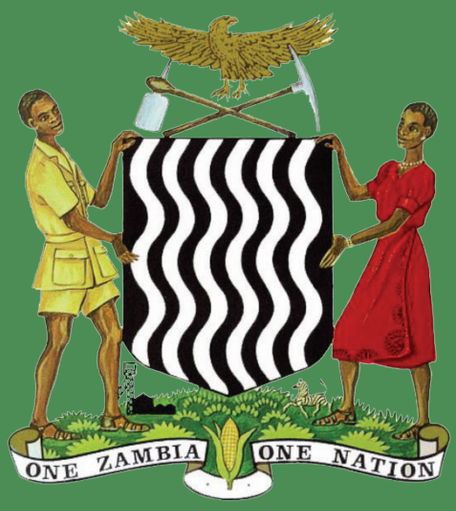
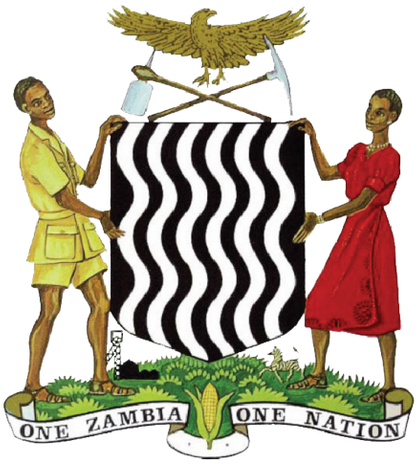


ZAMBIA NATIONAL FORMULARY

06

2025



REPUBLIC OF ZAMBIA

Ministry of Health

ZAMBIA NATIONAL FORMULARY

2025

Version 06

Foreword

The Zambia National Formulary (ZNF) is an integral component of the Zambia National Medicines Policy that is aimed at making available and accessible essential medicines of proven efficacy, safety and quality at an affordable cost. The ZNF is a major strategy in the promotion of rational use of medicines.

This edition of the ZNF has maintained the basic objectives and organization of the previous edition. This edition emphasizes the need for evidence-based treatments as derived from the Standard Treatment Guidelines (STGs). The development of this document was consultative and participatory. The ZNF is a very dynamic document that needs regular review and updates to make it truly relevant in meeting the health needs of our communities.

The Zambia National Formulary Committee (ZNFC) responsible for development and dissemination of this document welcomes the active participation of all stakeholders to achieve our goal of promoting rational use of medicines in the delivery of quality health care.

Dr Kennedy Lishimpi
Permanent Secretary – Technical Services
MINISTRY OF HEALTH

Changes to the 6th version of the Zambia National Formulary Document

In this document, changes have been made from its previous version to improve the delivery of information and for the purpose of ensuring that this document is updated based on current treatment guidelines of the conditions that the drugs are being used for.

These are some of the changes and improvements made to this document:

- The Children's administration on every applicable drug has been added and this has been highlighted in a green box after the adult administration for easy visibility and guidance.
- The section for Medicines used in Obstetrics and Gynaecology has been separated from Section 5: Medicines acting on the Endocrine System and is now appearing as Section 6 in this document.
- Medicines used in the treatment of Covid-19 have been added
- Medicines have been classified based on their generations where applicable.
- Rearranged medicines used in the treatment of diseases of the cardiovascular system to start with antihypertensives, cardiac glycosides.

These are the medicines deleted from this version as they are no longer (absolute)part of the current treatment guidelines for various conditions.

Deletions

1. Medicines acting on the Central Nervous System

Amisulpride	Flupenthixol decanoate	Orphenadrine hydrochloride
Thioridazine hydrochloride	Zuclopenthixol decanoate	Benztropine mesylate
Disulfiram		

2. Medicines used in the treatment of Infections

Zalcitabine (DDC)	Stavudine (D4T)

3. Medicines acting on the Endocrine system

Chlorpropamide	Tolbutamide

4. Nutrition

Calcium gluconate

These are the medicines added to this version following the current treatment guidelines for various conditions.

Additions

1. Medicines used in anaesthesia

Etomidate	Succinycholine	Sevoflurane	Bupivacaine
Propofol	Rocuronium	Atracurium	Cisatracurium
Isoflurane			

2. Medicines Acting on the Gastro-Intestinal System

Famotidine	Rabeprazole

3. Medicines acting on the Central Nervous System

Clozapine	Gabapentine	Naloxone
Risperidone	Lamotrigine	Acamprosate
Olanzapine	Levetiracetam	Methadone
Quetiapine	Midazolam	Buprenorphine
Levodopa (combination with carbidopa)	Lamotrigine	Aceclofenac
Citalopram	Levetiracetam	Diclofenac sodium/potassium
Clomipramine	Alprazolam	Celecoxib
Escitalopram	Naltrexone	Ketorolac trometamol
fluoxetine	Clonidine	Mefenamic acid
Sertraline	Fentanyl	Indomethacin
Divalproex sodium		Tramadol

4. Medicines used in the treatment of Infections

Cefixime	Levofloxacin	Albendazole
Cefepime	Terbinafine tablets/cream	Valganciclovir
Meropenem	Miconazole cream	Etravirine
Carbapenems	Itraconazole	Atazanavir + Ritonavir
Itraconazole	Deltaprim	Darunavir+ Ritonavir
Miconazole cream	Artesunate	Cabotegravir
Terbinafine tablets and cream	Hydrochloroquine	Moxifloxacin

5. Medicines acting on the Endocrine system

Rapid acting insulin	Dapagliflozin	Insulin glargine
Semaglutide	Vildagliptin	Insulin Detemir
Pioglitazone	Sitagliptin	Insulin Degludec
Tadalafil	Propylthiouracil	

6. Medicines used in Gynaecology and Obstetrics

Carbetocin

7. Medicines used in the treatment of diseases of the respiratory system

Formoterol Fumerate	Aminophylline	Caffeine Citrate
Surfactant	Cetrizine	Baricitinib
Fexofenadine	Montelukast	Tocilizumab

8. Medicines used in the treatment of diseases of the cardiovascular system

Antihypertensives				
Torasemide	Magnesium sulphate	Enalapril	Methyldopa	Losartan
Eplerenone	Verapamil	Prazosin	Spironolactone	Telmisartan
Sacubitril + valsartan	Bosentan			
Antiarrhythmics				
Atropine	Labetalol	Bisoprolol	Ivabradin	
Anti-anginas				
Nitroglycerine	Amlodipine	Diltiazem hydrochloride	Nimodipine	Isosorbide dinitrate
Anti-cholesterol				
Atorvastatin				

9. Medicines used in the treatment of malignant disease

Daunorubicin	Melhalan	Fludarabin
Liposomal doxorubicin	Letrozole	Imatinib
Carboplatin	Mitomycin	Filgrastim
Etoside	Paclitaxel	Interferon
Ifosfamide	Procabazine	Lomusatine
Irinotecan	Tacrolimus	All-Trans Retinoid Acid (ATRA) or TRETINOIN

10. Medicines acting on the Eye

Ganciclovir eye gel	Prednisolone eye drops	Cyclopentolate hydrochloride
Dexamethasone eye drops	Sodium cromoglycate eye drops	Tropicamide
Hydrocortisone eye drops	Ciprofloxacin eye drops	

11. Blood Products

Glycopyrrolaten	Alteplase	Dabigatran etexilate
Etamsylate	Tenecteplase	Fondaparinux sodium
Clopidogrel	Rivaroxaban	Iron sucrose
Erythropoietin (epoietin)		

12. Nutrition

Calcium carbonate	Tacrolimus	Ketoconazole cream
Colecalciferol (vitamin D) with calcium carbonate	Selenium	Terbinafine
Tazarotene		

13. Medicines used in the treatment of diseases of the Ear, Nose and Oropharynx

Ciprofloxacin	Mometasone furoate	Loratidine
Clotrimazole	Xylometazoline hydrochloride	Cetirizine
Fluticasone	Itraconazole	

14. Medicines used in the treatment of Musculoskeletal disorders

Meloxicam	Hydroxychloroquine	Febuxostat
Celecoxib	Infliximab	Chlorzoxazone
Glucosamine /chondroitin		

15. Vaccines

Rotavirus vaccine	HPV (quadrivalent)
Tetanus + diphtheria (TD) vaccine	Measles/rubella
Diptheria, pertussis, tetanus (DPT)	

Preface

The publication of this 6th Edition of the Zambia National Formulary (ZNF) is yet another milestone of the ZNFC. The ZNF is an authentic publication that reflects the priorities of the Zambia National Medicines Policy. It is accepted by health workers as a reliable guide for prescription of medicines.

The ZNF is considered by the government of the Republic of Zambia as the national standard reference formulary to be used in the management of diseases in the country. The formulary contains information about essential and rational medicines available on the Zambia Essential Medicines List (ZEML). The indications, contraindications, drug interactions, side effects and dosages are provided.

It is hoped that this publication will equip health workers both in the public and private sectors with enough information for rational and safe use of medicines.

The Ministry of Health will update this document every two (2) years to keep it relevant for evidence-based healthcare practice.

Dr Justo Banda
Chairperson
Zambia National Formulary Committee

Acknowledgement

The Zambia National Formulary Committee is grateful to the Ministry of Health (MoH) for its support during the preparation of this edition of the Formulary. The Committee would also like to thank Clinton Health Access Initiative (CHAI), World Health Organization (WHO), United Nations Population Fund (UNFPA), and PATH with support from Flemming Fund for financial and technical support towards the preparation of the Formulary. The Committee further acknowledges the technical advice and contributions received from various health professionals across various institutions in the country. Special thanks go to PATH for the support rendered in editing, proof-reading, typesetting and graphical designs of this document.

The Committee would also like to thank the following Pharmacists from ZNFC Secretariat for their support in facilitating the review of this document: Mr. Maxwell Kasonde (MoH), Mr. Kandandu Chibosha (MoH), Mrs. Thikondane Mphande-Muyunda (UTH-WNH), and Mr. Pious Haachizo (UTH-CDH).

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Director - Clinical Care & Diagnostics Services
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Introduction

The sixth edition of the ZNF seeks to provide a list of Medicines suitable for use in Zambia as well as essential information about their use.

The drug selection has been based on proven efficacy and potential availability.

Arrangement of Information

The main text consists of classified notes and preparations. These have been divided into chapters according to a particular system of the body or an aspect of medical care.

Chapters are further divided into necessary sections with introductory notes for health care providers who include doctors, pharmacists, nurses and other health professionals. This information is intended to facilitate the selection of appropriate treatment.

Drug monographs and details of relevant preparations follow the notes.

Guidance on Prescribing and Prescription Writing

This part of the formulary contains information on prescription writing, prescribing for children and the elderly, advice on promoting compliance, drug stability, storage conditions and the Vital-Essential-Nonessential (VEN) classification system for setting procurement and stocking priorities.

For the sake of this document, the words "Drug" and "Medicine" are used interchangeably.

Drug Name: Appears under the approved name or non-proprietary title on the International Non-proprietary Name (INN).

Presentation: Indicates the dosage form in which the drug is available on the market.

Indications: Gives details of the use of the drug.

Administration: Explains how the drug is given, the dose, or how often it is given.

Side Effects: Gives details of common side effects and adverse effects of the drug.

Contraindications: Gives details of circumstances in which the drug should be avoided.

Caution: Highlights the precautions required. This may include counselling of patient on how to take the medication.

General Treatment of Poisoning

This chapter deals with the management of all cases of poisoning or suspected poisoning when first seen in the home through referral to a health facility.

Appendices and Indices

The appendices include information on immunisation schedules, drug interactions, haematological and clinical chemistry reference values for children, adults and during pregnancy, thyroid and reproductive hormones reference levels, additives to intravenous (I.V.) fluids and medicines in pregnancy.

A special section on patients' leaflets and instructions give information on how to administer and use nasal drops, aerosols, vaginal creams, ointments and gels, pessaries, suppositories, ear drops, eye drops and ointments. This section follows appendices.

The indices list the Medicines in alphabetical order by approved name or INN.

Prescriber Control and Drug Availability

Prescriber categories are not indicated in the text because it is expected that the drug availability will be controlled by:

i. Medicines and therapeutic committees actively defining policies for prescribing within an institution or District.

ii. The range of availability of Medicines in any institution is restricted according to the level of the institution and to the categories of staff prescribing.

Prescribers are advised to follow rational prescribing habits which emphasise the priority use of essential and economic treatment regimes.

Price of Medicines

Because of constant price fluctuations, it is impossible to include specific prices for medicines. However, the pharmacy staff will be able to give up-to-date information for guidance.

Revision of Formulary Contents

The ZNFC recognises that the healthcare industry and field of medicine are dynamic, thus a revision of the formulary contents will be a continuous process. Contributions can be submitted for consideration by the Committee to Secretariat at the Ministry of Health.

Dr Justo Banda
Chairperson,
Zambia National Formulary Committee

Prescription Writing

General Practice Prescriptions

A well-written prescription should contain the following information:

1. Name and address of the patient, and the age if for a child
2. Name, dosage form and strength of the preparation
3. The dosage and frequency together with the duration of treatment
4. PRN prescriptions should clearly state a time limit for treatment
5. The directions for use
6. The prescriber's name, initials in block letters and practising license number
7. The signature of the prescriber
8. Name and address of hospital or clinic
9. Date of prescription

Hospital prescriptions

There should be prescription sheets on which only prescriptions and a record of dispensing and administration are written.

At any one time use only one prescription sheet per patient.

Frequency of administration for "As Required" medicines should be indicated by clear and stated intervals or indications.

The route of administration should be indicated.

The prescription sheet should show the signed and dated cancellation of any prescriptions no longer current.

Quantities and strengths on a Prescription

1. For solids, quantities less than 1 gram should be written in milligrams, e.g. 500mg, not 0.5g; quantities less than 1mg should be written in mcg, e.g.100mcg, not 0.1mg.
2. Use the term millilitre (ml) for fluid measurements.
3. For liquid preparations suitable quantities of the preparations should be used viz: Elixirs, Linctus and paediatric mixtures (usually 5ml dose) 50ml, 100ml or 150 ml. Adult mixtures (10ml dose) 200ml.
4. Injections should be limited to cases where they are necessary.

Abbreviations

Routes of Administration

PO	Per Oral
I.M	Intramuscular
I.V	Intravenous
P.R	Per rectal
P.V	Per vaginal
S.C	Subcutaneous

Dosage Forms

Tabs	Tablets
Caps	Capsules
Susp	Suspension
Syr	Syrup
Inj	Injection
Amp	Ampoule
Oint	Ointment
Soln	Solution
Lot.	Lotion
Mixt.	Mixture
Suppos.	Suppository
Lin.	Liniment
Applic.	Application
Linct.	Linctus
Pess.	Pessary

Frequency

nocte	at night
on	at night
om	in the morning
od	once a day
bd	twice a day
tds	three times a day
qds	four times a day
qid	every 6 hours
prn	when required
sos	when necessary
ac	before food
cc	with food
pc	after food
stat	at once
ic	in between meals

Units

g	gram
mg	milligram
mcg	microgram
kg	kilogram
l	litre
ml	millilitre
iu	international units
Mmol	millimoles

Prescribing for Children

In children, the risk of toxicity is increased by inefficient renal filtration, relative enzyme deficiencies, differing target organ sensitivity and inadequate detoxifying systems causing delayed excretion.

In the neonatal period (first 28 days of life) and childhood, the dosage is usually calculated according to body weight (until 50kg or puberty is reached) and a set of scales should be available in all clinics where children are treated.

Approximate doses can be calculated from adult doses using the following age ranges and corresponding fractions:

first month (neonate): $^1/_8$
up to 12 months (infant): ¼
1 – 5 years: $^1/_3$
6 – 12 years: ½

The manufacturer's recommended dose should be checked.

Body Surface Area (BSA) estimates are more accurate for the calculation of paediatric doses than body weight since many physical phenomena are more closely related to the body surface area. The average body-surface area of a 70-kilogram human is about $1.8m^{2.}$ Thus, to calculate the dose for a child the following formula may be used:

Approximate dose for patient = the surface area of the patient (m^2) x adult dose (mg) / 1.8.

The percentage method below may be used to calculate paediatric doses of commonly used Medicines. In general, the use of oral medication is preferred by children and injection should be limited to when it is necessary

CHILDREN						
Age	**Ideal Body Weight Kg**	**Ib**	**Height Cm**	**Body Surface in m^2**	**%of adult dose**	
Newborn*	3.4	7.5	50	20	0.23	12.5
1 month*	4.2	9	55	22	0.26	14.5
3 month*	5.6	12	59	23	0.32	18
6 month*	7.7	17	67	26	0.40	22
1 year	10	22	76	30	0.47	25
3 year	14	31	94	37	0.62	33
5 year	18	40	108	42	0.73	40
7 year	23	51	120	47	0.88	50
12 year	37	81	148	58	1.25	75
ADULT						
Male	68	150	173	68	1.80	100
Female	56	123	163	64	1.60	100

*The figures relate to full-term and not preterm infants who may need reduced dosage according to their clinical condition.

More precise body-surface values may be calculated from height and weight using a nomogram.

Prescribing for the Elderly

Elderly patients are usually at a greater risk of adverse reactions to medicines and interactions because of multiple drug therapies for their multiple diseases.

Manifestations of normal ageing in very old patients are sometimes mistaken for disease and lead to inappropriate prescribing. For example, medicines such as Prochlorperazine are commonly misprescribed for giddiness due to age-related loss of postural stability.

Self-medication with medicines prescribed for a previous illness or even for another person may be an added complication. The ageing nervous system shows increased susceptibility to many commonly used medicines such as benzodiazepines and opioid analgesics. These should be used with caution.

Before prescribing one should always pose the question of whether a drug is indicated at all. It is also sensible to prescribe from a limited range of medicines and to be thoroughly familiar with their effects in the elderly.

Compliance

Patients often do not take their medicines correctly. Surveys show that many patients are not told what is wrong with them and how to take their medicines. Others start taking their medication for a while, they then stop or forget when they start feeling better or suffer side effects.

Patient compliance is a measure of the extent to which a patient follows instructions on the use of a drug. These instructions should be given by both the prescriber and the dispenser. The result of the use of the medicine will be better when compliance is high. Prescribers and dispensers should always aim at high patient compliance.

If patients do not take their medicines properly, they are unlikely to improve and they may return to the health facility for further treatment. Spending a small amount of time in improving patient compliance is a worthwhile investment in terms of saving time and money.

Do not give too many medicines

The more medicines a patient has the less likely they are to take any of them properly! Giving the most important medicines and ensuring that they are taken properly is much better than giving a lot of medicines which may not be taken properly.

Reduce the number of medication times

Compliance is improved by keeping the number of medicines and frequency of administration as low as possible. For example, 3 times a day dosage are better than 4 times a day dosage. Different medications with one being taken 3 times a day and another taken 4 times a day are bound to be taken wrongly.

Check compliance with chronic patients

Patients having medication for chronic conditions are most prone to non-compliance, especially those illnesses requiring long-term medications for suppression or prophylaxis during which time the patient has few, if any symptoms.

The attitude of the prescriber should be positive and helpful all the time.

MEDICINES STABILITY

Medicines deteriorate with time and this is worsened if they are not stored or handled properly. When medicines deteriorate, they may become useless or even harmful.

Usually, medicines carry expiry dates. This means that they should not be used after that date.

This date relies on the medicines being stored under suitable storage conditions.

Medicines are susceptible to heat, light, moisture and dirt. Exposure to one or all of these will affect the stability of the drug. Storage should be such as to minimise exposure to heat, light and moisture. Signs that could indicate that deterioration has occurred include:

- Bad smell
- Bad taste
- Change in colour
- Development of bubbles in liquids
- Growth of bacteria or fungus often appearing as brown spots
- Melting, sticking or cracking of tablets
- Liquid has separated from creams
- Development of turbidity or crystallization in liquids

Certain medicines, however, may not show visible signs of deterioration after the expiry date or when affected by adverse storage conditions. Patients need education on how to store medicines. It is best to advise patients to use and finish the medicine within the prescribed period.

Moisture

When containers for medicaments are not properly closed, moisture can easily get in and destroy the contents. Tablets may get wet and eventually break or stick to one another. Certain medicines like aspirin deteriorate in the presence of moisture emitting an acidic smell like vinegar.

Medicines should be stored in a dry cool place with good ventilation. Containers should be tightly closed and should not be left open. Only open containers when necessary and close them immediately after use. Do not remove the desiccant put in the containers by the manufacturer.

Light

The chemical breakdown can be caused by exposure of medicines to sunlight.

Medicines should be kept out of direct sunlight.

Heat

Heat affects many medicines. Medicines stored in cool conditions will remain effective for a longer period. Some medicines may require refrigeration during transportation and storage, e.g. Insulin and vaccines. Always check for and follow the manufacturer's recommended storage conditions.

Dirt

Medicines should be protected from dirt. The dispensary and store should be cleaned often and this should be done in such a way as to prevent the dust created from covering the products.

DRUG STORAGE INFORMATION

Below are storage conditions and signs of deterioration for some common medicines.

DRUG	STORAGE TEMPERATURE ^{0}C	PROTECT FROM	SIGNS OF DETERIORATION
Aspirin	15-30^{0}C	Excess heat and moisture	Vinegar smell
Amoxycillin capsules/tablets	15-30^{0}C	Moisture, heat	Changes in colour, odour and texture
Amoxycillin syrup	Room temperature	Heat, extreme cold	Change in colour and taste
Benzylpenicillin Injection	Refrigerated; As powder 14 days <30^{0}C As liquid: room temp. 24hrs. refrigerated: 14 days	Heat, freezing	Changes in colour, odour or consistency

DRUG	STORAGE TEMPERATURE ^{0}C	PROTECT FROM	SIGNS OF DETERIORATION
Chloramphenicol Injection	As liquid, <30^{0}C, 30 days	Moisture, heat	Cloudy (should be clear)
Artemeter-Lumenfatrine tablets	15-30^{0}C	Moisture, heat	Discolouration
Co-trimoxazole Tablets	15 - 30^{0}C	Moisture, Direct light, extreme cold	Distinct odour
Co-trimoxazole Syrup	15 - 30^{0}C	Direct light, extreme cold	Inconsistent syrup, clumped powder
Erythromycin tablets	15 - 30^{0}C	Moisture, heat direct light,	Discolouration, cracked or chipped tablets
Gentian Violet solution	15 - 30^{0}C	Moisture, freezing	Solids/crystals, failure to stain
Iron/folate tablet	15 - 30^{0}C	Moisture, light,	Changes in colour consistency, clumped and chipped tablets
Gentamycin injection	15 - 30^{0}C	Freezing	Cloudy solution
Mebendazole tablet	15 - 30^{0}C	Moisture	Dotted tablets, dissolution changes
Nalidixic acid tablet	15 - 30^{0}C	Moisture	Discolouration, broken blister pack
ORS	15 - 30^{0}C	Moisture	Clumped powder, dissolution changes
Paracetamol tablets	<40^{0}C	Moisture, direct light, heat	Odour, colour (dots, discolouration)
Quinine injection	<40^{0}C	Light, heat	Cloudy, crystals
Sulphadoxine + Pyrimethamine tablets	15 - 30^{0}C	Moisture, light	Tablets harder than normal, discoloured
Tetracycline eye ointment	15 - 30^{0}C	Moisture, light, freezing	Inconsistent ointment
Tetracycline tablet	15 - 30^{0}C	Moisture, light	Tablets stuck together, discoloured.
Vitamin-A tablets	15 - 30^{0}C	Moisture, light, heat	Clumping, odour

VEN CLASSIFICATION

One way to maximise the effectiveness of health care when funds are limited is to set procurement and stock-keeping priorities according to the potential health impact of individual medical supplies. A method of doing this is the VEN classification system, in which all of the items on the supply list are placed into one of the following three categories:

VITAL items are potentially lifesaving and have significant withdrawal side effects.

ESSENTIAL items are effective against less

severe, but significant forms of illness.

NON-ESSENTIAL items for minor or self-limited illness, items which are of questionable efficacy, and items with a high cost for marginal therapeutic advantage.

Guiding purchases with the VEN system

Often requirements exceed available resources. Under these constraints, requests need to be revised, but the process for doing so is frequently haphazard.

Purchase quantities should be reduced in proportion to the quantities requested. Items which are unfamiliar to the person adjusting may be omitted despite their medical importance.

The VEN system helps to minimise these and other distortions in the procurement process, and thus maximize the health impact of available funds.

Once the VEN categories have been established, adjustments in purchases can be made quickly and easily.

1 Medicine used in Anaesthesia

1.1 Medicines used in General Anaesthesia

These should only be used by experienced personnel and on premises where adequate resuscitation equipment is available.

1.1.1 Intravenous and Intramuscular Anaesthetics

ETOMIDATE

Presentation: Available in 2mg/ml emulsion for injection

Indications: General anaesthesia used for induction

Administration: It is given as IV slow infusion at a dose of 0.2-0.6mg/kg over 30-60 seconds in **adults and 150-200 mcg/kg over 30-60 minutes.**

Children:

<10 years: safety and efficacy not established
>10 years: same as adults.

Side effects: Common side effects include; transient injection site pain, skeletal muscle movements, hiccups, opsoclonus, hyperventilation, hypotension, and adrenal suppression.

Contraindications: Hypersensitivity

Caution: Adrenal suppression (and prolonged therapy), and risk of toxicity may increase in patients with renal impairment and elderly patients require lower doses.

KETAMINE

Presentation: Injection containing 50mg/ml, 100mg/ml ketamine hydrochloride.

Indications: Induction and maintenance of anaesthesia for operations of short duration. May also be used for operations of longer duration if given by continuous intravenous infusion.

Administration: By slow intravenous injection 1 - 2mg/kg over 60 seconds, repeated according to the patient's response. By deep intramuscular injection, 4 - 10mg/kg repeated according to the patient's response.

Children:

by IM injection; 4–13 mg/kg, adjusted according to response. by IV injection; Initially 0.5–2 mg/kg, followed by (by continuous intravenous infusion) 10–45 mcg/kg/minute, adjusted according to response.

Side effects: Recovery reactions include hallucinations, vomiting, transient rise in blood pressure and heart rate. N.B. Diazepam can reduce hallucinations.

Contraindications: Hypertension, history of mental illness.

Caution: Maintain full anaesthetic vigilance and avoid patient stimulation during recovery.

THIOPENTAL SODIUM

Presentation: Powder for reconstitution containing thiopentone sodium in 1g and 5g vials.

Indications: Induction of anaesthesia in operations of short duration.

Administration: By intravenous injection 100 - 150mg as 2.5% solution in water for injection (4- 6ml of 2.5% solution) repeated if necessary, according to the patient's response or up to 4mg/kg.

Child; induction, 2 - 7mg/kg

Side effects: Coughing, sneezing, laryngeal and bronchial spasm during induction, thrombophlebitis, sensitivity reactions, depression of respiration, depression of cardiac output and initially, fall in blood pressure.

Contraindications: Shock, dehydration and severe anaemia, porphyria.

Caution*:* Avoid injections outside a vein.

PROPOFOL

Presentation: Injectable solution 200mg/20ml emulsion ampule.

Indications: Used for induction of anaesthesia;

Administration: Adults 18-54 years 2-2.5mg/kg, to be administered at a rate of 20-40mg every 10 seconds until response; 55 years and older.

Children: <3 years not recommended.

3-16 years: 2.5-3.5mg/kg IV over 20-30 seconds when not premedicated or medicated with oral benzodiazepines or intramuscular opoiods.

Side effects: patients may commonly present with hypotension, apnea, burning at injection site, respiratory acidosis, pruritus and Arrythmia.

Contraindications: documented hypersensitivity; egg allergy, soybean/soy allergy

Caution: drug enulasion vehicle support antimicrobial growth, ensure aseptic technique, closely monitoring patients with anemia, hepatic impairement and renal impairement. It may cause hypotension especially in patients with hypovolemia.

1.1.2 Inhalational Anaesthetics

Inhalational anaesthetics may be gases or volatile liquids. They can be used both for induction and maintenance of anaesthetics. Gaseous agents must be given with an adequate concentration of oxygen to prevent hypoxia.

HALOTHANE

Presentation: Volatile liquid, available in 250ml liquid

Indications: All-purpose anaesthesia it is used in the induction of anaesthesia (in oxygen or nitrous oxide-oxygen)

Administration: Using a suitable vaporizer: *Adult:* Induction, increased gradually to 2% - 4% in oxygen or nitrous oxide/oxygen.

Child; induction, 2 - 7mg/kg

Side effects: May produce hypotension or arrhythmia, shivering and jaundice.

Contraindications: A history of unexplained jaundice or fever in a patient following exposure to halothane is an absolute contraindication.

Caution: Adrenaline infiltrations should be avoided in patients anaesthetised with halothane due to risk of adrenaline-induced ventricular dysrhythmias and pulmonary edema.

SEVOFLURANE

Administration: 12-25 years: 2.6% in oxygen or 1.4% with 65% N20/35% oxygen. 25-40 years; 2.1% in oxygen or 1.1% with 65% N2/35% oxygen. 40-60 years: 1.7% in oxygen or 0.9% with N2O/35% oxygen. 60 -80 years: 1.4% in oxygen or 0.7% N20/35% of oxygen.

Children:

0-1 month 3.3% in oxygen, 1-6 months; 3% in oxygen, 6 month-<3 years 2.8% in oxygen or 2% with 65% N2O/35% oxygen.2-12 years: 2.5% in oxygen or 2.5% with 65% N2O/35% oxygen. 12-25 years; 2.6% in oxygen or1.4% with 65% N2O/35%

Side effects: Malignant hyperthemia, dose dependent hypotension, bradycardia, tachycardia, hypotension, hypertension, cough, apnea, nausea and vomiting.

Contraindications: known or suscpected genetic susceptibility to malignancy hyperthemia, known sensitivity to sevoflurane or to other halogenated inhalation anaestathetics.

Caution: can trigger malignant hyperthemia; raised intracranial pressure (can increase cerebrospinal pressure) entricular arrhythmias may result.

ISOFLURANE

Presentation: available as an inhalation solution in 100ml and 250ml.

Indications: it is used for anaesthesia induction and maintenance.

Administration: Adult induction: 1.5-3% can produce surgical anaesthesia in 7-10 minutes. Maintainance: 1-2.5% with nitrous oxide. Additional 0.5-1% may be needed if given with oxygen alone.

Children: safety and efficacy not established

Side effects: Nausea, vomiting, shivering, dose-dependent hypotension, arrhythmias, and elevation in white blood count, may decrease creatine clearance.

Contraindications: hypersensitivity to isoflurane and halogenated agents, genetic susceptibility to malignant hyperthemia.

Caution: Caution in coronary heart disease, may decrease renal and hepatic blood flow, QTc prolongation, use with care high risk patients.

NITROUS OXIDE

Presentation: Compressed gas

Indications: Induction and maintenance of anaesthesia. Analgesic in sub-anaesthetic concentrations.

Administration: Anaesthetic; Induction, 80% nitrous oxide with 20% oxygen and maintained at 70% nitrous oxide with 30% oxygen. Analgesic; 50% nitrous oxide with 50% oxygen as required.

Side effects: Convulsions

Contraindications: Jaundice

1.1.3 Muscle Relaxants

These Medicines are mainly used as anaesthesia to enable muscle relaxation to be achieved using a minimal dose of anaesthetic.

Caution: Administration of these Medicines may conceal signs of returning consciousness.

Caution: Risk of addiction and megaloblastic anaemia. Always administer with oxygen. Care is needed in patients with pneumothorax.

ATRACURIUM

Presentation: Available as a solution for injection in 10mg/ml.

Indications: It is used in endotracheal intubation, mechanical ventilation, and skeletal muscle relaxant in surgery.

Administration: Endotracheal intubation, mechanical ventilation:0.4-0.5 mg/kg IVP over 60 seconds, then 0.08-0.1 mg/kg 20-45 minutes after the initial dose. Continue infusion 0.005-0.01 mg/kg/minutes. Skeletal muscle relaxation during surgery: 0.4-0.5mg/kg IVP over 60 seconds, then 0.005-0.013 mg/kg/minutes, block usually maintained at the rate of 0.0.11-0.013 mg/min

Children:

<1 month old: Safety and efficacy not established.

1- 2 years: 0.3-0.4 mg/kg IVP under halothane anesthesia. Maintenance dose: children may need more frequent doses than adults.

>2 years: 0.4-0.5mg/kg IVP over 60 seconds, then 0.08-0.1mg/kg 20-45 minutes after the initial dose to maintain neuromuscular block, repeat maintenance dose every 15-25 minutes as required.

Side effects: skin flush, erythema, wheezing, increased bronchial secretions, pruritus, and urticaria.

Contraindications: Hypersensitivity to the drug or components, lack of ventilation support, neuromuscular disease.

Caution: Additive synergistic effects if administered with or following an opioid, sedative, or anesthetic agent. closely monitor patients with bronchogenic carcinoma, dehydration, electrolyte imbalance, hypotension, hypothermia, myasthenia gravis, and pulmonary disease. Adequate ventilation is mandatory.

CISATRACURIUM

Presentation: available as a solution for injection in 2mg/ml strength and 10mg/ml as single dose vial.

Indications: It is indicated as an adjuct to general aesthesia to facilitate tracheal intubation.

Administration: initial dose in conjuction with propofol or thiopental/nitrous oxide/ oxygen induction technique; 0.15-0.2 mg/kg IV bolus initially. Maintainance 0.03mg/kg IV bolus; start 40-50 min (after initial dose of 0.15mg/kg) or 50-60 minutes (after initial dose of 0,2mg/kg)

Children:

For Trachea intubation; 1-23 months: 0.15mg/kg IV bolus and 2-12 years 0.1-0.15 mg/kg IV bolus.

Side effects: Bronchospasm, bradycardia, flushing, pruritus, hypotension and rash

Contraindications: hypersensitivity to cisatracurium or benzyl alcohol)

Caution: burns (resistance may occur and higher doses may be required. In cardiovascular, reduce the rate of administration, electrolytes disturbances and fluids disturbances.

SUCCINYLCHOLINE

Presentation: The drug is available as injection solution in 20m/ml and 100mg/ml.

Indications: Neuromuscular blocker used for both short and long prolonged procedures.

Administration: Loading dose; 0.3-1.1.mg/kg IV stat or 3-4mg/kg IM stat. Maintainace dose for long procedure; 0.04-0.07mg/kg IV every 5-10 minutes as per required, or 2.5mg/minute as an infusion.

Children:

Loading dose: infants and small children: 2mg/kg IV stat, order children 1mg/kg IV stat or 3-4mg/kg deep IM stat; not to exceed 150 mg total dose. Maintainance; 0.3-0.6mg/kg IV every 5-10 minutes as per required.

Side effects: Muscle fasciculation which may results in postoperative pain, jaw rigidity, apnea, respiratory depression, bradycardia, hypotension, cardiac arrythmia, sinus tachycardia, rash.

Contraindications: Hypersensitivity to the drug, history of malignant hyperthemia, myopathies associated wth increased serum creatinine kinase.

Caution: watch out for anaphylaxis reaction, use with caution in patients with abdominal infections.

SUXAMETHONIUM CHLORIDE

Presentation: Injection containing 50mg/ml suxamethonium chloride in 2ml ampoules.

Indications: Surgical procedures like endotracheal intubation, endoscopic examinations and electroconvulsive therapy (ECT) after general anaesthesia has been induced.

Administration: *Adult;* by intravenous injection, 700mcg - 1.4mg/kg/dose. The dose may be repeated.

Children

by intravenous injection 1.0mg - 2.0mg/kg/dose. By intramuscular injection infant, up to 2.0mg - 5.0mg/kg/dose.

Side effects*:* Prolonged apnoea, bradycardia, bronchospasm, hyperpyrexia and sensitization. *Caution:* Atropine should be given before suxamethonium to prevent bradycardia and bronchial secretion. Thiopental should be administered before Suxamethonium to diminish bradycardia and subjective feelings. Concomitant use with pancuronium may lead to a neostigmine resistant mixed block.

Contraindications: Burns, severe trauma, liver and kidney impairment, malnutrition, anaemia, myasthenia gravis and sensitization.

PANCURONIUM

Presentation: Injection containing 2mg/ml pancuronium bromide.

Indications*:* Muscle relaxation for long-duration surgery.

Administration: By intravenous injection, initially for intubation 0.05mg - 0.1mg/kg then 10 - 20 mcg/ kg as required.

Children;

initially 60 - 100mcg/kg then 10 -20mcg/kg. Neonate; 30 - 40 mcg/kg initially then 10 -20mcg/kg. Intensive care; by intravenous injection 60mcg/kg every 60 - 90 minutes.

Side effects: Vagolytic and sympathomimetic effects which can cause tachycardia and hypertension.

Caution: Allergic cross-reactivity between neuromuscular blocking agents has been reported, hypersensitivity, myasthenia gravis and hypothermia where low doses may be required. Resistance may develop in patients with burns who may require increased doses.

ROCURONIUM

Presentation: Available as injectable solution in 10mg/ml (5 and 10ml vials).

Indications: it is indictaed foe rapid sequence intubation, trachea intubation.

Administration: For rapid sequence intubation; 0.6-1.2mg/kg IV and 0.45-0.6mg/kg IV for trachea intubation. Maintainance; 0.1-0.2mg/kg repeat as per required or continuous infunsion: 0.01-0.2mg/kg IV/kg/minute IV.

Children:

3 months -14 years; initial 0.6mg/kg IV, maintainance: 0.07-0.125 mg/kg IV or continuous infusion at 0.012-mcg/kg/minute IV. >14 years 0.45-0.6mg/kg IV or continuous infusion: 0.01-0.012mcg/kg/minute IV.

Side effects: Transien hypotension, hypertension, dose related tachycardia, injection site edema, pruritus, wheezing

Contraindications: hypersensitivity, lack of ventilation support, neuromuscular disease.

Caution: additive synergistic effect when coadministered with opioid, sedative or aesthetic agent. To be administered only by trained personel, watch out for severe anaphylaxis reactions, use with caution in patients with liver dysfuction, some patients may experience prolonged recovery.

1.1.4 Anticholinesterases Used in Surgery

NEOSTIGMINE METHYLSULPHATE

Presentation: Injection containing

2.5mg/ml Neostigmine methylsulphate.

Indication: Reversal of muscular relaxation produced by non-depolarizing muscle relaxants e.g. pancuronium,

Administration: *Adult*; 2.5 - 5mg with Atropine sulphate by slow intravenous injection over 60 seconds.

Children;

80mcg/kg with 20mcg/kg atropine. Diagnosis of myasthenia gravis; 1.5mg intramuscularly with 600mcg Atropine sulphate. Treatment of Myasthenia gravis; 1.0mg - 3.5mg subcutaneously, intramuscularly or intravenously several times a day according to the severity of the condition.

1.2 Medicines used in Local Anaesthesia

LIGNOCAINE HYDROCHLORIDE

Presentation: 0.5% injection containing 5mg/ml Lignocaine in vials. 1% injection containing 10mg/ml Lignocaine hydrochloride solution in vials. 2% injection containing 20mg/ml lignocaine hydrochloride in vials.

Indications: Local anaesthesia, infiltration anaesthesia.

Administration: Local infiltration and peripheral nerve block using 0.5% solution adult up to 250mg (up to 50ml); using 1% solution, adult up to 250mg (up to 25ml).

Children:

Neonate-11 years; Up to 3 mg/kg, dose to be given according to patient's weight and nature of procedure, dose may be repeated not more often than every 4 hours, 3 mg/kg equivalent to 0.3 ml/kg of 1% solution.

12–17 years: (max. per dose 200 mg), dose to be given according to child's weight and nature of procedure, dose may be repeated not more often than every 4 hours.

Side effects: Bradycardia, hypotension, cardiac arrhythmias, cardiac arrest, anxiety, restlessness, tremor, dizziness, respiratory arrest, hypersensitivity reactions manifested by oedema, status asthmaticus or anaphylactic reaction.

Contraindications: In patients with known hypersensitivity to the drug.

Caution: It should be used with caution in severely debilitated patients and those with liver disease.

LIGNOCAINE + ADRENALINE

Presentation: 1% injection containing 10mg/ml Lignocaine hydrochloride and Adrenaline 1 in 200, 000 (5mcg/ml). 2% injection containing 20mg/ ml lignocaine hydrochloride and adrenaline 1 in 200,000 (5mcg/ml).

Indications: Local anaesthesia

Administration: Adjusted according to the site of operation and response of the patient. Maximum dose 200mg or 500mg with a solution which also contains adrenaline. Local infiltration and peripheral nerve block; using 1% solution with adrenaline, adult up to 400mg (up to 40ml). Using 2% solution (dental anaesthesia) with adrenaline, adult 20 - 100mg (1 - 5ml).

Side effects: See lignocaine.

Contraindications: Patients with known hypersensitivity to the particular drug.

Caution: See under lignocaine.

1.3 Medicines used in Spinal Anaesthesia

These require great care and should be used by people with experience.

BUPIVACAINE HYDROCHLORIDE

Presentation: Available as a solution for injection in 0.25% 10ml, 0.5% and 0.75%.

Indications: used for surgical anaesthesia, lumber epidural block.

Administration: By regional administration; 75-150mg, dose administered using a 5mg/ml (0.5%) solution. For surgical anesthesia, field block, regional administration; up to 150mg, dose administerd using a 2.5mg/ml (0.25%) or 0.5%. Peripheral nerve block: 0.25%; 12.5-125mg(5-70ml)

Children:
Not recommended for under 12, decrease dose by 30% in infants if necessary. For 12 years and above; Sympathetic blocker; 0.25% (50-125mg (20-50ml)), Peripheral nerve blocker; 0.25%; 12.5-175mg (5-70ml) or 0.5%: 25-175mg (5-35ml).

Side effects: Visible bruising, nausea, surgical site bleeding, headache, somnolence, dizziness, hypoesthesia, Anaemia, tinnitus.

Contraindications: Hypersensitivity to any amide local aneathetics or other products compounds.

Caution: Risk cardiac arrest in obstetrical anaesthesia. Cardiac arrest with difficult resuscitation or death reported during use for epidural for epidural anesthesia in obstetric patients.

BUPIVACAINE HYDROCHLORIDE WITH GLUCOSE

Presentation: Available in a solution for injection as 15mg/2ml(7.5mg/ml) in a glass ampule.

Indications: It is an amide-local anesthetic indicated in adults for subarachnoid injection for the production of subarachnoid block (spinal anesthesia).

Administration: The dose is depenedent on the exact procedure; Vaginal delivery 6mg, 7.5mg for spinal anesthesia for lower extremity and peripheral procedures. 12 mg for lower adominal procedures, and 7.5 -10.5mg for caesarean section.

Children:
Its administration in patients younger than 18 years is not recommended.

Side effects: Most common adverse effects are; hypotension, diaphragmatic paralysis,

Contraindications: septicemia, severe hemorrhage, svere hypotension or shock and arrythmias, such as incomplete heartblock, which severy reduce cardiac output. It also contraindicated in patients with a known hypersensitivity reaction to bupivacaine or local anaesthetic with amide-type.

Caution: use of spinal anesthetic during uterine contractions; spinal anesthetics should not be injected during uterine contractions because cerebrospineal fluid current may carry the drug further cephalad tham desired, resulting in a high motor block. Patients with hypertension, cardiac patients.

2 Medicines acting on the Gastro-Intestinal System

2.1 Antacids

Neutralization of gastric acid relieves the pain caused by hyperacidity in case of peptic ulcer disease. Non-absorbable antacids are preferable. These include aluminium and magnesium hydroxide and magnesium trisilicate. They are best given when symptoms occur or are expected, usually between meals and at bedtime, four or more times daily. Additional doses may be required up to once an hour to reduce gastric acidity throughout the day. Antacids should not be given at the same time as other Medicines like tetracycline, Chloroquine, rifampicin, ACE inhibitors, antifungals, and other Medicines. For an elaborate list of these other Medicines see appendix 2. The reason being that absorption of these Medicines may be impaired when given together with antacids.

Furthermore, they should not be given together with enteric-coated tablets.

ALUMINIUM HYDROXIDE

Presentation: Gel containing 4% of hydrated aluminium hydroxide. Tablets containing 500mg dried aluminium hydroxide. The oral suspension containing 4% aluminium hydroxide in water.

Indications: Hyperacidity, peptic ulcer disease, hyperphosphataemia.

Administration: Gel; adult; 7.5 - 15ml repeat as required. As an intragastric drip diluted with 2 - 3 parts of water, the rate of flow is 15 - 20 drops a minute throughout the day. Tablets; 1 - 4 tablets chewed in between meals and at bedtime when required.

Oral suspension, *adult*; 5 - 10ml 4 times daily between meals and at bedtime as required.

Children:
6 - 12 years; up to 5ml 3 times daily

Side effects: Constipation.

Contraindications: Hypophosphataemia, porphyria.

MAGNESIUM TRISILICATE

Presentation: Magnesium trisilicate tablet compound containing Magnesium trisilicate 250mg, dried Aluminium hydroxide 120mg mixture, each 10ml containing Magnesium trisilicate 500mg, light Magnesium carbonate 500mg, Sodium bicarbonate 500mg, concentrated Peppermint emulsion 0.25ml, double strength Chloroform water 5ml.

Indications: Hyperacidity, peptic ulcer disease, hyperphosphataemia

Administration: *Adult:* Tablets; 1 - 2 tablets to be chewed 3 - 4 times daily in between meals and at bedtime when required. Mixture; 10 - 20ml 3 - 4 times daily in between meals and at bedtime when required.

Children:
5–11 years: 5–10 ml 3 times a day, alternatively as required.
12–17 years: 10–20 ml 3 times a day, alternatively as required.

Side effects: Diarrhoea.

Caution: Impaired renal function

2.2 Antispasmodics

These are antimuscarinic medicines which reduce gastrointestinal motility. They reduce spasm, delaying gastric emptying time and thus prolonging the action of antacids. They are useful for all colics but may cause blurring of vision and dry mouth.

HYOSCINE BUTYL BROMIDE

Presentation: Tablets (coated) containing 10mg hyoscine butylbromide. An injection containing 20mg/ml hyoscine butylbromide.

Indications: Adjunct in gastro-intestinal disorders characterized by smooth muscle spasm, irritable bowel syndrome

Administration: *Adult*; 20mg 3 - 4 times daily. Intramuscular or intravenous injection for acute spasm and spasm in diagnostic procedures; 20mg repeated after 30 minutes if necessary.

Children:
6 - 12 years; 10mg 3 times daily. Irritable bowel syndrome; 10mg 3 times daily increased if necessary to 20mg, 4 times daily.

Side effects: Dry mouth, tachycardia, difficulty in micturition, dilatation of pupils, constipation and hyperpyrexia.

Caution: Patients with prostatic enlargement and cardiac disease

Contraindications: Glaucoma

PROPANTHELIN BROMIDE

Presentation: Tablets (sugar-coated) containing 15mg propantheline bromide.

Indications: Adjunct in gastro-intestinal disorders characterized by smooth muscle spasm, urinary frequency.

Administration: 15mg 3 times daily 1 hour before meals and 30mg at bedtime. Maximum 120mg daily. Not recommended in children.

Side effects: Dry mouth, dilatation of pupils, constipation and hyperpyrexia.

Contraindications: Glaucoma.

Caution: In patients with prostatic enlargement and cardiac disease

2.3 Ulcer healing Medicines

2.3.1 H_2-receptor antagonists
2.3.2 Complexes
2.3.3 Proton pump inhibitors
2.3.4 Prostaglandin analogues

Peptic ulceration often involves the stomach, duodenum and lower oesophagus. Healing can be promoted by general measures such as stopping smoking, taking antacids and by antisecretory treatment. Nearly all duodenal ulcers and most gastric ulcers not caused by NSAIDs are caused by *Helicobacter pylori*.

The management of *Helicobacter pylori* and NSAID associated ulcer is discussed below. The recommended treatment is acid inhibition combined with antibacterial treatment. One to two week triple therapy regimens that comprising a proton pump inhibitor, amoxicillin and metronidazole (see dosage table below) are indicated.

Esomeprazole	20mg twice daily
Amoxycillin	1g twice daily
Metronidazole	400mg twice daily
Omeprazole	20mg twice daily
Amoxycillin	1g twice daily
Metronidazole	400mg 3 times daily
Ranitidine bismuth citrate	400mg twice daily
Amoxicillin	1g twice daily
Metronidazole	400mg twice daily

2.3.1 H_2–receptor antagonists

These medicines heal ulcers by reducing gastric acid output as a result of H_2 – receptor blockade. They also help relieve peptic oesophagitis.

Maintainance treatment with low doses reduces the rate of ulcer relapse. They will not modify the natural course of the disease when treatment is stopped and *Helicobacter pylori (H.pylori*) eradication should be considered in such cases. Maintainance treatment may occasionally be used in frequent severe recurrences and in the elderly to prevent complications from peptic ulcer diseases.

These medicines are also used in healing ulcers associated with NSAIDs but cannot prevent complications from these ulcers.

CIMETIDINE

Presentation*:* Tablets containing 200mg, 400mg, 800mg Cimetidine. Syrup/suspension containing 200mg/5ml cimetidine. Injection containing 100mg/ml Cimetidine.

Indications: Benign gastric and duodenal ulceration, stomal ulcer, Zollinger-Ellison syndrome, prophylaxis of acid aspiration and other conditions where gastric acid reduction is beneficial.

Administration: Oral; tablets 400mg twice daily (with breakfast and at night) or 800mg at night (benign gastric and duodenal ulceration) for at least 4 weeks (at least 6 weeks in gastric ulceration and 8 weeks in NSAID associated ulceration). When necessary, dosage may be increased to 400mg 4 times daily or rarely (e.g. stress ulceration) increased to a maximum of 2.4g daily in divided doses. Maintainance; 400mg at night or 400mg in the morning and night.

Reflux oesophagitis; 400mg 4 times daily for 4 - 8 weeks.

Zollinger-Ellison syndrome; 400mg 4 times daily or occasionally more.

Gastric acid reduction (prophylaxis of acid aspiration), obstetrics 400mg start of labour, then up to 400mg every 4 hours.

Short bowel syndrome; 400mg twice daily with breakfast and at bedtime.

Intramuscularly 200mg 4 - 6 hourly, maximum 2.4g. Intravenously 200mg may be repeated every 4 - 6 hours.

Children: Infants; slow intravenous injection or intramuscular injection 20mg/kg daily in divided doses. A child over 1 year; 25 - 30mg/kg daily in divided doses.

Caution: Renal and hepatic impairment, pregnancy, breast-feeding. Cardiovascular impairment.

RANITIDINE

Presentation: Tablet containing 150mg, 300mg Ranitidine hydrochloride.

An oral solution containing 75mg/ml Ranitidine hydrochloride.

Effervescent tablets containing 150mg, 300mg Ranitidine hydrochloride.

An injection containing 25mg/ml Ranitidine hydrochloride.

Indications: See under cimetidine.

Administration: Oral, *adult*; 150mg twice daily or 300mg at night for 4 - 8 weeks. Prophylaxis of NSAID-induced duodenal ulceration; 150mg twice daily for 8 weeks. Reflux oesophagitis; 150mg twice daily or 300mg daily for up to 8 - 12 weeks. Long term treatment of healed oesophagitis; 150mg twice daily. Zollinger-Ellison syndrome; 150mg 3 times daily up to maximum 6g in divided doses.

Gastric acid reduction; 150mg on the onset of labour then every 6 hours. Surgical procedures by intramuscular or intravenous injection 50mg, 45 - 60 minutes before anaesthesia.

By intramuscular injection; 50mg every 6 - 8 hours. By intravenous injection 50mg diluted to 20ml and given over at least 2 minutes, may be repeated every 6 - 8 hours.

Child; 2 - 4mg/kg twice daily, maximum 300mg daily. Maintainance 150mg at night.

Side effects: See under cimetidine

Caution: See under cimetidine. Avoid in porphyria.

RANITIDINE BISMUTH CITRATE

This is a complex of ranitidine with bismuth and citrate which releases ranitidine and bismuth in the gastrointestinal tract and therefore possesses both the actions of the bismuth compounds and ranitidine.

Presentation: Tablet containing 400mg ranitidine bismuth citrate (equivalent to 162 mg of ranitidine base, 128 mg of trivalent bismuth, and 110 mg of citrate).

Indications*:* Management of peptic ulcer disease and may be given in combination with antibiotics for the eradication of *Helicobacter pylori* infection and the prevention of relapse of duodenal ulcer.

Administration: *Adult;* Duodenal ulceration, 400mg twice daily for 4 - 8 weeks.

Benign gastric ulceration, 400mg twice daily for 8 weeks. Duodenal ulceration with infection with *Helicobacter pylori* present, Ranitidine bismuth citrate 400mg twice daily is combined with amoxicillin 1g twice daily or Clarithromycin 500mg twice daily for 2 weeks and then Ranitidine bismuth citrate continued alone for a further 2 weeks. Not recommended in children

Side effects: Blackening of the tongue and stool, gastrointestinal disturbances, headache, hypersensitivity reactions (including anaphylaxis), mild anaemia, altered liver enzyme values.

Contraindications: Moderate to severe renal impairment, pregnancy and breastfeeding, porphyria.

Caution: Not suitable for long term treatment or maintenance therapy because of the risk of bismuth accumulation.

FAMOTIDINE

Presentation: Tablets containing 10mg, 20mg and 40 mg; powder for suspensions containing 40mg per 5ml; injection containing 10mg per ml and 0.4mg per ml.

Indications: Treatment of peptic ulcer diseases and gastroesophageal reflux disease (GERD)

Administration: In the acute phase – 40mg once daily at bed time for 8 weeks (orally and intravenously) or as 20mg 12-hourly intravenously. For GERD – 20mg 12 hourly for 6 weeks. For maintenance in ulcers, 20mg once daily at bed time.

Side effects: Headache, diarrhoea, dizziness, constipation, fever, arrhythmias, nausea and vomiting.

Contraindications: Hypersensitivity to famotidine or other H_2 receptor antagonists.

Caution: Use with caution in renal impairment and those with prolonged QT interval.

2.3.2 Complexes

SUCRALFATE

Sucralfate acts by protecting the mucosa from acid pepsin attack on gastric and duodenal ulcers. It is a complex of aluminium hydroxide and sulfated sucrose.

Presentation: Tablets containing Sucralfate 1g. A suspension containing sucralfate 1g/ml.

Indications*:* Benign gastric and duodenal ulceration, chronic gastritis, prophylaxis of stress ulceration.

Administration: Benign gastric & duodenal ulceration, chronic gastritis, 2g twice daily (on rising and at bedtime) or 1g 4 times daily before meals and at bedtime for 4 - 6 weeks up to 12 weeks, maximum. Prophylaxis of stress ulceration; (suspension) 1g 6 times daily (maximum 8g daily).

Not recommended in children.

Side effects: Constipation, diarrhoea, nausea, indigestion, gastric discomfort, dry mouth, rash, hypersensitivity reactions, back pain, dizziness, headache, vertigo and drowsiness.

TRIPOTASSIUM DICITRATO BISMUTHATE, TDB (COLLOIDAL BISMUTH SUBCITRATE, CBS)

Presentation: Tablet containing 10 mg, 25 mg, 50 mg or 100 mg.

Indications: Gastric and duodenal ulcers

Administration: 480 mg daily in two divided doses, half an hour before meals for 4 to 8 weeks

Side effects: Stools and tongue may become black, belching, diarrhoea and headache.

Contraindications: Children, pregnant women and renal impairment.

Caution: Do not crush or chew

2.3.3 Proton Pump Inhibitors

These inhibit gastric acid production by blocking the hydrogen-potassium adenosine triphosphate enzyme system (the "proton pump"). They are also used in combination with antibacterials for the eradication of *Helicobacter pylori*.

Presentation: Capsules containing 10mg, 20mg, 40mg Omeprazole enteric-coated granules. Tablets containing 10mg, 20mg, 40mg enteric coated Omeprazole. Intravenous infusion containing 40mg Omeprazole. An intramuscular injection containing 40mg omeprazole.

Indications: Benign gastric or duodenal ulcers, NSAID associated gastric or duodenal ulcers, duodenal erosions, prophylaxis in patients with a history of above.

Administration: Oral, Benign gastric and duodenal ulcers; 20mg once daily for 4 weeks in duodenal ulceration or 8 weeks in gastric ulceration; in severe or recurrent cases increase to 40mg daily; Maintenance for recurrent duodenal ulcers, 20mg once daily; Prevention of relapse in duodenal ulcer; 10mg daily increasing to 20mg once daily if symptoms return.

NSAID associated gastric or duodenal ulceration and gastroduodenal erosions 20mg once daily for 4 weeks; followed by a further 4 weeks if not fully healed; Prophylaxis in patients with a history of NSAID associated gastric or duodenal ulceration, gastroduodenal lesions, or dyspeptic symptoms who require continued NSAID treatment, 20mg once daily.

Duodenal ulcer associated with *Helicobacter pylori* see the table in 2.3 above.

Benign gastric ulcer associated with *Helicobacter pylori, Omeprazole* 40mg daily in 1 - 2 divided doses (plus amoxicillin 0.75 - 1g twice daily) for 2 weeks. Zollinger-Ellison syndrome; initially 60mg once daily; usual range 20 - 120mg daily (above 80mg in 2 divided doses).

Prophylaxis of acid aspiration, 40mg on a preceding evening then 40mg 2 - 6 hours before surgery. Gastro-oesophageal reflux disease, 20mg once daily for 4 weeks, followed by a further 4 - 8 weeks if not fully healed; 40 mg once daily has been given for 8 weeks - gastro-oesophageal reflux disease refractory to other treatment.

Acid reflux disease (long term management), 10mg daily increasing to 20mg once daily if symptoms return.

Acid related dyspepsia 10 - 20mg once daily for 2 - 4 weeks according to the response.

By intravenous injection over 5 minutes or by intravenous infusion, gastric acid reduction during anaesthesia (prophylaxis of acid aspiration), 40mg completed 1 hour before surgery. Benign gastric or duodenal ulceration and gastro-oesophageal reflux; 40mg once daily until oral administration possible.

Children: Not recommended in children less than 2 years. A child over 2 years; severe ulcerating reflux oesophagitis, 0.7 - 1.4mg/kg daily for 4 - 12 weeks' maximum 40mg daily (to be initiated by hospital paediatrician).

Side effects: Gastrointestinal disturbances, headache, hypersensitivity reactions, pruritis, dizziness, peripheral oedema, muscle and joint pain, malaise, blurred vision, depression and dry mouth. Proton pump inhibitors decrease gastric acidity and may increase the risk of gastrointestinal infection.

Caution: Proton pump inhibitors should be used with caution in patients with liver disease, in pregnancy and breastfeeding. They may also mask symptoms of gastric cancer; particular

care should be given in those whose symptoms change and those over 45 years of age. The presence of gastric malignancy should be excluded before treatment. DO NOT chew. Swallow capsule whole or dispense tablets in water or mix capsule contents or tablets with fruit juice or yoghurt.

ESOMEPRAZOLE

Presentation: Tablets and injection containing 20mg, 40mg Esomeprazole magnesium trihydrate.

Indications: Duodenal ulceration associated with *Helicobacter pylori*, gastro-oesophageal reflux disease.

Administration: Duodenal ulceration associated with *Helicobacter pylori;* 20mg twice daily. gastroesophageal reflux disease; 40mg once daily for 4 weeks followed by further 4 weeks if symptoms persist. Maintenance; 20mg daily. Symptomatic treatment in the absence of oesophagitis 20mg daily for up to 4 weeks followed by 20mg daily when required.

Children: Not recommended in children less than 1 year. By mouth and injection

1–11 years: 10-20 mg once daily

12–17 years: 40 mg daily. Injection to be given over at least 3 minutes; oral can be given up to 8 weeks

Caution: Swallow tablet whole or disperse in water.

RABEPRAZOLE

Presentation: Tablet/injection containing 20mg

Indications: Treatment of peptic ulcer diseases, GERD, and hypersecretory conditions.

Administration: 20mg once daily for 4 weeks in adults generally. For *H. pylori* eradication, 20mg twice daily for 7 days together with amoxicillin 1000mg twice daily and clarithromycin 500mg twice daily. Maintenance dose can be given 20mg once daily for up to 12 weeks. For hypersecretory conditions, 60mg once daily initially, then increase to 100mg once daily. Continue use as long as clinically needed.

Side effects: Headache, diarrhoea, flatulence, constipation, abdominal pain, and pharyngitis.

Contraindications: Previous hypersensitivity to rabeprazole or other proton pump inhibitors. Also rilpivirini-containing products.

Caution: Associated with increased incidence of *Clostridium difficile* associated diarrhoea. May require dose reduction in liver disease.

2.3.4 Prostaglandin analogues

ESOMEPRAZOLE

This is a synthetic prostaglandin analogue with anti-secretory and protective properties promoting gastric and duodenal ulcer treating. This drug is mostly recommended for the elderly or frail maintained on NSAIDs

Presentation: Tablets containing 200mcg misoprostol.

Indications: Prevention of NSAID associated ulceration in the elderly and the frail. Healing of gastric and duodenal ulcers.

Administration: Benign gastric or duodenal ulcer 800mcg (in 2 - 4 divided doses) with breakfast (or main meals) and at bedtime. Treatment should be continued for at least 4 weeks. Treatment can go up to 8 weeks. Prophylaxis of NSAID associated ulcer 200mcg 2 - 4 times daily taken with the NSAID. Not recommended in children.

Side effects: nausea, vomiting, constipation, chills, headache, dizziness, skin reactions, uterine rupture. **Caution:** Inflammatory bowel disease, pregnancy, breastfeeding, cerebrovascular disease, cardiovascular disease.

2.4 Medicines used for the treatment of diarrhoea

Dehydration resulting from acute diarrhoea is the main cause of death in children and the elderly. The first-line treatment, regardless

of the cause of diarrhoea, must be the replacement of fluids and electrolytes. The use of oral rehydration salts (ORS) is the preferred method in mild and moderate dehydration but in severe dehydration, intravenous fluids need to be used.

There are a variety of pathogens (bacterial, viral, parasitic) that can cause diarrhoea but very few can be specifically treated. Antibiotics and sulphonamides are not indicated for routine treatment of acute diarrhoea.

When rehydration has been achieved; consideration can be given to the treatment of the cause of diarrhoea particularly if parasitic.

Many acute diarrhoeas are self-limiting and oral rehydration therapy alone is sufficient. In watery stool with vomiting, criteria for the treatment is decided upon by the degree of dehydration.

CODEINE PHOSPHATE

Presentation: Tablets containing 15mg, 30mg, 60mg; oral solution containing 3mg/ml and 5mg/ml codeine phosphate.

Indications: Diarrhoea, relief of nerve, muscular and abdominal pain

Administration: Adult and children >12 years*;* 15 - 60mg 3-4 times daily. Maximum 300mg in 24 hours.

Side effects: Constipation, nausea, vomiting and drowsiness

Caution: In children, in the elderly and severe respiratory depression. Dependence may occur with prolonged use. Not recommended in children <12 years old.

LOPERAMIDE

Presentation*:* Capsules containing 2mg Loperamide hydrochloride. Syrup containing 1mg/ml Loperamide hydrochloride.

Indications: Symptomatic treatment of acute diarrhoea, Chronic diarrhoea, Faecal incontinence, Pain of bowel colic in palliative care and AIDS-related diarrhoea.

Administration: *Adult,* Acute diarrhea; Initially 4 mg, followed by 2 mg for up to 5 days, dose to be taken after each loose stool; usual dose 6–8 mg daily; maximum 16 mg per day. Chronic diarrhoea; initially 4 - 8mg daily in divided doses, subsequently adjusted according to the response. Maintenance 16mg per day in 2 divided doses.

Children: 100–200 mcg/kg 3–4 times a day (max. per dose 2 mg), increased if necessary up to 1.25 mg/kg daily in divided doses; maximum 16 mg per day.

Side effects: Dizziness, abdominal pains, drowsiness, skin reactions including urticaria, paralytic ileus and abdominal bloating.

Caution: Prolonged use could aggravate irritable bowel syndrome.

ORAL REHYDRATION SALTS (ORS)

Presentation: The oral fluids can be made with chemicals as follows (WHO recommendations); Sodium chloride 3.5g, potassium chloride 1.5g, Sodium citrate 2.9g, anhydrous glucose 20g. The salts are dissolved in water up to 1 litre of solution. The recommended treatment of dehydration is shown in rehydration tables (see section on Oral Rehydration Salts)

ZINC SULPHATE

Zinc sulphate is a salt used for the treatment of zinc deficiency. Zinc sulphate contains 23 percentage of elemental zinc. Zinc sulphate is absorbed over a wide range of PH and may cause GI irritation. Zinc is an essential element of nutrition and traces are present in a wide range of foods. It is a constituent of many enzyme systems and it is present in all the tissues. Normal growth and tissue depend upon adequate zinc. Zinc acts as an integral part of several enzymes important to protein and carbohydrate metabolism. Features of zinc deficiency include growth retardation and defects of rapidly dividing tissues such as skin and the intestinal mucosa. Zinc facilitates wound healing and helps maintain normal growth rates, normal skin

hydration and senses of taste and smell. Zinc improves absorption of water electrolytes. Zinc supplements prevent subsequent episodes of diarrhoea (in the ensuing 2 - 3 months after treatment). Zinc deficiency in humans alters aspects of immune function. Immune defects associated with zinc deficiency include impaired function of lymphocytes, natural killer cells and neutrophils. Zinc deficiency has also been hypothesized to exacerbate malaria and other diseases (infection with human immunodeficiency virus and tuberculosis) that rely on macrophage killing of infected cells. An adequate intake of zinc shortens the duration of respiratory tract infections including the common cold.

ZINC SULPHATE DISPERSIBLE TABLETS

Presentation: Dispersible tablets, Zinc sulphate monohydrate USP 54.9mg equivalent to elemental Zinc 20mg

Indications: Used in acute and persistent diarrhoea in children, (along with oral rehydration salts (ORS), respiratory tract infections, common cold, malaria, acrodermatitis enteropathica sickle cell anaemia and Wilson's diseases.

Administration: **Acute diarrhoea:** *Adult*; 20mg daily**.** Wilson's disease: 25 – 50mg elemental Zinc two to three times daily. Acrodermatitis enteropathica: 1-2 mg/kg elemental zinc.

Children: Acute diarrhoea; below 6 months: 10mg elemental Zinc daily for 10 - 14 days. For children above six months: 20mg elemental Zinc daily for 10-14 days. Place the tablet in a teaspoon/tablespoon. Add 5ml water or breast milk. Allow tablet to disperse (about 45 seconds). Give the entire spoonful to the child.

Sickle cell anaemia: 10 - 15mg elemental zinc daily.

Zinc sulphate tablets should be taken between meals.

Side effects: It may cause copper deficiency if excessive doses are taken. Nausea and vomiting may occur. If GIT symptoms occur, Zinc sulphate tablets can be taken with food, but food high in calcium, phosphorus and phytates must be avoided. Caution: No problems have been observed in human beings especially paediatrics when taken in normal daily recommended doses.

Contraindications: Concomitant administration with penicillamine, sodium valproate and ethambutol which inhibit zinc absorption. It is contraindicated to patients with hypersensitivity to the active substance or any of the excipients.

REHYDRATION TABLES

MODERATE DEHYDRATION

Amount of ORS solution to give in the first 4 to 6 hours

Age	Under 4 months	4 to 11 months	12 to 23 months	2 to 4 years	5 to 14 years	15 years and over
Weight	under 5 kg	5 to 7.9 kg	8 to 10.9 kg	11 to 15.9 kg	16 to 29.9 kg	30 kg and over
ORS in ml	200 to 400	400 to 600	600 to 800	800 to 1200	1200 to 2200	2200 to 4000

Use the patient age if you do not know the weight. If the patient wants more ORS, give more

SEVERE DEHYDRATION OR WHERE PATIENT UNABLE TO DRINK

Guidelines for rehydration therapy

Age Group	Type of fluid	Amount of fluid (kg) body weight	Time of Administration
Infants (under 12 months)	i.v. Ringers lactate or half strength Darrows	30ml/kg	Within 1 hour
	i.v. Ringers lactate or half-strength Darrows	Followed by 40ml/kg	Within the next 2 hours
	ORS Solution	Followed by (if appropriate) 40ml/kg	Within the next 3 hours
Older children and adults	i.v. Ringer's lactate	100ml/kg	Within three hours; initially as fast as possible until the radial pulse is easily felt

2.5 Laxatives

2.5.1. Bulk-forming laxatives
2.5.2. Stimulant laxatives
2.5.3. Faecal softeners
2.5.4. Bowel cleansing solutions

2.5.1 Bulk-forming laxatives

These helps relieve constipation by increasing faecal mass which stimulates peristalsis; the full effect may take some days to develop and patients should be told this. A balanced diet with plenty of water and fibre is important in preventing constipation.

ISPAGHULA HUSK

Presentation: Granules or powder containing 3.5g of ispaghula husk.

Indications: Constipation, Colostomy, ileostomy, anal fissure, haemorrhoids, hypercholetocaemia

Administration: 1 sachet or 2 level 5ml spoonfuls in a glass of water twice daily, preferably after meals.

Children:
6-12 years ½ - 1 level 5ml spoonful in a glass of water.

Side effects: Intestinal obstruction, hypersensitivity.

SENNA

Presentation: Tablets containing 7.5mg sennocides.

Indications: Constipation

Administration: Adult 2-4 tablets at night. The initial dose should be low and then gradually increased. A child over 6 years; half adult dose (on Doctor's advise only).

Side effects: Abdominal colic and flatulence. **Contraindications:** Should not be given to patients with abdominal pain of unknown cause.

2.5.2 Stimulant laxatives

BISACODYL

Presentation: Tablet containing 5mg bisacodyl, Suppositories containing 10mg. Paediatric suppositories containing 5mg bisacodyl. **Indications:** Constipation

Administration: *Adult:* 5–10 mg PO once daily; increased if necessary, up to 20 mg once daily, dose to be taken at night. Suppository; 10 mg once daily, dose to be taken in the morning.

Children: 4–17 years: 5–10 mg PO once daily, adjusted according to response, dose to be taken at night. by rectum; 2–17 years: 5–10 mg once daily, adjusted according to response

GLYCEROL SUPPOSITORIES

Presentation: Adult size (4g) containing 2.8g glycerol. *Child* size (3G) containing 2.1g glycerol. Infant size (1g) containing 700mg glycerol.

Indications: Constipation especially when the stool is very hard

Administration: Oral, 5 - 10mg at night occasionally may be increased to 15 - 20mg. Before radiological procedures and surgery, 10mg orally at bedtime for 2 days before examination and, if necessary, a 10mg suppository 1 hour before the examination.

Children: Child under 10 years 5mg. By rectum in suppositories for constipation, 10mg in the morning. Child, under 10 years 5mg. Child; half the adult dose.

Side effects: Gripping, local irritation for suppositories, hypokalaemia and atonic non-functioning colon in prolonged use.

Caution: Intestinal obstruction.

2.5.3 Faecal softeners

ARACHIS OIL

Presentation: Enema containing Arachis oil (peanut) in 130ml single-dose disposable packs.

Indications: Constipation

Administration: To soften impacted stool, 130ml. The enema should be warmed before use. It is not recommended for children below 3 years. Children above 3 years reduce adult dose in proportion to body weight.

Glycerol suppositories (see 2.5.2 above)

2.5.5 Bowel cleansing solutions

These are used before colonic surgery, colonoscopy or radiological examination to ensure the bowel is free of solid contents. They are not treatments for constipation.

CITRAMAG

Presentation: Citramag prep oral effervescent powder containing magnesium carbonate 11.57g, anhydrous citric acid 17.79g/sachet.

Indications: Colonic surgery, colonoscopy or radiological examination to ensure the bowel is free of solid contents.

Administration: Bowel evacuation for surgery or radiological examination on day before the procedure; 1 sachet between 2 - 4 PM.

Side effects: Nausea and bloating; less frequently abdominal cramps (usually transient, this can be removed by taking the drug more slowly), vomiting.

Caution: Pregnancy, renal impairment, heart disease, ulcerative colitis, diabetes mellitus, reflux oesophagitis, impaired gag reflex, unconscious or semiconscious or the possibility of regurgitation or aspiration.

Contraindications: Gastrointestinal obstruction, gastric retention, gastrointestinal ulceration, perforated bowel, congestive cardiac failure, toxic colitis, toxic megacolon or ileus.

FLEET PHOSPHO-SODA

Presentation: An oral solution containing sugar-free Sodium dihydrogen phosphate dihydrate 24.4g, Disodium phosphate dodecahydrate 10.8g/45ml

Indications: See under Citramag

Administration: 45ml diluted with half a glass (120ml) of cool water, followed by one full glass (240ml) of cool water. Timing of doses is dependent on the time of the procedure; For morning procedure, the first dose should be taken at 7.00 am and the second at 7.00 PM on the day before the procedure. For afternoon procedure, the first dose should be taken at 7.00 PM on the day before and the second dose at 7.00 AM on the day of the procedure. Solid food must not be taken during the

dosing period; clear liquids or water should be substituted for meals.

Children:
Not recommended for children under 15 years old.

Contraindications: see under Citramag.

Caution*:* see under Citramag

3 Medicines acting on the Central Nervous System

3.1 Antipsychotics

The term "antipsychotic" refers to several classes of Medicines which includes conventional antipsychotic medicines (often referred to as" neuroleptics" and "atypical antipsychotics").

Antipsychotics vary in potency and propensity to induce side effects. The conventional antipsychotics are usually classified into 3 groups according to their anti-psychotic potency.

The high - potency agents include haloperidol and fluphenazine, the intermediate-potency include loxapine and perphenazine and the low-potency include chlorpromazine and thioridazine.

Side effects: Antipsychotic medications can cause a broad spectrum of side effects. Many are the result of pharmacological effects on the neurotransmitter systems in other regimes than the target site for the intended therapeutic effects. Common side effects include sedation, dry mouth, blurred vision, constipation, tachycardia and urinary retention, postural hypotension and tachycardia. Neurological (Extrapyramidal) side effects including medication-induced parkinsonism characterised by rigidity, tremor, akinesia and bradykinesia.

These symptoms arise in the early days of antipsychotic medication and are drug dependent. Dystonia characterised by the spastic contractions of discrete muscle groups.

Akathisia (characterised by somatic restlessness that is manifested subjectively and objectively. Patients complain of an inner sensation of restlessness and irresistible urge to move various parts of their bodies. Objectively this is seen as an increased motor activity. The most common form involves pacing and inability to sit still.

Neuroleptic Malignant Syndrome characterised by a triad of rigidity, hypothermia and autonomic instability (including hypertension and tachycardia). *Tardive dyskinesia* is a hyperkinetic abnormal involuntary movement disorder caused by sustained exposure to antipsychotic Medicines that can affect neuromuscular function in any body region but is most commonly seen in the 'oro-facial region'.

Other side effects include seizures, endocrine -galactorrhea, amenorrhea, reduced fertility, impotence, metabolic- weight gain, haematological- bone marrow depression and allergic-cholestatic jaundice.

IMPLEMENTATION

Antipsychotic Medicines have a wide therapeutic index. Thus, an overdose is rarely fatal unless they are complicated by pre-existing medical problems or concurrent ingestion of alcohol or other medication. Clinical features of overdose are generally characterised by exaggerations of the

adverse effects of respiratory depression and hypotension presenting the greatest danger.

ROUTE OF ADMINISTRATION

Administration of antipsychotic Medicines can be in form of oral, short-acting intramuscular injections or as long-acting depot medicines.

For maintenance therapy, long-acting, depot injections of antipsychotic Medicines are used because they are more convenient than oral preparations. They ensure better patient compliance. However, they may give rise to a higher incidence of extrapyramidal reactions than oral preparations. Depot antipsychotics are administered by deep intramuscular injections at intervals of 1-4 weeks. Patients should first be given a test dose as undesirable side effects are prolonged. Treatment requires careful monitoring for optimum effects. Extrapyramidal side effects occur frequently. When transferring from oral to depot therapy, dosage by mouth should be gradually phased out. Not recommended in children.

DRUG CHOICE

Different medicines differ in predominant actions and side effects. Selection is therefore influenced by the degree of sedation required and the patient's susceptibility to extrapyramidal side effects. However, the differences between psychotic Medicines are less important than the great variability in patients response. Moreover, tolerance to adverse effects usually develops.

DOSAGE

After an initial period of stabilisation, in most patients, the long half-life of antipsychotic Medicines allows the total daily dose to be given as a single dose.

WITHDRAWAL

Withdrawal of antipsychotic Medicines after long-term therapy should always be gradual and monitored to avoid the risk of withdrawal syndrome or rapid relapse.

IMPORTANT

- Prescribing of more than one antipsychotic drug is not recommended
- Consider potential drug interaction.
- Carry out ECG periodically to exclude abnormalities such as prolonged QT. interval
- Carry out regular pulse rate, blood pressure, temperature, ensure that the patient maintains adequate fluid balance
- Increase the dose slowly and not more than once a week.
- Consider high dose therapy to be for a limited period and review regularly. Abandon if no improvement after 3 months (return to standard dosage)

First Generation (typical)

CHLORPROMAZINE HYDROCHLORIDE

Presentation: Tablets containing 10mg, 25mg, 50mg, 100mg Chlorpromazine hydrochloride. Syrup containing 25mg/5ml Chlorpromazine hydrochloride. An injection containing 25mg/1ml Chlorpromazine hydrochloride.

Indications: Psychosis**,** autism, hiccup.

Administration: Oral, Short term adjunctive management of severe anxiety, psychomotor agitation, excitement and violent or dangerously impulsive behaviour; 25mg 3 times a day or (75mg at night) adjusted according to response to the usual maintenance dose of 75-300mg (but up to 2g may be required in psychosis). *Elderly* (or debilitated) $^{1}/_{3}$ to $^{1}/_{2}$ adult dose.

Injection, for relief of acute symptoms (note Caution and side effects); 25-50mg 6-8 hourly daily.

Intractable hiccup 25-50mg 3-4 times a day.

Children:

(childhood schizophrenia and autism) 1-5 years; 5mg/kg per day every 4-6 hours (maximum dose 40mg daily).

6-12 years; 1/3 to 1/2 adult dose (maximum dose 75mg daily).

Side effects: Sedation, drowsiness, apathy, constipation, urine retention, tachycardia, hypotension, arrhythmia, parkinsonism, dystonia, akathisia, neuroleptic, malignant syndrome, amenorrhoea, infertility, impotence, galactorrhea gynecomastia, cholestatic jaundice, pigmentary retinopathy after prolonged use, convulsions, leucopenia, weight gain and respiratory depression.

Contraindications: Coma caused by Central Nervous System depression, bone marrow depression, phaeochromocytoma.

Caution: Parkinsonism, epilepsy, acute infections, pregnancy and breastfeeding, renal and hepatic impairment, history of jaundice, leucopenia, cardiovascular, cerebrovascular and respiratory diseases, hypothyroidism, myasthenia gravis, prostatic enlargement, closed-angle glaucoma, the elderly.

HALOPERIDOL

Presentations: Capsule containing 500mcg Haloperidol. Tablets containing 1.5mg, 5mg, 10mg Haloperidol. Syrup containing 2mg/ml Haloperidol.

An injection containing 10mg/ml Haloperidol.
Indications: See 3.1, acute mania.

Administration: Oral*, Adult;* short term management of psychomotor agitation, excitement, violent or dangerously impulsive behaviour. Initially 3-5mg 2-3 times a day. In resistant schizophrenia up to 100mg daily adjusted according to clinical response, to the lowest effective maintenance dose of 5-10mg daily. *Elderly* or debilitated; initially ½ the adult dose.

Short term adjunctive management of severe anxiety adults 500mcg twice a day. Not recommended in children. Intractable hiccup; oral,1.5-3mg 3 times daily adjusted according to clinical response (not recommended in children). *Injection* intramuscularly 2-10mg, subsequent doses being given every 4-8 hours according to response (up to every hour if necessary) to maximum 60mg daily. Severely disturbed patients may require an initial dose of up to 30mg (not recommended in children). Nausea and vomiting 1-2mg/day.

Children: Child; 50mcg/kg daily in divided doses to a maximum of 10mg daily.

Side effects: See 3.1. The relative sedative antimuscarinic and adrenergic and extrapyramidal side effects such as akathisia and dystonic reactions are more frequent in thyrotoxicosis.

Contra-indications: See 3.1. Avoid in basal ganglia disease.

Caution: See 3.1.

HALOPERIDOL DECANOATE

Presentation: Injection containing 50mg/ml

haloperidol decanoate

Indications: *See 3.1.*

Administration: By deep intramuscular injection into the gluteal muscles initially 50mg every 4 weeks, if necessary, increase after 2 weeks by 50mg increments to 300mg every 4 weeks. Higher doses may be needed in some patients. *Elderly* initially 12.5mg every 4 weeks.

Side effects: See 3.1. **Caution:** See 3.1.

Contraindications: See 3.1.

FLUPHENAZINE DECANOATE

Presentation: Injection containing 25mg/ml, 100mg/ml Fluphenazine decanoate.

Indications: Maintenance in Schizophrenia and other psychosis

Administration: By deep intramuscular injection in the gluteal muscle test dose 12.5mg (6.5mg in the elderly) then after 4-7 days 12.5-100mg repeated at the interval of 4 - 35 days adjusted according to the response.

Side effects: See notes above. Extrapyramidal side effects usually appear a few hours after the dose has been administered and continue for 2 days but they may be delayed. Contra-indicated in severely depressed states.

Contra-indications: See 3.1.

Caution: See 3.1.

Second Generation (atypical)

CLOZAPINE

Presentation: Tablet containing 25mg and 50mg

Indications: Treatment resistant Schizophrenia (patients treated with at least two different medications one of which should be a second-generation antipsychotic), psychosis in Parkinson's disease.

Administration: Treatment resistant Schizophrenia (patients treated with at least two different medications one of which should be a second-generation antipsychotic)

Adult 18–59 years: 12.5 mg 1–2 times a day for day 1, then 25–50 mg for day 2, then increased, if tolerated, in steps of 25–50 mg daily, dose to be increased gradually over 14–21 days, increased to up to 300 mg daily in divided doses, larger dose to be taken at night, up to 200mg daily may be taken as a single dose at bedtime; increased in steps of 50–100 mg 1–2 times aweek if required, it is preferable to increase once aweek; usual dose 200–450 mg daily, max. 900mg perday, if restarting after interval of more than 48 hours, 12.5mg once or twice on first day (but may be feasibleto increase more quickly than on initiation)—extreme caution if previous respiratory or cardiac arrest with initial dosing

Adult 60 years and over: 12.5 mg once daily for day 1, then increased to 25–37.5 mg for day 2, then increased, if tolerated, in steps of up to 25 mg daily, dose to beincreased gradually over 14–21 days, increased to up to 300 mg daily in divided doses, larger dose at to be taken night, up to 200mg daily may be taken as a single dose at bedtime; increased in steps of 50–100 mg 1–2 times a week if required, it is preferable to increase once a week; usual dose 200–450 mg daily, max. 900mg per day, if restarting after interval of more than 48 hours, 12.5mg once or twice on first day (but may be feasible to increase more quickly than on initiation)—extreme caution if previous respiratory or cardiac arrest with initial dosing.

Psychosis in Parkinson's disease: Adult, 12.5 mg once daily, dose to be taken at bedtime, then increased in steps of 12.5 mg up to twice weekly, adjusted according to response; usual dose 25–37.5 mg once daily, dose to be taken at bedtime; increased in steps of 12.5 mg once weekly, this applies only in exceptional cases, increased if necessary up to 100 mg daily in 1–2 divided doses; Usual maximum50 mg/24 hours

Children: Not recommended for use in children.

Side effects: eosinophilia, fatigue, Fever, headache, hypertension muscle complaints, nausea, postural hypotension (dose-related), speech impairment,sweating, syncope, urinary disorders, blurred vision Anaemia, cardiac arrest, cardiomyopathy, circulatory collapse, Delirium, diabetes mellitus, dyslipidaemia, dysphagia, gastrointestinal disorders, glucose tolerance impaired, hepatic disorders, hyperglycaemia, increased risk of infection, intestinal obstruction (including fatal cases), ketoacidosis, nephritis tubulointerstitial, obsessive compulsive disorder, pancreatitis, pericardial effusion, respiratory disorders, restlessness, sexual dysfunction, skin reactions, sleep apnoea, thrombocytopenia, thrombocytosis.

Contraindications: Alcoholic and toxic psychoses, bone-marrow disorders, coma, drug intoxication, historyof agranulocytosis, history of circulatory collapse, historyof neutropenia, paralytic ileus, severe cardiac disorders (e.g. myocarditis), severe CNS depression, uncontrolledepilepsy

Caution: Myocarditis and cardiomyopathy (discontinue permanently in clozapine-induced myocarditis or cardiomyopathy), age over 60 years, prostatic hypertrophy, susceptibility to angle-closure glaucoma, taper off other antipsychotics before starting. Agranulocytosis, Neutropenia and potentially fatal agranulocytosis reported. Avoid drugs which depress leucopoiesis; patients should report immediately symptoms of infection, especially influenza-like illness.

RISPERIDONE

Presentation: Tablets containing 2mg, 1mg , powder for injection 25mg

Indications: schizophrenia and other psychoses, Aggresssion and violence in autism spectrum disorders.

Administration: *Adults:* By mouth 2mg 12 hourly in the acute phase usually 2 to 4 weeks and 2mg once daily at night during maintenance once the acute symptoms have resolved. By deep intramuscular injection, 25mg deep IM in the gluteal or deltoid muscle every two weeks upto a maximum of 50mg every two weeks.

Children:
> 12 years: 0.5mg PO once daily, then can increase to a maximum of 1.0 mg daily
< 12 years (not recommended)

Side effects: muscle stiffness, drooling, joint stiffness, stiffness of the tongue, abdominal discomfort, anaemia, weight gain, hypertension

Contraindications: acute porphyria, documented hypersentivity

Caution: use with caution in preganancy, breastfeeding, hepatic impairment and renal impairment.

OLANZAPINE

Presentation: tablets containing 5mg, 10mg, 20mg, IM injection 10mg

Indications: schizophrenia and other psychoses, mania in bipolr mood disorder, agitation and disorganised behaviour in mania

Administration: in schizophrenia 5-10 mg/ day initially; then titrate upward in increments of 5 mg/day at intervals >1 week Maintenance: 10-20 mg/day; not to exceed 20 mg/day

In bipolar Mania Monotherapy: 10-15 mg/ day PO initially; may be titrated upward in increments of 5 mg/day at intervals >24 hr Adjunct to valproate: 10 mg/day PO initially

Maintenance: 5-20 mg/day PO; not to exceed 20 mg/day

In children 3-17 years: 2.5-5 mg/day PO initially; target, dosage, 10mg/day; adjust by increments/decrements of 2.5-5 mg; dosage range, 2.5-20 mg/day

Side effects: Orthostatic hypotension, weight gain, dose-dependent hypertriglyceride, hypercholesterolemia, omnolence, dose-dependent extrapyramidal symptoms (EPS), dose-dependent xerostomia, weakness, dizziness, accidental injury, insomnia, elevated alanine aminotransferase (ALT) level, constipation, dyspepsia, hyperprolactinemia, hyperglycemia, hypotension, postural hypotension, tremor.

Contraindications: Documented hypersensitivity

Caution: Use with caution in patients with history of seizures or with conditions that potentially lower seizure threshold and patients with urinary retention.

QUETIAPINE

Presentation: immediate /extended release tablets containing 25mg, 50mg, 100mg, 200mg, 300mg, 400mg.

Indications: schizophrenia and other psychoses, bipolar 1 disorder, manic episode and major depressive disorder.

Administration: *Adult*, immediate release tablets initially 25 mg PO 12 hourly. Days 2-3: Dose increased daily in increments of 25 mg per dose 12 hourly. Dosage range: 150-750 mg/day. Extended release tablets 300 mg once daily for day 1, then 600 mg once daily for day 2, then, adjusted according to response. Maximum dose under specialist supervision is 800mg per day

Children:

In children older than 12 years

Day 1: 25 mg PO 12 hourly

Day 2: 25 mg 12 hourly

Day 3: 50 mg PO 12 hourly

Day 4: 75 mg PO 12 hourly

Day.5: 100mg/day PO 12 hourly;

Dosage range: 400-800 mg/day

Extended release tablets Day 1: 50 mg/day PO once daily

Day 2: 100 mg/day PO once daily

Day 3: 200 mg/day PO once daily

Day 4: 300 mg/day PO once daily

Day 5: 400 mg/day PO once daily

Extended release tablets are given once daily by summing up the total daily dose of the immediate release tablets.

Side effects: Appetite, increased asthenia, dysarthria, dyspepsia, dyspnea, fever, headache, hyperglycaemia, irritability, palpitations, peripheral oedema, rhinitis, sleep disorders, suicidal behaviour, syncope, blurred vision, withdrawal syndrome, anaemia, diabetes mellitus, dysphagia, hyponatreamia, hypothyroidism, sexual dysfunction.

Contraindications: documented hypersensitivity.

Caution: Use with caution in cardiovascular and cerebrovascular disease. May worsen hypotensive conditions. Use with caution in breast cancer and history of seizure.

3.2 Medicines used in parkinsonism and related disorders

3.2.1 Antimuscarinics

Antimuscarinic medicines exert their antiparkinsonian effect by correcting the relative central cholinergic excess thought to occur in parkinsonism as a result of dopamine deficiency.

These medicines also reduce the symptoms of drug-induced parkinsonism as seen for example with antipsychotic medicines.

There is no justification for giving them simultaneously with antipsychotic medicines unless parkinsonism side effects occur. Tardive dyskinesia is not improved with antimuscarinic medicines and may be made worse. No important differences exist between the many synthetic antimuscarinic medicines available but some patients tend to tolerate one better than the other. The most commonly used are Procyclidine and Benzhexol. Procyclidine may be given parenterally and is the effective emergency treatment of acute drug dystonic reactions which may be severe.

BENZHEXOL HYDROCHLORIDE

Presentation: Tablet containing 2mg, 5mg Benzhexol hydrochloride. Syrup containing Benzhexol hydrochloride 5mg/5ml

Indications: Drug-induced Parkinsonism

Administration: 1mg daily, gradually increased to a maintenance dose of 5-15mg daily in 3-4 divided doses. Elderly patients should preferably be put on the lower end of the dosage range.

Children:

3 months–17 years: Initially 1–2 mg daily in 1–2 divided doses, then increased in steps of 1 mg every 3–7 days, dose to be adjusted according to response and side-effects; maximum 2 mg/kg per day

Side effects: Dry mouth, dizziness, blurred vision, urinary retention, tachycardia, hypersensitivity, nervousness and with high dose in susceptible patients' mental confusion, excitement and other psychiatric disturbances.

Contraindications: Untreated urinary retention, closed-angle glaucoma and intestinal obstruction.

Caution: Cardiovascular disease, hepatic and renal impairment

PROCYCLIDINE HYDROCHLORIDE

Presentation: Tablet containing 5mg Procyclidine hydrochloride. Syrup containing 2.5mg/5ml Procyclidine hydrochloride. An injection containing 5mg/ml Procyclidine hydrochloride

Indications: See under benzhexol hydrochloride

Administration: *Oral*; 2.5mg 3 times daily gradually increasing to a maximum of 30mg daily (60mg in exceptional cases). *Elderly;* preferably lower end of the dosage range.

By injection in acute dystonia; 5-10mg intramuscularly if necessary repeat after 20 minutes. Maximum dose 20mg daily.

Children:

7–11 years: oral 1.25 mg 3 times a day. injection; 1 month–1 year: 0.5–2 mg for 1 dose; 2–9 years: 2–5 mg for 1 dose, 10–17 years: 5–10 mg, occasionally, more than 10 mg.

Dose usually effective in 5–10 minutes but may need 30 minutes for relief.

Side effects: See Benzhexol hydrochloride above.

Contraindications: See Benzhexol hydrochloride above.

Caution: See Benzhexol hydrochloride above.

LEVODOPA (COMBINATION WITH CARBIDOPA)

Presentation: Tablets containing a combination of carbidopa and levodopa in the proportions 10mg / 100mg, 25mg / 100mg and 25mg / 250mg respectively.

Indications: Parkinson Disease and Parkinson-like Disorders

Administration: *Adult*: Initially 25/100 mg 3 times a day, then increased in steps of 12.5/50 mg once daily or on alternate days, alternatively increased in steps of 25/100 mg once daily or on alternate days, dose to be adjusted according to response; dose increased until 800mg levodopa (with 200mg carbidopa) daily in divided doses is reached, then maintenance up to 200/2000 mg daily in divided doses, adjusted according to response, when cocareldopais used, the total daily dose of carbidopa should be at least 70 mg. A lower dose may not achieve full inhibition of extracerebral dopa-decarboxylase, with a resultant increase in side effects.

Side effects: Drowsiness, seizure, sleep disorders, agranulocytosis, alertness decreased, alopecia, anaemia, angioedema, anxiety, appetite decreased, asthenia, cardiac disorder, chest pain compulsions, confusion, constipation, delusions, dementia, depression, diarrhoea, dizziness, dopamine dysregulation syndrome, dry mouth, dyskinesia (may be dose-limiting), dysphagia, dyspnoea, eating disorders, euphoric mood, eye disorders, fall, focal tremor, gastrointestinal discomfort, gastrointestinal haemorrhage, haemolytic anaemia, hallucination, headache, Henoch-Schönlein purpura, hiccups, hoarseness, Horner's syndrome, exacerbated hypertension, hypotension, leucopenia, malaise, malignant melanoma, movement disorders, muscle complaints, nausea, neuroleptic malignant syndrome (on abrupt discontinuation), oedema, on and off phenomenon, oral disorders, palpitations, pathological gambling, postural disorders, psychotic disorder, respiration abnormal, sensation abnormal, sexual dysfunction, skin reactions, suicidal ideation, sweat changes, syncope, taste bitter, teeth grinding, thrombocytopenia, trismus, urinary disorders, vasodilation, vision disorders, vomiting, weight changes.

Contraindications: Hypersensitivity, concurrent administration of nonselective monoamine oxidase inhibitors (MAOIs) or use within last 14 days.

Cautions: Treatment with levodopa is associated with impulse control disorders, including pathological gambling, binge eating, and hypersexuality. Patients and their carers should be informed about the risk of impulse control disorders. Cushing's syndrome, diabetes mellitus, endocrine disorders, history of convulsions, history of myocardial infarction with residual arrhythmia, history of

peptic ulcer, hyperthyroidism, osteomalacia, phaeochromocytoma, psychiatric illness, severe cardiovascular disease, severe pulmonary disease, susceptibility to angle-closure glaucoma.

BROMOCRIPTINE

Presentation: Tablet containing 2.5mg

Indications: Prevention of lactation, suppression of lactation, hypogonadism, galactorrhoea, infertility, acromegaly, prolactinoma, parkinsons disease.

Administration:

Prevention of lactation: Initially 2.5 mg daily for 1 day, then 2.5 mg twice daily for 14 days.

Suppression of lactation: Initially 2.5 mg daily for 2–3 days, then 2.5 mg twice daily for 14 days.

Hypogonadism/Galactorrhoea/Infertility: Initially 1–1.25 mg daily, dose to be taken at bedtime, increase dose gradually; usual dose 7.5 mg daily in divided doses, increased if necessary, up to 30 mg daily, usual dose in infertility without hyperprolactinaemia is 2.5mg twice daily.

Acromegaly/ Prolactinoma: Initially 1–1.25 mg daily, dose to be taken at bedtime, then increased to 5 mg every 6 hours, increase dose gradually. Occasionally patients may require up to 30mg daily.

Parkinson's disease: Initially 1–1.25 mg daily for 1 week, dose to be taken at night, then 2–2.5 mg daily for 1 week, dose to be taken at night, then 2.5 mg twice daily for 1 week, then 2.5 mg 3 times a day for 1 week, then increased in steps of 2.5 mg every 3–14 days, adjusted according to response; maintenance 10–30 mg daily

Side effects: Constipation, drowsiness, headache, nasal congestion, nausea, allergic dermatitis, alopecia, confusion, dizziness, dry mouth, fatigue, hallucination, hypotension, leg cramps, movement disorders, vomiting, abdominal pain, arrhythmias, cardiac valvulopathy, diarrhoea, dyspnea, gastrointestinal disorders, gastrointestinal haemorrhage, neuroleptic malignant-like syndrome, pallor, paraesthesia, pericardial effusion, pericarditis, peripheral oedema, psychotic disorder, respiratory disorders, sleep disorders, tinnitus, vision disorder, eating disorders, hypertension, myocardial infarction, pathological gambling, psychiatric disorders, seizure, sexual dysfunction, stroke.

Contraindications: Cardiac valvulopathy (exclude before treatment), hypertension in postpartum women or in puerperium, hypertensive disorders of pregnancy (e.g. pre-eclampsia, eclampsia or pregnancy-induced hypertension)

Cautions: Cardiovascular disease, history of peptic ulcer (particularly in acromegalic patients), history of serious mental disorders (especially psychotic disorders), Raynaud's syndrome.

3.3 Antidepressants

Antidepressants are used to treat depression and manic-depressive disorders. Other methods of treatment include psychotherapy, which may be all that is required for the milder forms of depression, and electroconvulsive therapy (ECT) which is used in severe depression or where antidepressants have failed.

Classification

The two traditional categories of tricyclic antidepressants (typified by amitriptyline) and monoamine oxidase inhibiting antidepressants (MAOIs) (typified by phenelzine) continue to be widely used.

Of late there is a recent generation of antidepressants called selective serotonin reuptake inhibitors (SSRIs) typified by fluoxetine which has come into use.

Imipramine and amitriptyline despite having marked antimuscarinic or cardiac side effects than compounds such as the SSRIs and MAOIs are well established and relatively safe and effective to treat depression.

Choice

There is a relatively widespread view that certain types of depression respond preferentially to certain classes of antidepressants. Tricyclic and related antidepressants are usually considered to be more effective than monoamine oxidase inhibitors in major depression or endogenous depression, whereas the converse may be true in atypical depression or reactive depression. Choice of an antidepressant within a given class lies, therefore, not primarily in supposed efficacy, but in the ability to select or avoid an agent possessing known pharmacological properties unrelated to antidepressant action. For example, some tricyclics possess marked sedative properties and if given at night this effect may be of particular advantage in patients with insomnia, whereas Medicines with less of a sedative action or those with a stimulant action may be preferred in apathetic or hypersomniac patients. Additionally, some antidepressants appear to have less of an antimuscarinic action or exhibit reduced cardiotoxicity or epileptogenic potential, factors which may be of importance in individual patients.

Withdrawal

All antidepressants should generally be withdrawn gradually to prevent withdrawal symptoms. It should be remembered that a characteristic feature of several types of depression is that remissions and relapses are likely to occur and that re-introduction of therapy may become necessary.

First Generation

AMITRIPTYLINE HYDROCHLORIDE

Presentation: Tablets containing 10mg, 25mg, 50mg Amitriptyline hydrochloride. Syrup containing 25mg/5ml Amitriptyline hydrochloride. An injection containing 10mg/ml Amitriptyline hydrochloride.

Indications: Depression (especially where sedation is needed), nocturnal enuresis.

Administration: *Oral,* Depression initially 75mg daily (adolescents and elderly 30 -75mg daily) in divided or single doses at bedtime to a maximum dose of 150mg daily. Maintenance dose 50-100mg daily.

Children:

Not recommended in children under 16 years.

Nocturnal enuresis, Child; 7-10 years 10-20mg daily, 11-16 years 25-50mg daily at night (maximum period of treatment including gradual withdrawal is 3 months).

Injection, depression; 10-20mg 4 times daily (not recommended in children under 16 years)

Side effects: Sedation, dry mouth, blurred vision, nausea, constipation, difficulty in micturition, arrhythmias, postural hypotension, tachycardia, sweating, syncope (in high doses), urticaria, hypomania/mania, confusion (in elderly). Increased appetite and weight gain, testicular enlargement, fever.

Contraindications: Severe liver disease, manic phase, cardiac arrhythmias especially heart block, recent myocardial infarction.

Caution: History of epilepsy, hepatic disease (avoid if severe), thyroid disease, pheochromocytoma, mania and psychosis (may aggravate psychosis), urine retention, concurrent electroconvulsive therapy (ECT), anaesthesia (increase the risk of arrhythmia and hypotension), cardiac arrhythmias and porphyria, caution in elderly. Avoid abrupt withdrawal.

IMIPRAMINE HYDROCHLORIDE

Presentation: Tablet containing 10mg, 25mg imipramine hydrochloride. Syrup containing 25mg/5ml imipramine hydrochloride

Indications: See Amitriptyline hydrochloride above.

Administration: Depression; initially up to 75mg daily in divided doses increasing gradually to 150-200mg daily (up to 150mg may be given as a single dose at bedtime). Maintenance dose; 50-100mg daily. *Elderly*;

initially 10mg/day increasing gradually to 30-50mg daily.

Children: not recommended for depression. Nocturnal enuresis, 7 years; 25mg daily. 8-11 years; 25-50mg daily. Over 11 years, 50-75mg daily at bedtime. The maximum period of treatment (including gradual withdrawal) is 3 months.

Contraindications: See Amitriptyline hydrochloride above. Less sedating.

Caution: See Amitriptyline hydrochloride above

CLOMIPRAMINE

Presentation: Capsule containing 25mg, 50mg, and 75mg.

Indications: Depressive illness, obsessive compulsive disorder.

Administration: *Depressive illness:* Adult: Initially 10 mg daily, then increased if necessary to 30–150 mg daily in divided doses, dose to be increased gradually, alternativelyincreased if necessary to 30-150mg once daily. Dose to bet taken at bedtime. Maximum dose 250mg per day.

Phobic and obsessional states: Adult Initially 25 mg daily, then increased to 100–150 mg daily, dose to be increased gradually over 2 weeks; maximum 250 mg per day. *Elderly:* Initially 10 mg daily, then increased to 100–150 mg daily, dose to be increased gradually over 2 weeks, maximum 250 mg per day.

In children above 10 years 25 mg PO once daily

Side effects: Aggression, anxiety, arrhythmias, breast enlargement, concentration impaired, confusion, constipation, delirium, depersonalization, depression, exacerbated diarrhoea, dizziness, drowsiness, dry mouth, fatigue, galactorrhoea, gastrointestinal disorder, hallucination, headache, hot flush, hyperhidrosis, hypotension, memory loss, mood altered, movement disorders, muscle tone increased, muscle weakness, mydriasis, nausea, palpitations, paraesthesia, photosensitivity reaction, sexual dysfunction, skin reactions, sleep disorders, speech disorder, taste altered, tinnitus, tremor, urinary disorders, vision disorders, vomiting, weight increased, yawning.

Contraindications: Acute porphyrias, arrhythmias during the manic phase of bipolar disorder, heart block, immediate recovery period after myocardial infarction.

Caution: Cardiovascular disease, chronic constipation, epilepsy, history of bipolar disorder, history of psychosis, hyperthyroidism (risk of arrhythmias), increased intraocular pressure, patients with a significant risk of suicide, phaeochromocytoma (risk of arrhythmias), prostatic hyprtrophy, risk factors for QT interval prolongation (correct hypokalemia before initiating treatment), susceptibility to angle-closure glaucoma, urinary retention.

Second Generation

CITALOPRAM

Presentation: Tablets containing 10mg, 20mg, 40mg

Indications: Depression, obsessive compulsive disorder, panic disorder, generalized anxiety disorder and eating disorders.

Administration: In adults start with 10mg once daily with a target dose of 20 to 40 mg per day after 1 week.

In children under 12 years 10mg once daily and in children above 12 years start with 10mg once daily, then increase to 20mg once daily in intervals of 5mg by the beginning of the second week.

Side effects: Dry mouth, sausea, somnolence, insomnia, xerostomia, increased sweating, anxiety, pruritus, rhinitis, orthostatic, hypotension, tremor, diarrhea, ejaculation disorder, polyuria, tachycardia, weight change, orthostatic hypotension, upper respiratory infection, paraesthesia, rash, dyspepsia, fatigue, vomiting, anorexia, abdominal pain,

agitation, impotence, sinusitis, dysmenorrhea, amenorrhoea, confusion, cough, decreased libido, yawning, arthralgia, myalgia, flatulence, increased saliva, migraine, QTc prolongation.

Contraindications: Hypersensitivity, coadministration with pimozide; coadministration with serotonergic drugs; concomitant use or within 14 days of MAOIs increases the risk of serotonin syndrome.

Caution: Use with caution in pregnancy, in individuals with uncompensated heart failure, those with eye problems, in patients with history of seizure disorder

ESCITALOPRAM

Presentation: Tablets containing 5mg, 10mg and 20mg

Indications: Depressive illness, generalised anxiety disorder, obsessive-compulsive disorder.

Administration: *Adult:* 10 mg once daily; increased if necessary up to 20 mg daily.

In children above 12 years, 5mg once daily but may increase to 10mg over 3 weeks

Side effects: Sinusitis, oedema, headache, nausea, insomnia, diarrhoea, ejaculation disorder, decreased libido, fatigue, indigestion.

Contraindications: Hypersensitivity to escitalopram or citalopram, pimozide

Caution: use with caution in pregnancy and breastfeeding, causes discontinuation syndrome, risk of serotonin syndrome when used with other antidepressants, increased risk of bleeding tendencies and risk of mydriasis.

FLUOXETINE

Presentation: Tablets containing 10, 20 and 60 mg and capsules containing 10, 20 and 40mg

Indications: Indicated for acute and maintenance treatment of major depressive disorder (MDD), Bulimia Nervosa, obsessive compulsive disorders.

Administration: *Major Depressive Disorder: Adult;* Initial 20mg PO once daily in the morning. May consider gradually increasing dose after a few weeks to 40mg once daily in the morning.

Bulimia nervosa: Adult; 60 mg daily, daily dose may be administered as a single or divided dose. *Elderly*: Up to 40 mg daily, daily dose may be administered as a single or divided dose, usual maximum dose is 40 mg daily but doses up to 60 mg daily can be used

Obsessive-compulsive disorder: Adult; 20 mg daily, increased, if necessary, up to 60 mg daily, daily dose may be administered as a single or divided dose, dose to be increased gradually, review treatment if inadequate response after 10 weeks maximum 60 mg per day. *Elderly:* 20 mg daily, increased if necessary up to 40 mg daily, daily dose may be administered as a single or; divided dose, dose to be increased gradually, review treatment if inadequate response after 10 weeks, usual maximum dose is 40 mg daily but doses up to 60 mg daily can be used.

Children

lder than 7 years, 10mg PO per day once daily and can be increased up to 20 mg once daily.

Side effects: Headache, insomnia, agitation, heart palpitations, chills, GI Bleeding, vasodilation, blurred vision, cold sweat, dysphagia, dyspnoea, hypotension, mood altered, muscle twitching, self injurious behaviour, temperature sensation.

Contraindications: Hypersensitivity, breastfeeding.

Caution: Risk of bleeding (GI and other) when used in combination with NSAIDs, aspirin, or drugs affecting coagulation; may impair platelet aggregation.

MIRTAZAPINE

Presentation: Tablets containing 30mg mirtazapine.

Indication: Treatment of major depressive episodes.

Administration: Tablet swallowed whole without chewing with sufficient amount of water. Adult the initial dose is 15-30mg taken preferably in the evening. The maintenance dose is 15-45mg daily.

Side effects: Mirtazapine may impair concentration and alertness, sleepiness, increased appetite, weight gain, dry mouth constipation, strange dreams. Attempt to commit suicide.

Caution: Operation of machinery, heart problems.

SERTRALINE

Presentation: Tablets containing 25mg, 50mg and 100mg, capsules containing 150mg and 200mg. Solution containing 20mg/ml.

Indications: depressive illness, obsessive compulsive disorder, panic disorder, social anxiety disorder, post-traumatic stress disorder and premenstrual dysphoric disorder.

Administration: *Depressive illness/ Obsessive-compulsive disorder: Adult;* Initially 25 mg daily, then increase in steps of 25 mg at intervals of at least 1 week if required, maintenance 50 mg daily, maximum 200 mg per day.

Panic disorder/Post-traumatic stress disorder/ Social anxiety disorder: Adult; Initially 25 mg daily for 1 week, then increased to 50 mg daily, then increased in steps of 25 mg at intervals of at least 1 week if required, increase only if response is partial and if drug is tolerated; maximum 200mg per day.

In children: 6-12 years, 25 mg PO once daily and in those 12 – 17 years 25 – 50 mg once daily.

Side effects: Gastrointestinal disturbances, increased risk of infection, neuromuscular dysfunction, vasodilation, back pain, burping, chills, cold sweat, dysphagia, dyspnoea, ear pain, euphoric mood, hypertension, hypothyroidism, migraine, muscle complaints, muscle weakness, oedema, oral disorders, osteoarthritis, periorbital oedema, thirst, agitation, insomnia.

Contraindications: hypersensitivity, concomitant use with disulfiram and pimozide.

Caution: Coadministration with other drugs that enhance the effects of serotonergic neurotransmission (eg, tryptophan, fenfluramine, fentanyl, 5-HT agonists, meperidine, methadone, St. John's Wort) should be undertaken with caution, use with caution in people with seizure disorders

LITHIUM CARBONATE (See 3.4 Below)

3.4 Antimanics

3.4.1 Lithium Carbonate

3.4.2 Carbamazepine See 3.5 below

LITHIUM CARBONATE

Presentation: Tablet containing 250mg and 400mg of Lithium.

Indications: Treatment and prophylaxis of mania, manic depressive illness and recurrent depression.

Administration: Initially 1.5 - 2g per day (Elderly 0.5-1.2g per day). Prophylaxis; 0.5 - 1.2g per day (Elderly 0.5 – 1 g per day). Dose must be adjusted to attain a plasma Lithium concentration of 0.4 - 1.0mmol/L after 12 hours from the preceding dose, on the 4th and 7th day of treatment, then weekly until dosage has remained constant for 4 weeks and every 3 months thereafter. Initially, the doses are in divided doses but after a stable plasma concentration, single dose per day is preferable. Lithium 250mg should be given in divided doses, whereas Lithium 400mg may be given either in single or divided doses.

Not recommended in children.

Side effects: Nausea, vomiting, mild diarrhoea, fine tremors, weight gain and oedema, anorexia, coarse tremor, drowsiness, vertigo, dysarthria, cardiac arrhythmias, blurred vision, sluggishness to giddiness, ataxia and lack of co-ordination, convulsions, toxic psychoses,

syncope, circulatory failure, hypothyroidism, diabetes insipidus, hyperuricaemia and non-toxic goitre.

Contraindications: Renal impairment, cardiac insufficiency, conditions with sodium imbalance such as Addison disease.

Caution: Lithium has a narrow therapeutic/toxic index; therefore, it must be administered where facilities to monitor plasma concentration are available. The normal Lithium plasma concentration range is 0.4 - 1.0 mmol/L. Thyroid, renal and cardiac function tests must be done before starting treatment and thereafter annually. Lithium should only be used in low doses, and under frequent supervision in patients who have thyroid, renal and cardiac impairment. Lithium used in the 1st trimester of pregnancy is said to be teratogenic but is safe after this period. Use with caution in breastfeeding and myasthenia gravis (reduce the dose).

3.5 Anticonvulsants

The rationale of treatment is to prevent the occurrence of seizures by maintaining an effective plasma concentration of the drug, careful adjustment of doses if necessary, starting with low doses and increasing until seizures are controlled. The use of more than two anti-epileptics is rarely justified. Abrupt withdrawal of anti-epileptics should be avoided, as this may precipitate severe rebound seizures. Reduction in dosage should be carried out in stages; the withdrawal process may take months. The changeover from one anti-epileptic drug regimen to another should be made cautiously, withdrawing the 1st drug when the new regimen has been established. The decision to withdraw all anti-epileptic medicines from a seizure-free patient, and its timing, is often difficult and may depend on individual factors. Even in patients who have been seizure-free for several years, there is a significant risk of seizure reoccurring on drug withdrawal.

First Generation

CARBAMAZEPINE

Presentation: Tablet containing 100mg, 200mg and 400mg Carbamazepine. Liquid, sugar-free containing 100mg/5ml Carbamazepine. Suppositories containing 125mg Carbamazepine.

Indications: Partial and generalised tonic-clonic seizures, temporal lobe epilepsy, idiopathic trigeminal neuralgia. Prophylaxis of manic-depressive illness unresponsive to lithium.

Administration: *Oral*, epilepsy; initially 100 - 200mg 1 - 2 times daily, increased slowly to the usual dose of 0.8 - 1.2g daily in divided doses. In some cases, 1.6 - 2g daily may be needed. Elderly; reduce the initial dose. Trigeminal neuralgia, initially 100mg 1 - 2 times daily (some patients may require higher initial dose), increased gradually according to response; usual dose 200mg 3 - 4 times daily, up to 1.6g daily in some patients. Prophylaxis of bipolar disorder, unresponsive to lithium, initially 400mg daily in divided doses increased until symptoms are controlled, usual range 400 - 600mg daily, maximum 1.6g daily.

Children

Daily in divided doses, up to 1 year 100-200mg, 1 - 5 years 200 - 400mg, 5 - 10 years 400 - 600mg, 10 - 15 years 0.6 - 1g.

Side effects: Nausea, vomiting, dizziness, bone marrow depression, Steven Johnson's syndrome, impotence.

Contraindications: History of bone marrow depression, porphyria, AV conduction abnormalities.

Caution: Hepatic, renal and cardiac diseases and Glaucoma.

DIVALPROEX SODIUM

Presentation: Tablet containing 250mg, 500mg.

Indications: Management of manic episodes associated with bipolar disorder, prophylaxis for migraine headache, epilepsy.

Administration: *Treatment of manic episodes associated with bipolar disorder: Adult;* Initially 500 mg 12 hours then increased to 1–2 g daily in two divided doses, adjusted according to response.

Migraine prophylaxis: Adult; Initially 250 mg 12 hourly, then increased if necessary to 1g in two divided doses.

Epilepsy: Adult; Initially 600 mg daily in 2–4 divided doses, increased in steps of 150–300 mg every 3 days; usual

maintenance 1–2 g daily in 2–4 divided doses, max. 2.5 g daily in 2–4 divided doses.

Children:

Older than 10 years; 10-15 mg/kg/day PO initially; may increase by 5-10 mg/kg/week to achieve optimal clinical response; not to exceed 60 mg/kg/day. Less than 10 years; not recommended.

Side effects: Abdominal pain, alertness increased, alopecia (regrowth may be curly), anaemia, behaviour, teratogenicity, bone disorders, bone fracture, cerebral atrophy, coma, confusion, consciousness impaired, dementia, diarrhoea, diplopia, drowsiness, encephalopathy, fine postural tremor, gastrointestinal disorder, gynaecomastia, haemorrhage, hallucination, hearing loss, hepatic disorders, hirsutism, hyperammonaemia, leucopenia, menstrual cycle irregularities, movement disorders, nail disorder, nausea, obesity, pancreatitis, pancytopenia, parkinsonism, peripheral oedema, seizure, severe cutaneous adverse reactions (SCARs), skin reactions, suicidal behaviours, thrombocytopenia, urine abnormalities, vasculitis, vomiting, weight increased.

Contraindications: Hypersensitivity, hepatotoxicity (causing significant hepatic impairment), pregnant women, panreatitis.

Caution: hepatotoxicity, pancreatitis, thrombocytopenia, discontinue if hyperammonemia or encephalopathy occur.

ETHOSUXIMIDE

Presentation: Capsule containing 250 mg and syrup containing 250 mg/5ml.

Indications: Absence Seizures

Administration: *Adult;* Initially 500 mg daily in 2 divided doses, then increased in steps of 250 mg every 5–7 days; usual dose 1–1.5 g daily in 2 divided doses, increased if necessary up to 2 g daily.

Children:

1month–5 years: Initially 5 mg/kg twice daily (max. per dose 125 mg), dose to be increased every 5–7 days; maintenance 10–20 mg/kg twice daily (max. per dose 500 mg), total daily dose may rarely be given in 3 divided doses.

6–17 years: Initially 250 mg twice daily, then increased in steps of 250 mg every 5–7 days; usual dose 500–750 mg twice daily, increased if necessary up to 1 g twice daily.

Side effects: Aggression, agranulocytosis, appetite decreased, blood disorder, bone marrow disorders, concentration impaired, depression, diarrhoea, dizziness, drowsiness, erythema nodosum, fatigue, gastrointestinal discomfort, generalised tonic-clonic seizure, headache, hiccups, leucopenia, libido increased, lupus-like syndrome, mood altered, movement disorders, nausea, nephrotic syndrome, oral disorders, psychosis, rash, sleep disorders, Stevens-Johnson syndrome, suicidal behaviours, vaginal haemorrhage, vision disorders, vomiting, and weight decreased.

Contraindications: Hypersensitivity.

Caution: Avoid in acute porphyria. The drug should be used in lactating mothers only if the benefits clearly outweigh the risks.

PHENOBARBITONE

Presentation: Tablet containing 15mg, 30mg phenobarbitone. Syrup containing 15mg/5ml phenobarbitone. An injection containing 200mg/1ml.

Indications: All forms of epilepsy except absence seizures; status epilepticus.

Administration: Oral, 60 - 180mg at night. Intramuscular injection, 200mg repeated after 6 hours if necessary.

Children:

Oral, 5.8mg/ kg daily. Intramuscular injection 15mg/kg.

Status epilepticus, (dilute injection 1 in 10 with water for injection) 10mg/kg at a rate of not more than 10mg/minute, maximum 1g.

Side effects: Fatigue, listlessness, tiredness, depression, restlessness, insomnia, distractability, aggression, poor memory, decreased libido, impotence, folate deficiency, neonatal haemorrhage, hypocalcaemia and osteomalacia.

Caution: Elderly, debilitated, avoid long term usage in children, renal and hepatic impairment, respiratory depression, pregnancy and breastfeeding.

PHENYTOIN SODIUM

Presentation: Tablet containing 50mg phenytoin sodium. Capsule containing 25mg, 50mg, 100mg phenytoin sodium. Syrup containing 30mg/5ml phenytoin sodium. An injection containing 50mg/ml phenytoin sodium in 5ml ampoule.

Indications: All forms of epilepsy such as trigeminal neuralgia and status epilepticus except absence seizures.

Administration: Orally, Seizures; initially 3 - 4mg/kg daily or 150 - 300mg daily (as a single dose or in two divided doses) increased gradually as necessary; usual dose 200 - 500mg daily (exceptionally higher doses may be used). Maintainance dose 100mg every 6 - 8 hours, monitored by measurement of plasma concentration.

Children:

Initially 5mg/kg daily in 2 divided doses, usual dose ranges 4 - 8mg/kg daily (maximum 300mg).

Status epilepticus, by intravenous infusion 15 - 18mg/kg at a rate not exceeding 50mg/ minute as a loading dose.

Neonates 15 -20mg/kg at a rate of 1 - 3mg/ minute.

NOTE: Plasma concentration for optimum response 10- 20mg/litre (40 - 80micrpmpl/ litre). Preferably take with or after food.

Side effects: Anorexia, dyspepsia, nausea, vomiting, aggression, ataxia, cognitive impairment, depression, drowsiness, headache, nystagmus, paradoxical seizures, gum hypertrophy, coarse facies, hirsutism, megaloblastic anaemia, hypoglycaemia, osteomalacia, neonatal haemorrhage, Steven-Johnson syndrome, aplastic anaemia, thrombocytopenia, agranulocytosis, peripheral neuropathy, cardiovascular depression.

Contraindications: Active liver disease, family history of severe hepatic dysfunction.

Caution: Hepatic impairment.

SODIUM VALPROATE

Presentation: Tablet containing 200mg sodium valproate. Syrup containing 200mg/5ml sodium valproate.

Indications: Primary generalised epilepsies,
Administration: Orally, initially 600mg daily given in 2 divided doses, preferably after food, increasing by 200mg/ day at 3-day intervals to a maximum of 2.5g daily in divided doses, usual maintenance 1 - 2g daily (20 - 30mg/kg daily). By intravenous injection (when oral valproate is not possible) over 3 - 5 minutes 400 - 800mg (up to 10mg/kg) followed by intravenous infusion up to maximum 2.5g daily.

Children:

Up to 20kg, initially 20mg/kg daily in divided doses, may be increased provided plasma concentrations are monitored in partial seizures, and prophylaxis of febrile convulsions. (above 40mg/kg also monitor clinical chemistry and haematological parameters).

Over 20kg, initially 400mg daily in divided doses increased until control (usually 20 - 30mg/kg daily) maximum 35mg/kg daily.

By intravenous injection, usually 20 - 30mg/ kg daily.

Side effects: Anorexia, dyspepsia, nausea, vomiting, hair loss, rash, peripheral oedema, drowsiness and tremors.

Contraindications: All active liver diseases and family history of severe hepatic dysfunction, the first trimester of pregnancy.

Presentation: Tablet containing 500mcg, 2mg Clonazepam. Injection containing 1mg/1ml Clonazepam.

Indications: Myoclonic and generalised tonic-clonic seizures, status epilepticus.

Administration: 1mg (elderly 500mcg) initially at night for 4 nights, increased over 2 - 4 weeks to a usual maintenance dose of 4 - 8mg daily in divided doses.

Children:

Up to 1-year 250mcg increased as above to 0.5 to 1mg.

1- 5 years 250mcg increased to 1 - 3mg.

5 - 12 years 500mcg increased to 3 - 6mg.

Side effects: Fatigue, dizziness, drowsiness (may affect the performance of skilled tasks such as driving), ataxia, irritability, aggression, hyperkinesia, hypersalivation, weight gain, muscle hypotonia.

Contraindications: Respiratory depression and acute pulmonary insufficiency.

Caution: Renal, hepatic and respiratory disease, pregnancy and breastfeeding, elderly and debilitated, porphyria, avoid sudden withdrawal.

Second Generation

GABAPENTINE

Presentation: Tablet containing 100mg, 300mg, 400mg and solution containing 250mg/5ml.

Indications: Adjunctive treatment of focal seizures with or without secondary generalisation, monotherapy for focal seizures with or without secondary generalisation, peripheral neuropathic pain, menopausal symptoms particularly hot flushes in women with breast cancer, Oscillopsia in multiple sclerosis, spasticity in multiple sclerosis, muscular symptoms in motor neurone disease

Administration: *Adjunctive treatment of focal seizures with or without Secondary generalization/Monotherapy for focal seizures with or without secondary generalization::* Adult; Initially 300 mg once daily on day 1, then 300 mg twice daily on day 2, then 300 mg 3 times a day on day 3, alternatively initially 300 mg 3 times a day on day 1, then increased in steps of 300 mg every 2–3 days in 3 divided doses, adjusted according to response; usual dose 0.9–3.6 g daily in 3 divided doses (max. per dose 1.6 g 3 times a day)

Peripheral neuropathic pain: Adult: Initially 300 mg once daily on day 1, then 300 mg twice daily on day 2, then 300 mg 3 times a day on day 3, alternatively initially 300 mg 3 times a day on day 1, then increased in steps of 300 mg every 2–3 days in 3 divided doses, adjusted according to response; maximum 3.6 g per day.

Menopausal symptoms, particularly hot flushes, in women with breast cancer: Adult; 300 mg 3 times a day, initial dose should be lower and titrated up over three days.

Oscillopsia in multiple sclerosis: Adult; Initially 300 mg once daily, then increased in steps of 300 mg, every 4–7 days, adjusted according to response; usual maximum 900 mg 3 times a day.

Spasticity in multiple sclerosis/ Muscular symptoms in motor neuron disease: Adult; Initially 300 mg once daily for 1–2 weeks, then

300 mg twice daily for 1–2 weeks, then 300 mg 3 times a day for 1–2 weeks, alternatively initially 100 mg 3 times a day, then increased in steps of 100 mg 3 times a day, every 1–2 weeks, adjusted according to response; usual maximum 900 mg 3 times a day.

Children:

6–11 years: 10 mg/kg once daily (max. per dose300 mg) on day 1, then 10 mg/kg twice daily (max. per Dose 300 mg) on day 2, then 10 mg/kg 3 times a day (Max. per dose 300 mg) on day 3; usual dose25–35 mg/kg daily in 3 divided doses, some childrenMay not tolerate daily increments; longer intervals (upto weekly) may be more appropriate, daily dosemaximum to be given in 3 divided doses; maximum 70 mg/kg per day.

12–17 years: Initially 300 mg once daily on day 1, then 300 mg twice daily on day 2, then 300 mg 3 times a day on day 3, OR alternatively, initially 300 mg 3 times a day on day 1, then increased in steps of 300 mg every2–3 days in 3 divided doses, adjusted according to response; usual dose 0.9–3.6 g daily in 3 divided doses (max. per dose 1.6 g 3 times a day), some children may not tolerate daily increments; longer intervals (up toweekly) may be more appropriate.

Side effects: Ataxia, dizziness, drowsiness, somnolence, fatigue, diplopia, nystagmus, tremor, back pain, constipation, depression, dry mouth, myalgia, peripheral oedema.

Contraindications: Hypersensitivity.

Caution: Anaphylaxis and angioedema reported after first dose or at any time during treatment; CNS depression, respiratory depression.

LAMOTRIGINE

Presentation: Tablet containing 25mg and 100mg.

Indications: Monotherapy of focal seizures, monotherapy of primary and secondary generalised tonic-clonic seizures, adjunctive therapy of focal seizures with valproate, adjunctive therapy of primary and secondary, generalised tonic-clonic seizures with valproate, adjunctive therapy of seizures associated with Lennox Gastaut syndrome with valproate, adjunctive therapy of focal seizures (with enzyme inducing drugs) without valproate, adjunctive therapy of primary and secondary generalised tonic-clonic seizures (with enzyme inducing drugs) without valproate, adjunctive therapy of seizures associated with Lennox Gastaut syndromes (with enzyme inducing drugs) without valproate, monotherapy or adjunctive therapy of bipolar disorder (without enzyme inducing drugs) without valproate, adjunctive therapy of bipolar disorder with valproate.

Administration: *Monotherapy of seizures associated with LennoxGastaut syndrome:* Adult; initially 25 mg once daily for 14 days, then increased to 50 mg once daily for further 14 days, thenincreased in steps of up to 100 mg every 7–14 days; maintenance 100–200 mg daily in 1–2 divided doses; increased if necessary up to 500 mg daily, dose titrationshould be repeated if restarting after interval of morethan 5 days.

Adjunctive therapy of focal seizures with valproate Adjunctive therapy of primary and secondary generalised tonic-clonic seizures with valproate Adjunctive therapy of seizures associated with LennoxGastaut syndrome with valproate: Adult; initially 25 mg once daily on alternate days for14 days, then 25 mg once daily for further 14 days, then increased in steps of up to 50 mg every 7–14 days; maintenance 100–200 mg daily in 1–2 divided doses, dose titration should be repeated if restarting after interval of more than 5 days

Monotherapy or adjunctive therapy of bipolar disorder (without enzyme inducing drugs) without valproate: Adult; Initially 25 mg once daily for 14 days, then 50 mg daily in 1–2 divided doses for further 14 days, then 100 mg daily in 1–2 divided doses for further 7 days; maintenance 200 mg daily in 1–2 divided doses, patients stabilised on lamotrigine for bipolar disorder may require dose adjustments if other drugs are added to or withdrawn from their treatment regimens dose titration should be repeated if restarting after interval of more than 5 days; maximum 400 mg per day.

Adjunctive therapy of bipolar disorder with valproate: Adult; Initially 25 mg once daily on alternate days for 14 days, then 25 mg once daily for further 14 days, then 50 mg daily in 1–2 divided doses for further 7 days; maintenance 100 mg daily in 1–2 divided doses, patients stabilised on lamotrigine for bipolar disorder may require dose adjustments if other drugs are addedto or withdrawn from their treatment regimens dose titration should be repeated if restarting after interval of more than 5 days; maximum 200 mg per day

Adjunctive therapy of bipolar disorder (with enzyme inducing drugs) without valproate: Adult; Initially 50 mg once daily for 14 days, then 50 mg twice daily for further 14 days, then increased to 100 mg twice daily for further 7 days, then increased to 150 mg twice daily for further 7 days; maintenance 200 mg twice daily, patients stabilised on lamotrigine for bipolar disorder may require dose adjustments if other drugs are added to or withdrawn from their treatment regimens dose titration should be repeated if restarting after interval of more than 5 days

Children:

Monotherapy of seizures associated with LennoxGastaut syndrome:

12–17 years: Initially 25 mg once daily for 14 days, then increased to 50 mg once daily for further 14 days, then increased in steps of up to 100 mg every7–14 days; maintenance 100–200 mg daily in1–2 divided doses; increased if necessary up to 500 mg daily, dose titration should be repeated if restarting after interval of more than 5 days

Adjunctive therapy of focal seizures with valproate Adjunctive therapy of primary and secondary generalised tonic-clonic seizures with valproate Adjunctive therapy of seizures associated with LennoxGastaut syndrome with valproate:

12–17 years: Initially 25 mg once daily on alternatedays for 14 days, then 25 mg once daily for further14 days, then increased in steps of up to 50 mg every 7–14 days; maintenance 100–200 mg daily in 1–2 divided doses, dose titration should be repeated ifrestarting after interval of more than 5 days.

2–11 years (body-weight 13 kg and above): Initially 150 mcg/kg once daily for 14 days, then 300 mcg/kg once daily for further 14 days, then increased in steps of up to 300 mcg/kg every 7–14 days; maintenance 1–5 mg/kg daily in 1–2 divided doses, dose titration should be repeated if restarting after interval of more than 5 days; maximum 200 mg per day.

2–11 years (body-weight up to 13 kg): Initially 2 mg once daily on alternate days for first 14 days, then 300 mcg/kg once daily for further 14 days, thenincreased in steps of up to 300 mcg/kg every7–14 days; maintenance 1–5 mg/kg daily in 1–2 divided doses, dose titration should be repeated ifrestarting after interval of more than 5 days; maximum200 mg per day.

Side effects: Aggression, agitation, arthralgia, diarrhoea, dizziness, drowsiness, dry mouth, fatigue, headache, irritability, nausea, pain, skin rashes, steven Johnson syndrome, sleep disorders, tremor, vomiting, alopecia, movement disorders, vision disorders, confusion, conjunctivitis, disseminated intravascular coagulation, facial oedema, fever, hallucination, hepatic disorders, lupus-like syndrome, lymphadenopathy, meningitis, aseptic, multi organ failure, nystagmus, seizure, severe cutaneous reactions.

Contraindications: Hypersensitivity

Caution: Use with caution in renal impairment and hepatic impairment; dose adjustments may be necessary, risk of serious rash

LEVETIRACETAM

Presentation: Tablet containing 250mg, 500mg, 750mg and 1000mg. Solution for injection containing 100mg/ml, oral suspension containing 500mg/5ml.

Indications: Partial onset seizures, primary generalised tonic clonic seizures and myoclonic seizures

Administration:

Myoclonic Seizures: Adult; Immediate-release 500 mg IV/PO every 12hours; may

increase in the second week by 500 mg/dose to recommended dose of 1500 mg every 12 hours.

Partial Onset Seizure: Adult; immediate-release 500 mg PO 12hourly; may increase weekly by 500 mg/dose; not to exceed 3000 mg/day.

Extended-release 1000 mg PO once Daily; may increase weekly by 1000 mg/day; not to exceed 3000 mg/day

IV: 500 mg 12hourly; may increase weekly by 500 mg/dose; not to exceed 3000 mg/day.

Primary Generalized Tonic-Clonic Seizures: Adult; Immediate-release 500 mg IV/PO 12 hourly; may increase every 2 weeks by 500 mg/dose to recommended dose of 1500 mg every 12 hourly

Children:

Myoclonic Seizures:

Older than 12 years; 500 mg PO every 12 hours; increase by 500 mg every 12 hours per week to recommended dose of 1500 mg every 12 hours.

Partial Onset Seizure: Immediate release (1-6 months): 7 mg/kg PO every 12 hours; increase every 2 weeks by increments of 7 mg/kg every 12 hours to recommended dose of 21 mg/kg every 12 hours

6 months-4 years: 10 mg/kg PO every 12hours, increase every 2 weeks in increments of 10 mg/kg 12 hourly to recommended dose of 25 mg/kg 12hourly.

4-16 years: 10 mg/kg PO 12hourly; increase by 10 mg/kg/dose every 2 weeks to 30 mg/kg 12 hourly.

>16 years: 500 mg PO 12hourly, increase by 500 mg 12hourly every 2weeks to recommended dose of 1500 mg 12hourly.

Extended release (for children older than 12 years): 1000 mg PO once Daily initially; may adjust dose by 1000 mg increments every 2 weeks to a maximum of 3000 mg/day

Primary Generalized Tonic-Clonic Seizures:

Immediate release (6-16 years): 10 mg/kg PO 12 hourly; increase every 2 weeks by 10 mg/kg/dose to recommended dose of 30 mg/kg 12 hourly.

>16 years: 500 mg PO 12 hourly, increase by 500 mg 12 hourly every 2 weeks to recommended dose of 1500 mg every 12 hourly.

Side effects: Asthenia, headache , infection, increased blood pressure in children < 4 years, somnolence, drowsiness, fatigue, anorexia, weakness, nasopharyngitis, cough, viral infection, asthma , dizziness, nervousness, amnesia, anxiety, ataxia depression, hostility, paresthesia, sinusitis, diplopia amblyopia , conjunctivitis, albuminuria, abnormal hepatic function tests, dyskinesia, eczema, neutropenia, decreased hematocrit, leukopenia, suicidal tendencies, hepatitis, pancreatitis, bone marrow suppression, epidermal necrolysis.

Contraindications: Hypersensitivity.

Caution: Serious dermatological reactions including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis, haematological abnormalities including decreases in white blood cell (WBC), neutrophil, and red blood cell (RBC) counts; decreases in hemoglobin and hematocrit; and increases in eosinophil counts; cases of agranulocytosis, pancytopenia, and thrombocytopenia, nonpsychotic behavioral symptoms (eg, aggression, agitation, anger, anxiety, apathy, depersonalization, lability, hostility, hyperkinesis, irritability, nervousness, neurosis, and personality disorder).

3.6 Hypnotics and Anxiolytics

Prescribing of hypnotics and anxiolytics is widespread but dependence (physical and psychological) and tolerance occurs. This may lead to difficulty in withdrawing the drug after the patient has been taking it for a few weeks. Hypnotics and anxiolytics should not be prescribed indiscriminately and should never be used for long term treatment. They should be restricted to short courses to alleviate acute conditions after causal factors have been established. Benzodiazepines are the most commonly used anxiolytics and hypnotics.

PARADOXICAL EFFECTS

An increase in hostility and aggression may be observed in patients taking benzodiazepines. The effects will range from talkativeness and excitement to aggressive and antisocial acts. Adjustment of dose either upwards or downwards usually effectively controls these acts.

Hypnotics and anxiolytics impair judgement. This affects the ability to drive or perform skills requiring concentration. Withdrawal of these Medicines should be gradual as abrupt withdrawal may cause withdrawal effects such as confusion, toxic psychosis or delirium.

3.6.1 Hypnotics

Before prescribing a hypnotic, the cause of insomnia should be established and the causative factors should be attended to appropriately. Hypnotics should not be prescribed for more than 3 weeks (preferably 1 week) in short term insomnia while one or two doses are adequate in transient insomnia.

Hypnotics should never be prescribed in children except in cases such as in night terrors and sleepwalking. They should also be avoided in the elderly, as they are more at risk of ataxia and confusion.

CHLORMETHIAZOLE

Presentation: Capsule containing 192mg chlormethiazole base. Syrup containing 250mg/5ml chlormethiazole edisylate (1 capsule = 5ml syrup). Intravenous infusion containing 8mg/ ml chlormethiazole edisylate.

Indications: Hypnosis (especially useful in the elderly as it does not give hangover). It is also used in status epilepticus and sedation during regional anaesthesia. **Administration:** Oral, severe insomnia in the elderly; 1 – 2 capsules or 5 – 10ml syrup at bedtime.

Side effects: Nasal congestion and irritation, conjunctival irritation, headache, rarely paradoxical excitement, confusion, dependence, gastro-intestinal disturbances, rash.

Contraindications: Acute pulmonary insufficiency, alcohol-dependent patients who are continuing with alcohol drinking.

Caution: Cardiac and respiratory disease, renal and hepatic insufficiency, history of drug abuse, marked personality disorders.

LORAZEPAM

Presentation: Tablet containing 1mg Lorazepam. Injection containing 4 mg/ml Lorazepam.

Indications: Short-term use in anxiety or insomnia; status epilepticus; peri-operative.

Administration: By mouth, anxiety, 1–4 mg daily in divided doses; *Elderly* (or debilitated) half adult dose Insomnia associated with anxiety, 1–2 mg at bedtime; By intramuscular or slow intravenous injection (into a large vein), acute panic attacks, 25–30 mcg/kg (usual range 1.5–2.5 mg), repeated every 6 hours if necessary.

Note: Only use the intramuscular route when oral and intravenous routes not possible. For intramuscular injection, it should be diluted with an equal volume of water for injections or physiological saline.

Children: NOT recommended.

Sideeffects: See under Diazepam

Contra-indications: See under Diazepam

Cautions: See under Diazepam; short-acting; when given parenterally, facilities for managing respiratory depression with mechanical ventilation must be at hand.

NITRAZEPAM

Presentation: Tablet containing 5mg Nitrazepam. Oral suspension containing 2.5mg/5ml Nitrazepam.

Indications: Insomnia (short term).

Administration: *Adult*; 5 – 10mg taken 30 minutes before bedtime. *Elderly* or debilitated; 2.5 – 5mg. Not recommended in children.

Side effects: Drowsiness, light-headedness the following day, confusion and ataxia (particularly in the elderly).

Caution: Should never be used for long term treatment, respiratory disease, muscle weakness, history of drug abuse, pregnancy, breastfeeding, personality disorders, hepatic and renal impairment, porphyria. Drowsiness may persist the following day and hence affect the performance of skilled tasks such as driving.

Contraindications: Respiratory depression, pulmonary insufficiency, myasthenia gravis, severe hepatic impairment.

3.6.2 Anxiolytics

Anxiolytics are widely prescribed and are useful in alleviating anxiety states. However, their use in most of these instances is unjustified. They should not be used to treat depression or chronic psychosis. Treatment should be limited to the lowest possible dose and for the shortest possible time. Dependence occurs especially in patients with a history of drug or alcohol abuse and those with marked personality disorders.

CHLORDIAZEPOXIDE

Presentation: Tablet or capsule containing 5mg, 10mg, 20mg chlordiazepoxide hydrochloride.

Indications: Anxiety (short term use), adjunct in acute alcohol withdrawal.

Administration: *Anxiety;* 10mg 3 times daily increased to 60 – 100mg daily in divided doses if necessary. *Elderly and debilitated:* half adult dose.

Alcohol withdrawal syndrome; first day 100mg in divided doses; day two 80mg; day three 60mg; day four 40mg; day five 20mg; day six 10mg.

Not recommended in children.

Side effects: Drowsiness, light-headedness the following day, confusion and ataxia (especially in the elderly), dependence, amnesia may occur, headache, vertigo, hypotension, gastrointestinal disturbances.

Contraindications: Respiratory depression, acute pulmonary insufficiency, severe hepatic impairment, chronic psychosis, should not be used alone in depression or anxiety with depression.

Caution: Respiratory disease, muscle weakness, history of drug or alcohol abuse, pregnancy and breastfeeding, hepatic and renal impairment, marked personality disorders, avoid prolonged treatment and abrupt withdrawal thereafter.

DIAZEPAM

Presentation: Tablet containing 2mg, 5mg and 10mg Diazepam. Oral solution containing 2mg/5ml Diazepam. Injection (solution) containing 5mg/ ml Diazepam (do not dilute except for intravenous infusion). Injection (emulsion) containing 5mg/ml Diazepam.

Indications: Short term treatment of anxiety or insomnia, adjunct in acute alcohol withdrawal, psychiatric disorders associated with anxiety, febrile convulsions, status epilepticus.

Administration: *Adult*, anxiety, oral; 2mg 3 times daily increased if necessary to 15 – 30mg daily in divided doses. *Elderly* or debilitated; half adult dose. Insomnia associated with anxiety; 5 – 15mg daily at bedtime. By intramuscular or slow intravenous injection (into the large vein at a rate of not more than 5mg/ minute, for severe acute anxiety, acute panic attacks; 10mg repeated if necessary after not less than 4 hours.

Status epilepticus; *Adult;* 10mg intravenously if fits continue to give further 10mg over 30 seconds.

Children:

Night terrors; 1 – 5mg orally at bedtime.

Status epilepticus; Intravenously titrate up to 1mg/kg (maximum 10mg under 3 years, 15mg over 3 years).

Rectally, 5mg infants 6 months to 3years; more than 3 years 10mg.

Side effects: Drowsiness and light-headedness the following day, confusion, ataxia, dependence, paradoxical increase in aggression.

Contraindications: Respiratory depression, acute pulmonary insufficiency, severe hepatic impairment, phobic and obsessional conditions, not to be used alone in depression or anxiety with depression.

Caution: Special precaution in intravenous injection because of the risk of respiratory depression.

ALPRAZOLAM

Presentation: Tablet containing 0.25 mg and 0.5mg

Indications: Short term use in anxiety.

Administration: *Adult*; 250–500 mcg 3 times a day, increased if necessary up to 3 mg daily, for debilitated patients, use elderly dose.

Elderly; 250 mcg 2–3 times a day, increased if necessary up to 3 mg daily.

Side effects: Concentration impaired, constipation, dermatitis, dry mouth, memory loss, movement disorders, sexual dysfunction, weight changes, menstruation irregularities, angioedema, autonomic dysfunction, hepatic disorders, hyperprolactinaemia, peripheral oedema, photosensitivity reaction.

Contraindications: Respiratory depression

Cautions: Breastfeeding, renal impairment, muscle weakness, organic brain changes.

3.7 Medicines used in substance abuse and dependence

Sedatives are used to reduce symptoms of alcohol withdrawal and if administered promptly can prevent further development of more serious symptoms, like seizures and delirium tremens. Benzodiazepines and Chlormethiazole are the most widely used. To prevent dependence these Medicines should only be used for short periods.

Once the initial acute withdrawal symptoms have been treated, long-term abstinence has to be maintained. Disulfiram can be used as an adjunct to treat alcohol dependence. A patient who takes alcohol after taking adequate doses of disulfiram will experience severe and unpleasant reactions, which it is hoped, will deter the patient from further ingesting alcohol. These include flushing of the face, palpitations, tachycardia, throbbing headache, nausea and vomiting. With large doses of alcohol, the following will also occur arrhythmias, hypotension and collapse. It must be noted that even small amounts of alcohol contained in some medications may be enough to precipitate a reaction.

CLONIDINE

Presentation: Solution for injection containing 100mcg/ml,500mcg/ml. Patch containing 0.1mg/day, 0.2mg/day, 0.3mg/day. Tablets containing 0.1 mg, 0.2mg and 0.3mg.

Indications: Hypertension, cancer pain, ethanol withdrawal, smoking cessation, opioid withdrawal, restless leg syndrome, ADHD.

Administration:

Hypertension: immediate-release tablets;0.1mg every 12 hrs not to exceed 2.4mg/day.

Cancer pain: not relieved by opioids; 30mcg/hr.

Ethanol withdrawal: 0.3-0.6 mg PO every 6hrs.

For smoking cessation: PO administration 0.1mg/day; increase by 0.1mg/day to 0.15-0.75mg/day and for patches 100-200mcg/day every 7 days.

Restless legs syndrome: 100-300mcg PO 2 hours before bedtime, up to 900mcg.

Opioid withdrawal: 0.1-0.3 mg every 4-6 hrs, increase by 0.1mg/day to 0.15-0.75mg/day. For a patch 100- 200mcg/day every 7 days, initiate 0.1-0.3 mg PO every 4-6hrs for the first two days. Psychosis; 0.4-1.4mg/day in divided doses.

Children:

For hypertension <immediate release and transdermal patch; safety and efficacy not established.

ADHD;

< *6 years old* not established;

6 years and above: 0.1mg/day and not to exceed 0.4mg/day.

Side effects: Skin reactions, dry mouth, somnolence, fatigue, dizziness, hypotension, anxiety.

Contraindications: Hypersensitivity.

Caution: Hemodynamically unstable patients, watch out for hypotension, do not discontinue suddenly, patch may need to be removed in cases of erythema.

NALTREXONE

Presentation: Implant containing 765mg, 1000mg, 1200mg and 1800mg. Tablet containing 50mg and solution for injection containing 380mg.

Indications: Alcohol dependence and opioid dependence

Administration:

Implant: implant is implanted under the abdominal skin and releases a standard daily amount of naltrexone in the blood stream. Implant lasts to 2-6 months depending on the naltrexone content

Opioid Dependence: Prevention of relapse after opioid detoxification; to be used only after patient has been opioid-free for 7-10 days and after negative naloxone challenge (no symptom withdrawal after naloxone administration). *Orally;* 25 mg initially, then observation for 1 hr, then 50 mg once daily starting on day 2; flexible dosing regimens can be employed to accommodate patient convenience or ensure compliance. *By injection;* 380 mg in gluteal muscle every 4 weeks for maintenance of abstinence

Alcohol Dependence: Treatment in patients who have been able to abstain from alcohol in outpatient settings before treatment initiation. *Orally;* 50 mg once daily for ≤12 weeks. By injection; 380 mg in gluteal muscle every 4 weeks for maintenance of abstinence.

Side effects: Injection site reaction, nausea, headache, decreased appetite, insomnia, vomiting, diarrhoea, dizziness, upper respiratory tract infection, anxiety, arthralgia, pharyngitis, depression, muscle cramps, dry mouth, dyspnoea, hepatocellular injury.

Contraindications: Patients who are on opioid analgesics; are opioid-dependent (eg, opioid agonists [methadone], opioid partial agonists [buprenorphine]); are in acute opioid withdrawal; have positive urine test for opioids or fail to pass naloxone challenge, hypersensitivity.

Caution: Depression, suicide, vulnerability to opioid overdose, risk of hepatotoxicity with increasing doses.

DIAZEPAM

Presentations: See 3.6.2

Indications: Acute alcohol withdrawal symptoms. For other indications see 3.6.2

Administration: 10mg repeated, if necessary, after not less than 4 hours.

Side effects: See 3.6.2

Caution: See 3.6.2

Contra-indications: See 3.6.2

MIDAZOLAM

Presentation: Solution for injection containing 1mg/ml.

Indications: Status epilepticus, febrile seizures, conscious sedation for procedures, premedication, sedation in combined anaesthesia, induction of anaesthesia, sedation of patient receiving intensive care, adjunct to antipsychotics for confusion and restlessness.

Administration: ***Adult;***

Status epilepticus: 10 mg IM stat

Conscious sedation for procedure: initially 2–2.5 mg, to be administered 5–10 minutes

before procedure at a rate of approximately 2 mg/minute, increased in steps of 1 mg if required, usual total dose is 3.5–5 mg; maximum 7.5 mg. *Elderly;* initially 0.5–1 mg, to be administered 5–10 minutes before procedure at a rate of approximately 2 mg/minute, increased in steps of 0.5–1 mg if required; maximum 3.5 mg.

Sedative in combined anaesthesia: Adult; 30–100 mcg/kg, repeated, if necessary, alternatively (by continuous intravenous infusion) 30–100 mcg/kg/hour. *Elderly;* Lower doses needed

Premedication: 70–100 mcg/kg IM, to be administered 20–60 minutes before induction OR 1–2 mg IV slowly, repeated if necessary, to be administered 5–30 minutes before procedure. *Elderly;* 25–50 mcg/kg, to be administered 20–60 minutes before induction OR 0.5 mg IV slowly, repeated if necessary, initial dose to be administered 5–30 minutes before procedure, repeat dose slowly as required

Sedation for patient needing intensive care: initially 30–300 mcg/kg, dose to be given in steps of 1–2.5mg every 2 minutes, then (by slow intravenous injection or by continuous intravenous infusion) 30–200 mcg/kg/hour, reduce dose (or reduce or omit initial dose) in hypovolaemia, vasoconstriction, or hypothermia, lower doses may be adequate if opioid analgesic also used.

Adjunct to antipsychotic for confusion and restlessness: initially 10–20 mg/24 hours, adjusted according to response by subcutaneous infusion. usual dose 20–60 mg/24 hours OR 5mg IV slowly stat dose.

Children: use buccal route and NOT IV

1–2 months: 300 mcg/kg (max. per dose2.5 mg), then 300 mcg/kg after 10 minutes (max. per dose 2.5 mg) if required

3–11 months: 2.5 mg, then 2.5 mg after 10 minutes if required

1–4 years: 5 mg, then 5 mg after 10 minutes if required

5–9 years: 7.5 mg, then 7.5 mg after 10 minutes if required

10–17 years: 10 mg, then 10 mg after 10 minutes if required.

Side effects: Vomiting, skin reactions, dry mouth, dyspnoea, hiccups, movement disorders, respiratory disorders, level of consciousness decreased, apnoea, bradycardia, cardiac arrest, constipation, physical assault, vasodilation, increased falls, saliva altered, thrombosis, angioedema, apnoea, bradycardia, cardiac arrest, constipation, drug abuse, drug withdrawal, seizure, embolism.

Contraindications: CNS depression, compromised airway, severe respiratory depression.

Caution: Cardiac disease, children, debilitated patients (reduce dose), hypothermia, hypovolaemia (risk of severe hypotension), neonates, risk of airways obstruction and hypoventilation in children under 6 months (monitor respiratory rate and oxygen saturation), vasoconstriction

ACAMPROSATE

Presentation: Tablet containing 333mg.

Indications: Maintenance of abstinence in alcohol-dependent patients.

Administration: *Adult 18–65 years (body weight up to 60 kg):* 666 mg once daily at breakfast and 333 mg at midday and at night.

Adult 18–65 years (body weight 60 kg and above): 666 mg 3 times a day.

Side effects: Abdominal pain, diarrhoea, flatulence nausea, sexual dysfunction, skin reactions, vomiting.

Contraindications: Pregnancy, breastfeeding, renal impairment, hypersensitivity.

Caution: Continued alcohol use, hepatic impairment.

NALOXONE

Presentation: Solution for injection containing 0.042mg/2ml, and 0.42mg/ml buprenorphine/naloxone, combination tablet containing 2mg buprenorphine and 0.5mg naloxone. Solution for injection containing 0.4mg/ml, 1mg/ml naloxone.

Indications: Acute opioid overdose–high-dose regimen, Opioid overdose–low-dose regimen, Opioid overdose in non-medical and medical settings.

Administration:

Acute opioid overdose-highdose regimen (when rapid titration with naloxone is necessary to reverse potentially life-threatening effects). Adult: Initially 400 mcg, then 800 mcg for up to 2 doses at 1-minute intervals if no response to preceding dose, then increased to 2 mg for 1 dose if still no response (4 mg dose may be required in seriously poisoned patients), then review diagnosis.

Opioid overdose–low-dose regimen [when there is risk of acute withdrawal, or when a continued therapeutic effect is required (e.g. postoperative use, palliative care)

Adult: Initially 100–200 mcg, then 100 mcg for up to 2 doses at 1-minute intervals, if no response to preceding dose, continue titrating up to a max. of 2mg until adequate response achieved. If still no response, give a further 2 mg dose (4mg dose may be required in seriously poisoned patients), then review diagnosis

Opioid overdose in non-medical and medical settings

Adult: 400 mcg every 2–3 minutes, each dose given in subsequent resuscitation cycles if patient not breathing normally, continue until consciousness regained, breathing normally, medical assistance available, or contents of syringe used up; to be injected into deltoid region or anterolateral thigh.

Children

Acute opioid overdose-highdose regimen (when rapid titration with naloxone is necessary to reverse potentially life-threatening effects).

12–17 years: Initially 400 mcg, then 800 mcg for up to 2 doses at 1-minute intervals if no response to preceding dose, then increased to 2 mg for 1 dose if still no response (4mg dose may be required in seriously poisoned patients), then review diagnosis.

1 month–11 years: Initially 100 mcg/kg (max. per dose 2 mg), if no response, repeat at intervals of 1 minute to a total max. of 2 mg, then review diagnosis.

Opioid overdose–low-dose regimen [when there is risk of acute withdrawal, or when a continued therapeutic effect is required

12–17 years: Initially 100–200 mcg, then 100 mcg for up to 2 doses at 1minute intervals if no response to preceding dose, continue titrating up to a max. of 2mg until adequate response achieved. If still no response, give a further 2 mg dose (4mg dose may be required in seriously poisoned patients), then review diagnosis.

1 month–11 years: Initially 1–10 mcg/kg (max. per dose 200 mcg), if no response, repeat at intervals of 1 minute up to 5 times, if no response then give a single dose of 100 mcg/kg (max. dose 2 mg) then review diagnosis if still no response.

Note: further doses may be required if respiratory function deteriorates following initial response, intravenous administration has a more rapid onset of action, doses may be given by intramuscular route but only if intravenous route is not feasible.

Side effects: Arrhythmias, dizziness, headache, hypertension, hypotension, nausea, vomiting, diarrhoea, dry mouth, hyperhidrosis, hyperventilation, tremor, cardiac arrest, erythema multiforme, pulmonary oedema.

Contraindications: hypersensitivity

Cautions: Cardiovascular disease or those receiving cardiotoxic drugs (serious adverse cardiovascular effects reported), chronic opioid use (risk of acute withdrawal), maternal chronic opioid use (risk of acute withdrawal in newborn), palliative care (risk of returning pain and acute withdrawal), post-operative use (risk of returning pain), pregnancy.

METHADONE

Presentation: Solution for injection containing 10mg/ml, 50mg/ml; Tablet containing 5mg, 10mg; Oral solution containing 1mg/ml, 10mg/ml and 20mg/ml.

Indications: Opioid dependence, severe pain and cough in palliative care

Administration: *Severe pain; Adult:* 5–10 mg PO/SC/IM every 6–8 hours, adjusted according to response, on prolonged use not to be given more frequently than every 12 hours.

Children: Not recommended for use in children

Adjunct in treatment of opioid dependence; Adult: Initially 10–30 mg PO daily, increased in steps of 5–10 mg daily if required until no signs of withdrawal nor evidence of intoxication, dose to be increased in the first week, then increased every few days as necessary up to usual dose, maximum weekly dose increase of 30 mg; usual dose 60–120 mg daily.

Adjunct in treatment of opioid dependence if tolerance low or not known

Adult: Initially 10–20 mg PO daily, increased in steps of 5–10 mg daily if required until no signs of withdrawal nor evidence of intoxication, dose to be increased in the first week, then increased every few days as necessary up to usual dose, maximum weekly dose increase of 30 mg; usual dose 60–120 mg daily.

Adjunct in treatment of opioid dependence if tolerance high (under expert supervision)

Adult: Initially up to 40 mg PO daily, increased in steps of 5–10 mg daily if required until no signs of withdrawal nor evidence of intoxication, dose to be increased in the first week, then increased every few days as necessary up to usual dose, maximum weekly dose increase of 30 mg; usual dose 60–120 mg daily

Cough in palliative care; Adult: 1–2 mg every 4–6 hours PO reduced to 1–2 mg twice daily, use twice daily frequency if prolonged use.

Side effects: Asthma exacerbated, dry eye, dysuria, hyperprolactinaemia, hypothermia, menstrual cycle irregularities, mood altered, nasal dryness, QT interval prolongation, galactorrhoea, increased intracranial pressure, biliary spasm, muscle rigidity, oedema, restlessness, sexual dysfunction, sleep disorder, ureteral spasm, neonatal withdrawal syndrome.

Contraindications: Phaeochromocytoma, children

Cautions: Patients with risk factors for QTc prolongation such as history of cardiac conduction abnormalities, family history of sudden death, heart or liver disease, electrolyte abnormalities, or concomitant treatment with drugs that can prolong QT interval; patients requiring more than 100mg daily should also be monitored.

BUPRENORPHINE

Presentation: Tablet containing 200mcg, 400mcg, 2mg, 8mg; injection containing 300mcg/ml; transdermal patch 5mcg/hr.

Indications: Moderate to severe pain, premedication, intra-operative analgesia and adjunct in the treatment of opiod dependence

Administration:

Moderate to severe pain; By sublingual administration

Adult: 200–400 mcg every 6–8 hours*; By intramuscular injection or slow intravenous injection:* 300–600 mcg every 6–8 hours.

Premedication: Adult:

By sublingual administration: 400 mcg

By intramuscular injection; 300 mcg

Intra-operative analgesia

By slow IV injection; Adult: 300–450 mcg

Adjunct in the treatment of opioid dependence

By sublingual injection; Adult: Initially 0.8–4 mg for 1 dose on the first day, adjusted in steps of 2–4 mg daily if required; usual dose 12–24 mg daily; maximum 32 mg per day

By mouth using oral psyphilate; Adult: Initially 2 mg daily, followed by 2–4 mg if required on day one, adjusted in steps of 2–6 mg daily if required, for adjustment of dosing interval following, stabilisation, consult product literature; maximum 18 mg per day

Children:

By sublingual administration:

Body-weight 50 kg and above: 200–400 mcg every 6–8 hours

Body-weight 37.5–50 kg: 200–300 mcg every 6–8 hours.

Body-weight 25–37.5 kg: 100–200 mcg every 6–8 hour.

Body-weight 16–25 kg: 100 mcg every 6–8 hours.

By intramuscular injection or slow intravenous injection:

12–17 years: 300–600 mcg every 6–8 hours

Child 6 months–11 years: 3–6 mcg/kg every 6–8 hours (max. per dose 9 mcg/kg.

Side effects: Anxiety, appetite decreased, depression, diarrhoea, dyspnoea, syncope, tremor, arthralgia, asthenia, asthma, gastrointestinal disturbance, hypersensitivity.

Contraindications: Hypersensitivity, significant respiratory depression, acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment, known or suspected gastrointestinal obstruction, including paralytic ileus.

Caution: Hepatitis B infection, hepatitis C infection, pre-existing liver enzyme abnormalities, nervous system abnormalities, fever or external heats, impaired consciousness.

3.8 Medicines used for the treatment of Nausea and Vomiting

Anti-emetics should only be prescribed when the cause of the vomiting is established. This is particularly important in children as the symptomatic relief may affect accurate diagnosis. They may not be necessary and may be harmful in cases where the cause of emesis can be treated. If nausea treatment is indicated, the choice of the drug will depend on the aetiology of the illness. Nausea in the first trimester of pregnancy does not require drug treatment. Occasionally when vomiting becomes severe an antihistamine may be required. If symptoms do not subside in 48-hours then specialist opinion must be sought.

DOMPERIDONE

Presentations: Tablet containing 10mg Domperidone maleate. Syrup containing 5mg/5ml Domperidone maleate.

Indications: Nausea and vomiting in gastrointestinal disorders and during treatment with cytotoxic medicines.

Administration: *Nausea and vomiting*, oral; 10 – 20mg every 4 – 8 hours. The maximum period of treatment is 2 weeks.

Children:

Nausea and vomiting following cytotoxic therapy or radiotherapy;

200 – 400mcg/kg body weight every 4 - 8 hours.

Side effects: Galactorrhoea, reduced libido, rashes and other allergic reactions, acute dystonic reactions.

Contraindications: Routine prophylaxis of postoperative vomiting or chronic administration.

Caution: Renal impairment, pregnancy and breastfeeding

ONDANSETRON

Presentation: Tablet containing Ondansetron hydrochloride 4 mg, Injection containing Ondansetron hydrochloride 2 mg/ml, Syrup containing sugar-free, strawberry-flavoured, Ondansetron hydrochloride 4 mg/5 ml, Suppositories containing Ondansetron 16 mg.
Indications: see under Dose.

Administration:

Moderately emetogenic chemotherapy or radiotherapy, adult: by mouth, 8 mg 1–2 hours before treatment; or by rectum, 16 mg 1–2 hours before treatment; or by intramuscular injection or slow intravenous injection, 8 mg immediately before treatment then by mouth, 8 mg every 12 hours for up to 5 days; or by rectum, 16 mg daily for up to 5 days;

Severely emetogenic chemotherapy, adult: by intramuscular injection or slow intravenous injection, 8mg immediately before treatment, where necessary followed by 2 further doses of 8 mg at intervals of 2–4 hours (or followed by 1 mg/hour by continuous intravenous infusion for up to 24 hours) then by mouth, 8 mg every 12 hours for up to 5 days or by rectum, 16 mg daily for up to 5 days; alternatively, by intravenous infusion over at least 15 minutes, 32 mg immediately before treatment or by rectum, 16 mg 1–2 hours before treatment then by mouth, 8 mg every 12 hours for up to 5 days or by rectum, 16 mg daily for up to 5 days.

Prevention of postoperative nausea and vomiting, adult: by mouth, 16 mg 1 hour before anaesthesia or 8mg 1 hour before anaesthesia followed by 8 mg at intervals of 8 hours for 2 further doses alternatively, by intramuscular or slow intravenous injection, 4 mg at induction of anaesthesia;

Treatment of postoperative nausea and vomiting, by intramuscular or slow intravenous injection, 4 mg.

Children:

Moderately and severely emetogenic chemotherapy or radiotherapy; by slow intravenous injection, 5 mg/ml immediately before chemotherapy then 4 mg by mouth every 12 hours for up to 5 days.

Prevention and treatment of postoperative nausea and vomiting Over 2 years, by slow intravenous injection, 100 mcg/kg (max. 4 mg) before, during, or after induction of anaesthesia

Side effects: Constipation, headache, flushing, injection site-reactions, hiccups, hypotension, bradycardia, chest pain, arrhythmias, movement disorders, seizures, dizziness, transient visual disturbances (very rarely transient blindness), suppositories may cause rectal irritation.

Caution: QT interval prolongation (avoid concomitant administration of Medicines that prolong QT interval); hepatic impairment, pregnancy, breast-feeding.

METOCLOPRAMIDE

Presentation: Tablet containing 10mg metoclopramide hydrochloride. Oral solution containing 5mg/5ml metoclopramide hydrochloride. An injection containing 5mg/ml metoclopramide hydrochloride.

Indications: Nausea and vomiting particularly in gastro-intestinal disorders and in treatment with cytotoxics or radiotherapy.

Administration: *Adult*: Oral or by intramuscular or intravenous injection; 10mg (5mg in those below 60kg) 3 times daily.

Children:

up to 1 year; 1mg twice daily

1 – 3 years; 1mg 2 – 3 times daily

3 – 5 years; 2mg 2 –3 times daily

5 – 9 years; 2.5mg 3 times daily.

9 – 14 years; 5mg 3 times daily.

Side effects: Diarrhoea, drowsiness, extrapyramidal effects especially in children and young adults.

Contraindications: Undiagonised nausea and vomiting especially in children and young adults.

Caution: Renal and hepatic impairment, elderly, children and young adults, pregnancy and breastfeeding, porphyria.

PROCHLORPERAZINE

Presentation: Tablet containing 5mg, 25mg prochlorperazine maleate.

Indications: Severe nausea, vomiting, vertigo.

Administration: A*dults*; 20mg initially, then 10mg after 2 hours. Prevention; 5 – 10mg 2 – 3 times daily.

Children: *(over 10kg only)*; 250mcg/kg body weight 2 – 3 times daily.

Side effects: Dry mouth, drowsiness, extrapyramidal effects may occur in children, young adults and the elderly.

Contraindications: Children less than 10kg, depression, coma caused by Central Nervous System depressants.

Caution: Liver dysfunction, cardiac insufficiency, epilepsy, pregnancy.

PROMETHAZINE

Presentation: Tablet containing 10mg, 25mg promethazine hydrochloride. Syrup containing 5mg/5ml promethazine hydrochloride. An injection containing 25mg/ml promethazine hydrochloride.

Indications: Nausea, vomiting, vertigo, allergies, pre-operative medication**.**

Administration: *Adult*; 20 – 50mg daily. Maximum 100mg daily.

Children:
Up to 2 years; not recommended
2 – 5 years; 5 – 15mg daily
5 – 10 years; 10 –25mg daily.

Side effects: Drowsiness.

Contraindications: Porphyria, severe hepatic disease. **Caution:** Epilepsy, hepatic disease, glaucoma.

TRIFLUOPERAZINE

Presentation: Tablet containing 1mg, 5mg trifluoperazine hydrochloride. Oral solution containing 5mg/5ml trifluoperazine hydrochloride.

Indications: Severe nausea and vomiting.

Administration: *Oral*; 2 – 4mg daily in divide doses, maximum 6mg daily.

Children:
3 – 5 years; up to 1mg daily.
6 – 12 years; up to 4mg daily.

Side effects: Extrapyramidal symptoms, drowsiness.

Contraindications: Bone marrow depression, coma caused by CNS depressants.

Caution: Cardiovascular and cerebrovascular disease, parkinsonism, epilepsy, respiratory disease, acute infections, pregnancy and breastfeeding, renal and hepatic impairment (avoid if severe), myasthenia gravis, elderly, children, avoid abrupt withdrawal.

3.9 Analgesics

Analgesics may be divided into those for mild or moderate pain and those for severe pain.

3.9.1 Non-opioid analgesics

The non-opioid medicines e.g. Acetylsalicylic acid and Paracetamol are more suitable for pain in musculoskeletal conditions whereas opioid analgesics are more suitable for severe visceral pain. Acetylsalicylic acid has anti-inflammatory properties and is an anti-pyretic. Gastric irritation may be a problem and this is minimised by taking it after food. Acetylsalicylic acid interacts with several other medicines such as other analgesics (NSAIDs), antacids, adsorbents, cytotoxics, diuretics, antiepileptics and anticoagulants (particularly its hazardous interaction with warfarin).

Paracetamol is similar in efficacy to acetylsalicylic acid but has weak anti-inflammatory activity. Overdose with paracetamol is of particular danger as it may cause hepatic damage, which may not be apparent for 4 to 6 days.

Anti-inflammatory analgesics are particularly useful in chronic disease accompanied by pain and inflammation. Other uses include dysmenorrhoea and pain caused by secondary tumours.

ACETYL SALICYLIC ACID (ASPIRIN)

Presentation: Tablet containing 75mg, 300mg Acetylsalicylic acid.

Indications: Mild to moderate pain, pyrexia, prophylaxis of cerebrovascular disease or myocardial infarction (secondary prevention of thrombotic cerebrovascular or cardiovascular disease), inflammatory conditions.

Administration:

Anti-inflammatory/analgesia; *Adults*; 300 – 900mg every 4–6 hours when necessary, maximum: 4g daily.

Secondary prevention of thrombotic cerebrovascular or cardiovascular disease; 75 – 300mg daily

After myocardial infarction; 150mg daily

Following bypass surgery; 75mg or 100mg daily (low dose).

Side effects: Gastrointestinal irritation, easy bleeding, bronchospasm and skin reaction in hypersensitive patients.

Contraindications: Gastro-intestinal ulceration, children under 12 years (except for juvenile arthritis) due to association with Reye's syndrome, breastfeeding, haemophilia and other bleeding disorders, history of hypersensitivity to aspirin and other NSAIDs includes those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or other NSAIDS, concurrent anticoagulant therapy.

Caution: Asthma, allergic disease, impaired renal or hepatic function, dehydration and pregnancy.

PARACETAMOL

Presentation: Tablet containing 100mg, 500mg Paracetamol; Syrup (paediatric) containing 120mg/5ml, 125mg/5ml Paracetamol.

Indications: Mild to moderate pain, pyrexia. As an alternative for patients who are sensitive to Acetylsalicylic acid.

Administration: *Adult;* 500mg to 1g every 4 – 6 hours., maximum 4g daily.

Children:

under 3 months (on doctors advise only): 10mg/kg body weight.

3 months-1 year; 60 – 120mg.

1–5 years; 120 – 250mg.

6 – 12 years; 250 – 500mg.

These doses are repeated every 4–6 hours (maximum of 4 doses in 24 hours).

Side effects: Liver damage on prolonged use or overdosage. (See section 15).

Caution: Impaired kidney or liver function, alcoholism.

IBUPROFEN

Presentation: Tablet containing 200mg, 400mg Ibuprofen; Syrup containing 100mg/5ml Ibuprofen.

Indications: Fever and pain, mild to moderate pain including dysmenorrhoea, postoperative analgesia. (see musculoskeletal medicines in section 15)

Administration: *Adult*; initially 1.2 – 1.8g daily in 3 – 4 divided doses preferably after food; increased if necessary to maximum 2.4g daily. Maintainance dose of 0.6 – 1.2g daily may be adequate.

Children:

Neonate: (under specialist supervision) Initially 10 mg/kg for 1 dose, followed by 5 mg/kg every 24 hours for 2 doses, the course may be

repeated after 48 hours if necessary.

Above 1 month: 5 mg/kg 3–4 times a day, maximum daily

dose to be given in 3–4 divided doses; maximum 30 mg/kg per day.

Not recommended for children under 7kg.

Side effects: see notes above (section 3.9.1.)

Contraindications: History of hypersensitivity to acetylsalicylic acid or any other NSAID.

Caution: see notes above (section 3.9.1.).

DICLOFENAC SODIUM/ POTASSIUM

Presentation: Tablet containing 50mg and 100mg; Injection containing 75mg/3ml ampoule; suppository containing 50mg and 100mg of Diclofenac sodium; Spray containing 4% of Diclofenac.

Indications: Mild to moderate pain, inflammation in musculoskeletal conditions, acute gout, arthritis, postoperative pain, ankylosis spondylitis, dysmenorrhea, migraine.

Administration: *Adult*; by mouth- 50-150mg daily in 2-3 divided doses. By deep IM injection: 75mg 1-2 times daily for a maximum of 2 days. Per rectal: 75-150mg in divided doses. Spray: 4-5 sprays 3 times daily.

Children:

6 months–17 years: orally; 1.5–2.5 mg/kg twice daily, total daily dose may alternatively be given in 3 divided doses; maximum 150 mg per day.

6 months –17 years: by IV infusion, or by deep IM injection or by rectum 0.3–1 mg/kg 1–2 times a day for maximum of 2 days.

For intramuscular injection, to be injected into the gluteal muscle; maximum 150 mg per day.

Side effects: Appetite decreased, diarrhea, dizziness, gastrointestinal discomfort, gastrointestinal disorders,

Headache, nausea, oedema, rash (discontinue), skin reactions, vertigo, vomiting.

Contraindications:

*With intravenous use***:** Dehydration, history of asthma, history of cerebrovascular bleeding, history of haemorrhagic diathesis, hypovolaemia, operations with high risk of haemorrhage.

*By mouth***:** Active gastro-intestinal bleeding and ulceration, avoid suppositories in proctitis, cerebrovascular disease, history of gastrointestinal bleeding and perforation related to previous NSAID therapy, ischaemic heart disease, heart failure, peripheral arterial disease.

ACECLOFENAC

Presentation: Tablet containing 100mg of Aceclofenac

Indications: Pain, pain and inflammation in rheumatoid arthritis, osteoarthritis and ankylosing spondylitis

Administration: *Adult*: 100 mg twice daily

Side effects: See above on Diclofenac oral

Contraindications: Active bleeding, active gastrointestinal bleeding, active gastro-intestinal ulceration, bleeding disorders, cerebrovascular disease, history of gastro-intestinal bleeding related to previous NSAID therapy, history of gastro-intestinal perforation related to previous NSAID therapy, history of recurrent gastrointestinal, haemorrhage (two or more distinct episodes), ischaemic heart disease, mild to severe heart failure, peripheral arterial disease, varicella infection.

CELECOXIB

Presentation: Capsules containing 100mg and 200mg of Celecoxib.

Indications: Pain and inflammation in osteoarthritis, rheumatoid arthritis, Ankylosing spondylitis.

Administration: *Adult;* 200 mg daily in 1–2 divided doses, then increased if necessary up to 400 mg daily in 1–2 divided doses, discontinue if no improvement after 2 weeks on maximum dose**.**

Children: No or insufficient experience in children and adolescents, therefore its use is not recommended.

Side effects: Headache, hypertension, diarrhoea, dizziness, upper respiratory tract infection, abdominal pain, insomnia, flatulence, rash, peripheral oedema.

Contraindications: Active GI bleeding, active GI ulceration, cerebrovascular disease, inflammatory bowel disease, ischaemic heart disease, mild to severe heart failure, peripheral arterial disease, patients with sulphonamide

sensitivity, allergy and cross-sensitivity: History of hypersensitivity to aspirin or any other NSAIDs.

KETOROLAC TROMETAMOL

Presentation: Injection containing 30 mg/ml of Ketorolac.

Indications: Short-term management of moderate to severe acute postoperative pain only

Administration: *Adult*; By IM or IV injection: Initially 10 mg, then 10–30 mg every 4–6 hours as required for maximum duration of treatment of 2 days; frequency may be increased to up to every 2 hours during initial postoperative period. Maximum 120mg per day.

Children: IV or IM

Below 2 years: Safety and efficacy not established

2–16 years: Single dose: 0.5 mg/kg once; not to exceed 15 mg. Multiple dose: 0.5 mg/kg every 6 hours; not to exceed 5 days.

Over 16 years, <50 kg: IV; 15 mg as single dose or 15 mg every 6 hours; not to exceed 60 mg/day. IM: 30 mg as single dose or 15 mg every 6 hours; not to exceed 60 mg/day

Over 16 years, over 50 kg IV: 30 mg as single dose or 30 mg every 6 hours; not to exceed 120 mg/day. IM: 60 mg as single dose or 30 mg every 6 hours; not to exceed 120 mg/day.

Side effects: Headache, somnolence, dyspepsia, oedema, increase in BUN, increase in serum creatinine, agranulocytosis, angioedema, azotemia, constipation.

Contraindications: see Diclofenac above

INDOMETHACIN

Presentation: Capsule containing 25mg and 50mg of Indomethacin

Indications: Acute Gout, moderate to severe pain in arthritis and rheumatoid disorders, dysmenorrhea, closure of Patent Ductus Arteriosus.

Administration: Adult 50-200mg daily in 2 divided doses.

Children: 0.5–1 mg/kg twice daily

Side effects: Transient renal insufficiency, jaundice, headache, dyspepsia, indigestion.

Contraindications: See above under Diclofenac and Ibuprofen.

MEFENAMIC ACID

Presentation: Tablet containing 250mg and 500 mg of Mefenamic Acid.

Indications: Dysmenorrhoe/Menorrhagia; Pain and inflammation in rheumatoid arthritis an osteoarthritis, Postoperative pain, Mild to moderate pain.

Dose: *Adult*: 500 mg 3 times a day

Children:

12–17 years: 500 mg 3 times a day.

Side effects: Diarrhea, haemolytic anaemia, renal impairment, thrombocytopenia, tinnitus, vertigo, constipation, agranulocytosis.

Contraindications: Late pregnancy, active gastro-intestinal bleeding, active gastro-intestinal ulceration, history of gastrointestinal bleeding related to previous NSAID therapy, inflammatory bowel disease, severe heart failure

Cautions: Acute porphyrias, allergic disorders, cardiac impairment (NSAIDs may impair renal function), cerebrovascular disease, coagulation defect, connective tissue disorders.

3.9.2 Opioid analgesics

Opioid analgesics are used to relieve moderate to severe pain, particularly of visceral origin.

Side effects: Most common are nausea, vomiting, constipation and drowsiness. Larger doses produce respiratory depression and hypotension.

Opioid analgesics interact with many medicines notably anti-depressants, anti-epileptics, anxiolytics, alcohol (see appendix 2).

Morphine is the most valuable for severe pain although it causes nausea and vomiting when used frequently. It also gives a state of euphoria and mental detachment. It is the treatment of choice for oral treatment of severe pain in terminal care.

Codeine is effective in relieving mild to moderate pain but is too constipating for long term use. Dihydrocodeine has analgesic efficacy similar to codeine.

Pethidine produces prompt but short-lasting analgesia. It has less constipating effect than morphine but is less potent. It is not suitable for severe continuing pain but is useful in labour and neonates.

Caution: Medicines in this group should not be administered repeatedly when used for acute pain as dependence and tolerance occur.

TRAMADOL

Presentation: Capsule containing 50mg; Injection containing 50mg/ml (2ml Ampoule) of Tramadol Hydrochloride

Indications: Moderate to severe pain where alternative therapies are inadequate. Useful for mixed pain- neuropathic and nociceptive.

Administration: *Adult; By oral:* Initially 25mg, titrate upwards by 25-50mg every 3 days up to 50-100mg every 4-6 hours when required, do not exceed 400mg in 24 hours

By IM, bolus, slow IV or SC: Initially 50mg every 4–6hours then adjust the dose according to the patient's response. Do not exceed 400mg in 24 hours.

Postoperative pain, by IM, bolus, slow IV or SC: Initially 100mg (in the first hour), then 50mg every 10-20 minutes if required up to 250mg (including the initial dose). Maintenance dose: 50-100mg every 4-6 hours. For IV give over 2-3 minutes. Do not exceed 400mg in 24 hours.

Elderly >65 years: give the initial dose at the lower end of dosing range. Do not to exceed 300 mg in 24 hours if

>75 years. Titrate doses cautiously.

Children:

1 month to 11 years: Safety and efficacy is not established, with life-threatening respiratory depression and death have occurred on receiving tramadol.

12–17 years: Adult doses as above.

Side effects: Fatigue, constipation, nausea, dizziness, headache, somnolence, vomiting, CNS stimulation, dyspepsia, asthenia, pruritis, dry mouth, sweating, euphoria, myosis, vasodilatation.

Contraindications: Acute intoxication with alcohol, acute intoxication with analgesic, acute intoxication with hypnotics, acute intoxication with opioids, compromised respiratory function (in children), not suitable for narcotic

withdrawal treatment, uncontrolled epilepsy.

Caution: Excessive bronchial secretions, history of epilepsy, susceptibility to seizures, impaired consciousness, not suitable in some types of general anaesthesia.

FENTANYL

Presentation: Injection containing 50mcg/ml of Fentanyl.

Indications: Intractable pain not currently treated with a

strong opioid analgesic; spontaneous respiration and assisted ventilation: analgesia and enhancement of anaesthesia during operation; assisted ventilation: analgesia and respiratory depression in intensive care; In surgery premedication; in general anaesthesia and as analgesia.

Administration: *Spontaneous respiration: analgesia and enhancement of anaesthesia, during operation*:

By slow IV injection; Adult: Initially 50–100 mcg (max. per dose 200 mcg), dose maximum

on specialist advice, then 25–50 mcg as required

By IV infusion: Adult: 3–4.8 mcg/kg/hour, adjusted according to response.

Assisted ventilation: analgesia and enhancement of

anaesthesia during operation, and Assisted ventilation: analgesia and respiratory depression in intensive care:

By slow intravenous injection; Adult: Initially 300–350 mcg, then 100–200 mcg as required.

By intravenous infusion; Adult: Initially 10 mcg/kg, dose to be given over 10 minutes, then 6 mcg/kg/hour, adjusted according to response, may require up to 180 mcg/kg/hour during cardiac surgery.

Surgery premedicated; 50-100 mcg/dose IM or slow IV 30-60 minutes prior to surgery.

For general anesthesia; minor surgical procedures: 0.5-2 mcg/kg/dose IV initially; 1-2mcg/kg/hr maintainance infusion IV. Discontinue infusion 30-60 minutes before end surgery.

Analgesia; 1-2mcg/kg IV bolus or 25-100mcg/dose, as per required or 1-2mcg/kg/hr by continuous infusion or 25-200mcg/hr.

Anaesthesia for severe pre-eclampsia: Fentanyl 2.5 **µ**g/kg or up to 200 **µ**g iv Alfentanil 10 **µ**g/kg iv.

Children:

Spontaneous respiration: analgesia and enhancement of anaesthesia, during operation; By intravenous injection

1 month–11 years: Initially 1–3 mcg/kg, then 1 microgram/kg as required, dose to be administered over at least 30 seconds

12–17 years: Initially 50–100 mcg (max. per dose 200 mcg), dose maximum on specialist advice, then 25–50 mcg as required, dose to be administered over at least 30 seconds

Assisted ventilation: analgesia and enhancement of anaesthesia during operation; and Assisted ventilation: analgesia and respiratory depression in intensive care; By intravenous injection:

Neonate: Initially 1–5 mcg/kg, then 1–3 mcg/kg as required, dose to be administered over at least 30 seconds.

1 month–11 years: Initially 1–5 mcg/kg, then 1–3 mcg/kg as required, dose to be administered over at least 30 seconds

12–17 years: Initially 1–5 mcg/kg, then 50–200 mcg as required, dose to be administered over at least 30 seconds.

Surgery premedication

1-12 years: 0.5-2mcg/kg IV given 3 minutes prior to procedusre and may repeat every 1-2 hours.

>12 years: 0.5-2mcg/kg IV, not exceed 50mcg/dose. May repeat upto 5 times at 25mcg/dose maximum.

For alnalgesia

<2 years, safety and efficacy not established.

>2 years; 2-3mcg/kg IV/IM every 1-2 hours as per required

Side effects: Apnoea, hiccups, hypothermia, hypertension, hypotension, movement disorders, muscle rigidity, post procedural complications, respiratory disorders, vascular pain, visual impairment, sthenia, confusion, constipation, dry mouth, nausea, somnolence, sweating, vomiting, abdominal pain.

Contraindications: Significant respiratory depression, acute/severe broncho-asthma, GIT obstruction including paralytic ileus, hypersensitivity, use within 2 weeks of monoamine oxidase inhibitor use.

Cautions: Bradyarrhythmias, cerebral tumour, impaired consciousness, repeated intra-operative doses should be given with care since the resulting respiratory depression can persist postoperatively and occasionally it may become apparent for the first time postoperatively when monitoring of the patient might be less intensive, in acute pancreatitis, Addison diseases, benign prostatic hyperplasia, cardiac arrhythmias, may cause serotonine syndrome.

CODEINE

Presentation: Tablet containing 15mg Codeine phosphate. Syrup containing 25mg/5ml Codeine phosphate.

Indications: Mild to moderate pain.

Administration: *Adult;* 30 – 60mg every 4 hours when necessary to a maximum of 240mg daily.

Children: 1 – 12 years, 3mg/kg body weight daily in divided doses.

Side effects, Caution, and Contraindications: see 3.9.2 above.

Use of cough suppressants containing Codeine or other similar opioid analgesics is generally not recommended in children and should be avoided altogether in those under 1 year.

DIHYDROCODEINE

Presentation: Tablet containing 30mg Dihydrocodeine tartrate. Syrup containing 10mg/ml Dihydrocodeine tartrate. An injection containing 50mg/ml Dihydrocodeine tartrate.

Indications: Moderate to severe pain.

Administration: Oral, *Adult;* 30mg every 4 – 6 hours when necessary, after food.

Children:
Over 4 years: 0.5mg – 1mg/kg body weight every 4 – 6 hours. By deep subcutaneous or intramuscular injection, up to 50mg every 4 – 6 hours.

Side effects: see 3.9.2 above; icluding dizziness, sedation.

Caution: see 3.9.2 above; not to be used in young children, dependence easily occurs.

MORPHINE

Presentation: An oral solution containing 5mg Morphine hydrochloride in 5ml of chloroform water; Tablet containing 10mg, 20mg Morphine sulphate; Suppository containing 15mg Morphine sulphate or hydrochloride; An injection containing 10mg/ml Morphine sulphate.

***Note*:** Both the strength of the suppositories and the morphine salt contained in them must be specified by the prescriber.

Indications: Severe persistent pain, acute pulmonary oedema, pre-operative analgesia.

Administration: Oral, subcutaneous or intramuscular injection; *Adult;* 5 to 20mg as required every 4 hours, adjusted according to response.

Myocardial infarction: By slow intravenous injection (2mg/minute), 10mg followed by a further 5 – 10mg if necessary.

Acute pulmonary oedema; by slow intravenous injection (2mg/ minute), 5 – 10mg.

Oral: Approximately double corresponding intramuscular dose.

Children:
up to 1 month; 0.15mg/kg body weight.
1–12 months; 0.2mg/kg body weight.
1–5 years; 2.5 – 5mg/kg body weight.
6–12 years; 5 – 10mg/kg body weight.
By slow intravenous injection; quarter to half corresponding intramuscular dose.

Side effects: See notes above. Cough suppression, urinary retention, dry mouth, sweating, facial flushing, tolerance, vertigo, bradycardia, palpitations, postural hypotension, hypothermia, hallucinations, mood changes, dependence, miosis, urticaria and pruritis.

Contraindications: Concomitant use with tranquillisers.

Caution: See 3.9.2 above. Patients taking MAOIs, pregnancy and breastfeeding. Drug dependence occurs easily

PETHIDINE

Presentation: Tablet containing 25mg, 50mg Pethidine hydrochloride. An injection containing 50mg/ml Pethidine hydrochloride.

Indications: Moderate to severe pain, obstetric analgesia and operative analgesia. Not suitable for severe continuing pain.

Administration: *Adult:* Oral*;* 50 – 150mg every 4 hours.

By subcutaneous injection, or by intramuscular Injection: 25–100 mg, then 25–100 mg after 4 hours,

By slow intravenous injection: 25–50 mg, then 25–50 mg after 4 hours

Obstetric analgesia; subcutaneous or intramuscular injection: 50 – 100mg repeated 1 – 3 hours later if necessary. Maximum 400mg in 24 hours.

Children:
By subcutaneous or intramuscular injection; 0.5–2mg/kg body weight. Maximum 25 - 100mg every 4 hours.

reported in overdosage. Avoid in acute abdomen paralytic ileus, head injury, raised intracranial pressure (affected papillary response). Less constipating than morphine.

Contraindications: Renal impairment

Caution: See 3.9.2 above.

3.9.3 Antimigraine Medicines

Most migraine headaches respond to non-opioid analgesics such an Acetylsalicylic acid or paracetamol. Ergotamine is used in patients who do not respond to non-opioid analgesics. It relieves migraine by constricting cranial arteries but visual and other prodromal symptoms are not affected and vomiting may be made worse. Repeated administration may cause habituation. Headache may be provoked by either chronic overdosage or rapid withdrawal of the drug.

ERGOTAMINE

Presentation: Tablet containing 1mg, 2mg Ergotamine tartrate.

Indications: Acute attacks of migraine unresponsive to analgesics.

Administration: 1–2mg at onset repeated after 30 minutes if necessary. Maximum 6mg in 24 hours at intervals of not less than 4 days. Maximum 10mg per week.

Side effects: Parasthesia of fingers and toes, nausea, vomiting, abdominal pain, and muscular cramps.

Contraindications: Pregnancy and peripheral vascular disease.

Caution: Withdraw treatment immediately if numbness or tingling of extremities develops, should not be used for migraine prophylaxis; if vomiting worsens, may add an anti-emetic.

3.10 Central nervous system stimulants

These include Amphetamines and related medicines. They have limited indications and should **NOT** be used to treat depression, obesity, senility, debility or for relief of fatigue. Patients with narcolepsy may derive benefit treatment with dexamphetamine. Dexamphetamine and methylphenidate may be of benefit in the management of hyperactive children. However, they must be used very selectively since they retard growth and the effect of long-term therapy has not been evaluated.

DEXAMPHETAMINE

Presentation: Tablet containing 5mg Dexamphetamine sulphate.

Indications: Narcolepsy, as an adjunct in the management of refractory hyperkinetic states in children.

Administration: *Narcolepsy*; 10mg (elderly 5mg) daily in divided doses increased by 10mg (elderly 5mg) daily at intervals of 1 week to a maximum of 60mg daily.

Children: Hyperkinesia;

Under 6 years not recommended

Over 6 years: 5 - 10mg daily, increased, if necessary, by 5mg at intervals of 1 week to the usual maximum dose of 20mg daily (older children have received maximum 40mg daily).

Side effects: Insomnia, restlessness, irritability and excitability, nervousness, night terrors, euphoria, tremor, dizziness, headache, convulsions (see Caution), dependence and tolerance, sometimes psychosis, anorexia, gastrointestinal symptoms, growth retardation in children (see under Caution), dry mouth, sweating, tachycardia and anginal pain, palpitations, increased blood pressure, visual disturbances, cardiomyopathy reported with chronic use, central stimulants have provoked choreoathetoid movements, tics and Tourette in predisposed individuals (see Caution).

Contraindications: Cardiovascular disease including moderate to severe hypertension, history of drug or alcohol abuse, glaucoma, pregnancy and breastfeeding, hyperthyroidism, hyperexcitability and or agitated states.

Caution: Mild hypertension, history of epilepsy, monitor growth in children, avoid abrupt withdrawal, porphyria. Treatment to be given strictly under specialist supervision.

METHYLPHENIDATE

Presentation: Tablet (scored) containing 5mg, 10mg, 20mg Methylphenidate hydrochloride.

Indications: Attention deficit, hyperactivity disorder when remedial measures alone prove insufficient.

Administration:

Children:

Under 6 years; not recommended;

Over 6 years: initially 5mg 1 - 2 times daily increased, if necessary, at weekly intervals by 5 - 10mg daily to maximum 60mg daily in divided doses. Discontinue if there is no response after 1 month, also suspend periodically to assess the child's condition (usually final discontinuation is during or after puberty).

NOTE: If effect wears off in the evening (with rebound hyperactivity) a dose at bedtime may be appropriate (establish need with trial bedtime dose).

Side effects: see under Dexamphetamine above; also sleep disturbances, pruritis, urticaria, fever, arthralgia, alopecia, exfoliative dermatitis, erythema multiforme, thrombocytopenic purpura, thrombocytopenia, leucopenia, urinary disorders, and very rarely liver damage.

4 Medicines used in the treatment of Infections

4.1 Antibacterials

Antibacterial agents are those Medicines that are used for the treatment of bacterial infections. Antibacterial agents should not be prescribed unless there are definite indications. Before selecting an antibacterial agent, the clinician must consider three factors: The patient and the known or likely causative microorganism and sensitivity of the organism. Factors related to the patient which must be considered include history of allergy, renal and hepatic function, resistance to infection, age and weight of the patient; if female whether pregnant and the stage of pregnancy; breastfeeding and concurrent medications. It may be necessary for some situations to prescribe therapy before laboratory results are available but it is essential that appropriate specimens are taken before therapy is initiated (where laboratory facilities exist).

The duration of the therapy depends on the nature of the infection, the severity and the response to treatment. Unless otherwise stated, the minimum duration of treatment should be five days.

4.1.1 Penicillins

These belong to the group of antibiotics called the Beta-lactam antibiotics. They are bactericidal and act by interfering with the synthesis of the bacterial cell wall. They diffuse well into body tissues and fluids but penetration into the cerebrospinal fluid is poor except when the meninges are inflamed. They are excreted in the urine in therapeutic concentrations. Probenecid blocks the renal tubular excretion of penicillins producing higher and more prolonged plasma concentrations. They are generally active against most gram-positive microorganisms and some gram-negative *Cocci bacteria*. The most common side effects associated with their use is hypersensitivity reactions which manifest as rashes and occasionally anaphylaxis reaction which may be fatal. Diarrhoea frequently occurs during oral penicillin therapy.

4.1.1.1 Natural penicillins

The first group of penicillins to be obtained by fermentation. They remain an important and useful group of antibiotics but they are inactivated by bacterial penicillinases (Beta-

lactamases). They are the drug of choice for *Streptococcal, Pneumococcal, Gonococcal, and Meningococcal* infections and also for anthrax, diphtheria, gas gangrene, leptospirosis, syphilis, tetanus and yaws. Most natural penicillins are inactivated by gastric acids and the absorption from the gut is low except for Phenoxymethlyl Penicillin.

BENZATHINE PENICILLIN

Presentation: Injection containing 2.4MU Benzathine penicillin equivalent to 1.4g of Benzylpenicillin powder for reconstitution. For intramuscular injection. Not to be administered by i.v. injection or infusion.

Indications: Penicillin sensitive infections particularly syphilis, bejel, yaws, pinta, prophylaxis of rheumatic fever.

Administration: *Primary/secondary syphilis*, adult; 2.4MU stat.

Late stage syphilis, 2.4MU intramuscularly once weekly for three weeks.

Prophylaxis of rheumatic fever; 1.2 MU every 3–4 weeks for at least 5 years or up to 21 years of age (whichever is longer).

Erysipelas, Yaws, Pinta Adult: 1.2 MU as a single dose

Children:

Syphilis

Neonate: 50 000 units/kg as a single dose.

1 month–11 years: 50 000 units/kg (max. per dose 2.4 million units) as a single dose (in primary/secondary) **OR** once weekly for 3 weeks (in late-stage)., if clinical symptoms recur or laboratory findings remain strongly positive - repeat treatment.

12–17 years: as Adult dose above

Prophylaxis of rheumatic fever:

Body-weight up to 30 kg: 0.6 million units every 3–4 weeks for at least 5 years or up to 21 years of age (whichever is longer).

Body-weight 30 kg and above: 1.2 million units every 3–4 weeks for at least 5 years or up to 21 years of age (whichever is longer)

Bejel & yaws

Less than 5 years: 0.6MU stat.

5 years and above: 1.2MU stat.

Note: mid-lateral thigh muscle is the preferred site of injection in children.

Side effects: Sensitivity reactions including urticaria, fever, joint pains, angioedema, anaphylactic shock.

Contraindications: History of hypersensitivity to penicillin.

Caution: Penicillin allergy, renal impairment.

BENZYL PENICILLIN

Presentation: Injection containing 5 mega Units (MU), equivalent to 3g of Benzylpenicillin powder for reconstitution.

Indications: See notes above (4.1.1.1).

Administration: *By slow intravenous injection or by infusion*.

Adult; 2.4MU 4 times daily increased if necessary to a maximum of 4 MU every 4 hours.

Bacterial endocarditis; 5 to 20 MU/day in equally divided doses every 4 to 6 hours

Meningitis: 24 MU/day IV in divided doses every 4 hours for 7 days

Children:

Premature infant and neonates; 50 000 MU/kg by IV injection every 12 hours

Infant 1–4 weeks; 50,000 units/kg IM or IV every 8 hours

1 month – 12 years; 100,000 to 300,000 units/kg/day IM or IV divided in 4 to 6 doses.

***Bacterial endocarditis*;**

Infants (1 – 4 weeks); 150mg/kg daily in 3 divided doses.

1 month – 12 years; 200,000 to 300,000 units/kg/day in divided doses every 4 hours; Maximum dose: 12 to 24 MU/day

Meningitis:

Premature infants and neonates; 150,000

units/kg/day IV in divided doses every 8 to 12 hours

Infants 1–4 weeks; 200,000 units/kg/day IV in divided doses every 6 to 8 hours

1 month – 12 years; 300,000 units/kg/day IV in divided doses every 4 to 6 hours.

Side effects: Sensitivity reactions including urticaria, fever, joint pains, angioedema, anaphylactic shock. **Contraindications:** History of hypersensitivity to Penicillin.

Caution: Penicillin allergy, renal impairment.

PHENOXYMETHYL PENICILLIN

Presentation: Tablet containing 250mg Phenoxymethylpenicillin potassium. A suspension containing 125mg/5ml Phenoxymethylpenicillin potassium.

Indications: Tonsillitis, otitis media, erysipelas, rheumatic fever, sinusitis, impetigo and prophylaxis of pneumococcal infection.

Administration: *Adult;* 500mg every 6 hours increased to 750mg every 6 hours in severe infection.

Children:

Neonates <7 days; 50mg/kg body weight in 2 divided doses in the first few days of life then in 3 –4 divided doses.

Neonate; 75mg/kg body weight daily in 3 divided doses.

0–1 year; 62.5mg every 6 hours.

1–5 years; 125mg every 6 hours.

6–12 years; 250mg every 6 hours.

Side effects: Sensitivity reactions including urticaria, fever, joint pains, angioedema, anaphylactic shock. **Contra-indications:** History of hypersensitivity to penicillin.

Caution: Penicillin allergy, renal impairment.

PROCAINE PENICILLIN

Presentation: Vial injection containing 3MU (3g) procaine penicillin and 1MU (1G) benzylpenicillin powder for reconstitution.

Indications: Penicillin sensitive infections including syphilis, anthrax and gas gangrene.

Administration: *Adult*; 600mg every 12 – 24 hours.

In syphilis:1.2MU intramuscularly daily for 10 days (up to 21 days for secondary and latent syphilis). The dose can be doubled for patients weighing over 80 kilograms.

Side effects: Sensitivity reactions including urticaria, fever, joint pains, angioedema, anaphylactic shock.

Contra-indications: History of hypersensitivity to penicillin.

Caution: Penicillin allergy, renal impairment.

4.1.1.2 Amino penicillins

They are synthetic derivatives of 6-amino penicillinoic acid and have a free amino group attached to the penicillin nucleus. Because of their enhanced polarity, they have enhanced activity against gram-negative bacteria compared to natural penicillins. They are active against gram-positive and gram-negative organisms but they are inactivated by penicillinases produced by *Staphylococcus aureus*. They are well excreted in the urine and bile. They are principally indicated in the treatment of exacerbation of chronic bronchitis and middle ear infections due to *Streptococcus pneumoniae* and *Haemophilus influenza* and urinary tract infections due to sensitive microorganisms.

AMOXICILLIN

Presentation: Capsule/Tablet containing 250mg, 500mg Amoxycillin trihydrate. Suspension containing 125mg/5ml Amoxycillin trihydrate. Injection containing 250mg, 500mg Amoxycillin sodium.

Indications: Urinary tract infections, otitis media, sinusitis, chronic bronchitis, invasive salmonellosis, prophylaxis adjunct in listerial meningitis.

Administration: *Adult*; 250-500mg orally, every 8 hours. Maximum dose 6g daily in divided doses.

Severe or recurrent purulent respiratory infections: 3g every 12 hours.

By IM/IV injection, 250 - 500mg every 8 hours, increased to 1g every 6 hours in severe infections.

Children:

Up to 10 years; 125mg every 8 hours, doubled in severe infections.

Severe or recurrent purulent respiratory infections

2 – 5 years; 750mg every 12 hours.

5–10 years; 1.5g every 12 hours.

By IV/IM injection: 50–100mg/kg body weight daily in divided doses.

Side effects: Nausea, diarrhoea, rashes (discontinue treatment), pseudomembranous colitis (rarely), on prolonged use leucopenia and thrombocytopenia may occur.

Contraindications: Penicillin hypersensitivity.

Caution: History of allergy, renal impairment, erythematous rashes common in glandular fever, chronic lymphatic leukaemia and HIV infection.

AMPICILLIN

Presentation: Capsule containing 250mg, 500mg Ampicillin. A suspension containing 125mg/5ml Ampicillin. An injection containing 250mg, 500mg Ampicillin sodium powder for reconstitution.

Indications: Urinary tract infection, otitis media, sinusitis, chronic bronchitis, invasive salmonellosis. **Administration:** Oral, *adult*; 0.25–1g every 6 hours at least 30 minutes before food depending on the severity of the infection.

Urinary tract infection; 500mg every 8 hours orally or by IM injection.

Meningitis; IV or by infusion, 500mg every 4 – 6 hours, higher doses may be required depending on the severity of the infection.

Children:

Newborn–5 years; 100mg/kg body weight daily in divided doses.

6 - 10 years; any route, half the adult dose.

Side effects: Nausea, diarrhoea, rashes (discontinue treatment), pseudomembranous colitis (rarely), on prolonged use, leucopenia and thrombocytopenia may occur.

Contraindications: Penicillin hypersensitivity.

Caution: History of allergy, renal impairment, erythematous rashes common in glandular fever and chronic lymphatic leukaemia.

4.1.1.3 Penicillinase-resistant Penicillins

They are semi-synthetic derivatives of 6 amino penicillinoic acid. They are stable against hydrolysis by most *Staphylococcal* penicillinases. They are effective in infections caused by penicillin-resistant *staphylococci*. Since they are acid-stable, they can be given by mouth as well as by injection.

AMOXYCILLIN + CLAVULANIC ACID

Presentation: Tablet containing 500mg Amoxicillin trihydrate and 125mg Clavulanic acid. A suspension containing 125mg Amoxicillin trihydrate and 31mg Clavulanic acid per 5ml. Injection containing 500mg Amoxicillin sodium and 100mg Clavulanic acid, 1g Amoxicillin and 200mg Clavulanic acid powder.

Indications: As for amoxicillin and the treatment of staphylococcal infections.

Administration: Expressed as amoxicillin, Oral, *adult*; 250mg every 8 hours, doubled in severe infections.

By *intravenous injection* (Over 3 minutes) or by infusion; 1g every 8 hours increased to 1g every 6 hours in more serious infections.

Surgical prophylaxis; 1g as induction, may be increased to 2 – 3 doses every 8 hours in the first 24 hours. (longer in high risk of infection).

Children:

Under 1 year; 0.8ml of the suspension/kg body weight daily in 3 divided doses.

1–6 years (10 – 18 kg); 125mg every 8 hours, doubled in severe infections.

6–12 years; 250mg every 8 hours, doubled in severe infections.

By intravenous injection (Over 3 minutes) or by infusion*;*

Infants up to 3 months; 25mg/kg body weight every 8 hours (every 12 hours in premature infants).

3 months – 12 years; 25mg/kg body weight every 8 hours increased to every 6 hours in a more serious infection.

Side effects: See under Amoxicillin above (4.1.1.2.)

Contra-indications: Penicillin hypersensitivity. **Caution:** See under Amoxicillin above (4.1.1.2.), Severe hepatic impairment, pregnancy and breastfeeding, hepatitis, cholestatic jaundice and erythema multiform. Treatment not to exceed 14 days without review.

CLOXACILLIN

Presentation: Capsule containing 250mg, 500mg Cloxacillin sodium; Suspension containing 125mg/5ml of Cloxacillin; An injection containing 250mg, 500mg Cloxacillin sodium powder for reconstitution.

Indications: Infections due to penicillinase-producing S*taphylococci* including otitis externa, adjunct in the treatment of pneumonia, impetigo, cellulitis and staphylococcal endocarditis.

Administration: Oral, *adult*; 500mg every 6 hours at least 30 minutes before food.

IM injection: 250mg every 4 – 6 hours.

By slow IV injection or by infusion: 500mg every 4 – 6 hours.

Children:

Under 2 years: Any route, quarter adult dose.

2 – 10 years: half adult dose.

Side effects: Sensitivity reactions including urticaria, fever, joint pains, angioedema, anaphylactic shock.

Contraindications: Penicillin hypersensitivity.

Caution: History of allergy, renal impairment.

4.1.1.4 Antipseudomonal Penicillins

PIPERACILLIN

Presentation: Injection 2.25g powder for reconstitution containing 2g piperacillin (as sodium salt) and tazobactam 250mg (as sodium salt). Injection 4.5g powder for reconstitution containing 4g piperacillin (as sodium salt) and tazobactam 500mg (as sodium salt). Infusion containing 4.5g piperacillin.

Indications: Hospital-acquired pneumonia, sepsis, complicated infections involving the urinary-tract, skin, and soft tissues; acute exacerbation of chronic obstructive

pulmonary disease and bronchiectasis, moderate and severe diabetic foot infection; leg ulcer infection

Administration: By intravenous injection over 3 - 5 minutes or by intravenous infusion

Adult and child over 12 years; 2.25 - 4.5g every 6 - 8 hours, usually 4.5g every 8 hours.

Complicated appendicitis, 4.5g every 6 - 8 hours, usually 4.5g every 8 hours

Infections in neutropenic patients (in combination with an aminoglycoside)

Adult and child over 50kg, 4.5g every 6 hours.

Children:

Complicated appendicitis

Under 2 years; not recommended.

2-12years, 112.5mg/kg every 8 hours (maximum 4.5g every 8 hours) for 5 - 14 days.

Infections in neutropenic patients (in combination with an aminoglycoside)

Neonate: 90 mg/kg every 8 hours.

Less than 50kg: 90mg/kg every 6 hours.

Side effects: Nausea and vomiting, rarely stomatitis, constipation, dry mouth, hepatitis, cholestatic jaundice, oedema, hypotension, fatigue, myalgia, erythema multiforme, hypokalaemia, injection site reaction. See also 4.1.1.1 above.

Contraindications: Penicillin hypersensitivity.

Caution: Renal impairment – adjust doses according to eGFR, history of allergy, discontinue if thrombocytopaenia or bleeding occurs, leucopenia associated with prolonged therapy.

FLUCLOXACILLIN

Presentation: Capsules containing 250mg, 500mg Flucloxacillin sodium. Oral solution (elixir or syrup) containing 125mg/5ml Flucloxacillin magnesium. An injection containing 250mg, 500mg Flucloxacillin sodium powder for reconstitution.

Indications: Infections due to penicillinase-producing *Staphylococci* including otitis externa, adjunct in the treatment of pneumonia, impetigo, cellulitis and staphylococcal endocarditis.

Administration: Oral, *adult*; 250mg every 6 hours at least 30 minutes before food

By IM injection, 250mg every 6 hours.

By slow IV injection or by infusion, 250mg – 1g every 6 hours.

The above doses can be doubled in severe infection.

Children:

Under 2 years, any route, quarter the adult dose.

2–10 years, half the adult dose.

Side effects: Sensitivity reactions including urticaria, fever, joint pains, angioedema, anaphylactic shock, and on prolonged use in old age it will cause thrombocytopenia, leucopenia, hepatitis and cholestatic jaundice.

Contraindications: Penicillin hypersensitivity.

Caution: History of allergy, renal impairment and porphyria.

4.1.2 Aminoglycosides

These are bactericidal antibiotics used primarily in the treatment of gram-negative infections. They bind irreversibly to 30s ribosomal subunit blocking the recognition step in protein synthesis and causing misreading of the genetic code. They are very poorly absorbed from the gastrointestinal tract and are thus administered parenterally. They are excreted principally via the kidneys and accumulation occurs in renal impairment. The major side effects are nephrotoxicity and ototoxicity and they may also impair neuromuscular transmission.

GENTAMICIN

Presentation: Injection containing 40mg/ml Gentamicin sulphate.

Indications: Septicaemia and neonatal sepsis, biliary tract infections, acute pyelonephritis, or prostatitis endocarditis caused by S*treptococcus viridans*, S*treptococcus faecalis*, pneumonia in hospital patients, adjunct in the treatment of listerial meningitis.

Administration: *Adults*; by IM or slow IV injection over at least 3 minutes or by infusion 2 – 5mg/kg body weight daily every 8-24 hours. Dosage should be reduced in patients with renal impairment.

Gonorrhoea; 240mg intramuscularly stat.

Children:

Neonate <7 day: 5 mg/kg every 24 hours

Up to 2 weeks; 3mg/kg body weight every 12 hours.

2 weeks–12 years; 2mg/kg body weight every 8 hours.

By *intrathecal injection (under specialist supervision)*; 1mg daily (increased if necessary to 5mg daily).

Side effects: Vestibular and auditory damage, nephrotoxicity, rarely hypomagnesaemia on prolonged therapy.

Contraindications: Myasthenia gravis, dehydrated patients, acute kidney injury.

Caution: Pregnancy, renal impairment, in infants and the elderly, in patients with hearing and vestibular problems or disturbances. Creatinine levels should be monitored.

KANAMYCIN

Presentation: Injection containing 1g kanamycin sulphate powder for reconstitution.

Indications: Similar to those of Gentamicin but it is more toxic, and resistance develops more rapidly. It is used primarily in the treatment of systemic and urinary tract infections caused by microorganisms which are sensitive to Gentamicin; Gonorrhoea.

Administration: By IM injection; 250mg every 6 hours or 500mg every 12 hours.

By infusion; 15 – 30mg/kg body weight daily in divided doses every 8–12 hours. *Gonorrhoea*; 2g stat.

Side effects: Same as for gentamicin but kanamycin has a lower therapeutic index. The major effect is damage to the eighth cranial nerve resulting in vertigo and deafness. Also, skin eruptions, nausea and vomiting may occur.

Contraindications: Same as for gentamicin

Caution: Same as for gentamicin.

AMIKACIN

Presentation: Injection containing 250mg/ml amikacin sulphate. A paediatric injection containing 50mg/ml amikacin sulphate.

Indications: Serious gram-negative infections resistant to gentamicin, neonatal sepsis.

Administration: By IM or slow IV injection or by infusion: to be administered over 3–5 minutes

Children:

1 month–11 years: 7.5 mg/kg every 12 hours OR 15mg/kg body weight once daily adjusted according to plasma-concentration monitoring

12–17 years: 7.5 mg/kg every 12 hours; increased to 7.5 mg/kg every 8 hours (max. per dose 500 mg every 8 hours) for up to 10 days, higher dose to be used in severe infection, maximum 15 g per course

Note: *one-hour peak concentration should not exceed 30mg/litre.*

Side effects: see under Gentamicin.

Contraindications: see under Gentamicin.
Caution*:* see under Gentamicin

4.1.3 Aminocyclitol

SPECTINOMYCIN

Presentation: Injection containing 2 g Spectinomycin hydrochloride powder.

Indications: Acute gonococcal urethritis, proctitis and acute gonococcal cervicitis to susceptible strains of *Neisseria gonorrhoeae*. It is only indicated in the treatment of gonorrhoea caused by penicillin-resistant organisms or in patients allergic to penicillins.

Administration: By deep IM injection; 2g, up to 4g can be given in difficult cases and in areas where there is resistance.

Children:
over 2 years; if there is no alternative treatment 40mg/kg body weight.

Side effects: Nausea, dizziness, urticaria, fever, insomnia.

Contraindications: Hypersensitivity

Caution: Pregnancy and breastfeeding.

4.1.4 Sulphonamides and Trimethoprim

Sulphonamides are derivatives of para-aminobenzoic acid. They act by inhibiting the enzyme dihydropteroate synthetase which is involved in incorporating para-aminobenzoic acid into pteridine in the formation of folic acid.

Trimethoprim is a 2,4 diaminopyrimidine derivative similar to pyrimethamine. It acts by blocking the enzyme dihydrofolate reductase which is involved in the reduction of folic acid to folinic acid.

This combination of sulphonamides and trimethoprim will provide a sequential blockade of the formation of folinic acid which is essential for DNA synthesis. The net effect is bactericidal action. The combination of sulphamethoxazole and trimethoprim is called Co-trimoxazole. The ratio of the combination is sulphamethoxazole 5: trimethoprim 1. The use of sulphonamides alone has decreased because of increasing bacterial resistance. The sulphonamides are bacteriostatic in action and are active against a wide range of gram-positive and gram-negative bacteria such as *Staphylococci, Streptococci, Enterobacter, E.coli, Klebsiella, Proteus mirabilis, Salmonella and Shigella*. They are also active against some strains of *Neisseria gonorrhoeae and Neisseria meningitis*. Some species of *Plasmodium* and *Chlamydia* are sensitive. The use of cotrimoxazole is decreasing due to resistance.

The major side effects associated with the use of sulphonamides are crystalluria, hypersensitivity reactions, haematological disorders and hepatic damage. They should be used with caution in patients with blood dyscrasia, in renal impairment and patients with Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency. They are also contraindicated in infants less than two months of age and the late third trimester of pregnancy because of the possibility of development of kernicterus.

Trimethoprim on the other hand is bactericidal in action. It is largely effective against many gram-positive, anaerobic bacteria and some gram-negative anaerobic bacteria. It is inactive against Bacteroides and has no established activity against strict anaerobes such as C*lostridium* or *Fusobacterium*. The volume of distribution of Trimethoprim is about nine times that of Sulphamethoxazole. It has been used alone in the treatment of pneumocystis carinii pneumonia (PCP), uncomplicated urinary tract infection caused by sensitive organisms and in the prophylaxis of chronic and recurrent urinary tract infections in men and women. It has also been used as prophylaxis in pneumocystis carinii pneumonia in HIV positive individuals particularly infants born to HIV positive mothers.

The combination of Trimethoprim with Sulphamethoxazole enhances activity, decreases resistance and reduces the net frequency of administration of each drug. However, some cumulative side effects have been recorded. The combination of Sulphamethoxazole with Trimethoprim is useful in the treatment of most urinary tract infections, gastrointestinal infections and pneumocystis carinii infection (high dose).

CO-TRIMOXAZOLE

Presentation: Tablets containing 400mg Sulphamethoxazole and 80mg Trimethoprim (480mg). Suspension containing 200mg Sulphamethoxazole and 40mg Trimethoprim (240mg). Intravenous infusion containing 80/16mg of Sulphamethoxazole /Trimethoprim per ml.

Indications: It should be limited to the role of drug of choice for the prophylaxis of opportunistic infections (OI), and treatment of pneumocystis carinii jirovencii. It is also

indicated for the treatment of toxoplasmosis and nocardiosis. It should only be considered for use in acute exacerbation of chronic bronchitis and infections of the urinary tract where there is good bacteriological evidence of sensitivity. Similarly, it should be used in acute otitis media where there is good reason to prefer it.

Administration: By mouth, *Adult*; 960mg every 12 hours increased to 1.44g in severe infections OR 480mg every 8 hours if treated for more than 14 days.

Prophylaxis of OIs: 960mg once daily

By intravenous infusion, *adult*; 960mg every 12 hours increased to 1.44g every 12 hours in severe infection.

High dose therapy for pneumocystis carinii pneumonia; 120mg/kg body weight in 2-4 divided doses for 14-21 days.

Children:

6 weeks–5 months; 120mg every 12 hours.

6 months–5 years; 240mg every 12 hours.

6–12 years; 480mg every 12 hours.

By intravenous infusion: 36mg/kg daily in divided doses increased to 54mg/kg daily in severe infections.

Prophylaxis in children born to HIV positive mothers; 240mg daily until HIV status is known.

Side effects: Nausea, vomiting, diarrhoea, glossitis, rashes, erythema multiform (including Stevens-Johnson syndrome), epidermal necrolysis, pancreatitis, eosinophilia, agranulocytosis, leucopenia, granulocytopenia, thrombocytopenia, megaloblastic anaemia due to the Trimethoprim component, pseudomembranous colitis, jaundice and hepatic necrosis. Diarrhoea, myocarditis, serum sickness, stomatitis, anorexia are indications for discontinuing treatment.

Contraindications: Infants under 6-weeks (risk of kernicterus), renal or hepatic failure, jaundice, blood disorders, porphyria.

Caution: Renal impairment, breastfeeding, photosensitivity, elderly patients, maintain adequate fluid intake during treatment.

TRIMETHOPRIM

Presentation: Tablets containing 100mg, 200mg trimethoprim. Injection containing 20mg/ml trimethoprim lactate.

Indications: Trimethoprim should be reserved as the drug of choice for the treatment of pneumocystis carinii pneumonia, in those who are hypersensitive to sulphonamides, urinary tract infections due to susceptible strains, acute and chronic bronchitis.

Administration: Oral; *adult*;

Acute infections: 200mg every 12 hours.

Chronic infections and prophylaxis: 100mg at night.

By slow IV injection or by infusion, 150 – 250mg every 12 hours.

Children:

Acute infections (Oral); *2–5 months*; 25mg twice daily.

6 month –5 years; 50mg twice daily.

6–12 years; 100mg twice daily.

Chronic infections and prophylaxis*;* 1 - 2mg/kg body weight at night.

By slow IV injection or by infusion:

Under 12 years; 6 – 9mg/kg body weight daily in 2 – 3 divided doses

Side effects: GIT disturbances including nausea and vomiting, pruritis, rashes, depression of haematopoiesis, erythema multiforme, toxic epidermal necrolysis and aseptic meningitis.

Contraindications: Severe renal impairment, neonates, blood dyscrasia, megaloblastic anaemia due to folate deficiency.

Caution: Renal impairment, breastfeeding, porphyria and in patients that are predisposed to folate deficiency.

4.1.5 Quinolones

These are generally effective against most gram-negative bacteria and some gram-positive bacteria. Most anaerobic bacteria are resistant. The fluorinated quinolones like ciprofloxacin

and norfloxacin have expanded spectrum of activity and increased activity compared with the non-fluorinated quinolones (e.g. nalidixic acid, oxolinic acid and cinoxacin). The piperazine group in most fluoroquinolones enhances the antipseudomonal activity.

They should be used with caution in patients with epilepsy, in hepatic or renal impairment, in pregnancy and breastfeeding. They should also be used with caution in children or adolescence (because of arthropathy).

The major side effects of the quinolones include nausea, vomiting, abdominal pain, diarrhoea, QT-prolongation, arthralgia. Less frequent side effects include anorexia, tendonitis and tendon rapture, restlessness, depression, hallucinations and confusion, peripheral neuropathy, hypo/hyper-glycaemia, photosensitivity.

NALIDIXIC ACID

Presentation: Tablets containing 500mg nalidixic acid. A suspension containing 300mg/5ml nalidixic acid.

Indications: Dysentery, urinary tract infections caused by susceptible gram-negative microorganisms, including the majority of *Proteus strains, Klebsiella, Enterobacterial species and E. Coli.*

Administration: *Adult*: 500mg-1g every 6 hours for 7 days, reduced in chronic infections to 500mg every 6 hours for 7 - 14 days.

Children:

Over 3 months: maximum dose 50mg/kg body weight daily in divided doses, reduced in prolonged therapy to 30mg/kg body weight daily.

Side effects: see notes above (4.1.5.). Also, paraesthesia, cholestasis, metabolic acidosis, increased intracranial pressure and jaundice.

Contraindications: Hypersensitivity to nalidixic acid, epilepsy or history of epilepsy.

Caution: see notes above (4.1.5.). Also, avoid exposure to strong sunlight during treatment, avoid in porphyria. Monitor blood counts, liver and renal function if treatment exceeds two weeks.

CIPROFLOXACIN

Presentation: Tablets containing 250mg, 500mg, 750mg Ciprofloxacin hydrochloride. Intravenous infusion containing 2mg/ml Ciprofloxacin lactate.

Indications: Gram-negative and gram-positive infections caused by susceptible bacteria. It is particularly active against gram-negative bacteria including *Salmonella, Shigella, Campylobacter, Neisseria* and *Pseudomonas species*. It is used in the treatment of pelvic inflammatory disease, urinary tract infections, infections of the GIT (including typhoid), gonorrhoea, septicaemia and for skin and soft tissue infections, post-exposure prophylaxis to meningococcal.

Administration: Oral*, Adult*;

Urinary tract infection: 250–500mg twice daily.

Gonorrhoea: 500mg single dose.

Most other infections; 500–750mg twice daily.

By intravenous infusion; 400mg twice daily (over 30 - 60 minutes).

Children:

Not recommended. However, where benefits outweigh the risk:

By mouth, 7.5–15mg/kg body weight daily in 2 divided doses **OR**

By intravenous infusion, 5–10mg/kg body weight daily in 2 divided doses.

Side effects: see notes above (4.1.5.)

Contraindications: Hypersensitivity to 4-Quinolones or quinolone group of antibacterials, pregnancy.

Caution: see notes above (4.1.5.) exacerbation of myasthenia gravis

LEVOFLOXACIN

Presentation: Premix, ready-to-use injection containing 5mg/ml. Oral solution containing 25mg/ml, and tablet containing 250mg, 500mg and 750mg; ear/eye drops.

Indications: Drug resistant Tuberculosis, community acquired pneumonia, nosocomial pneumonia, acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, inhalational anthrax, skin/skin structure infection, chronic bacterial prostatitis, complicated urinary tract infections and acute pyelonephritis, uncomplicated urinary tract infections, plaque, pseudomonas aeruginosa pulmonary infections

Administration: ***Adult;***

Management of Drug-resistant TB: 750mg to 1000 mg once daily for 18 to 20 months

Community-Acquired Pneumonia; Complicated Urinary Tract Infections & Acute Pyelonephritis: 500 mg PO/IV once daily for 7-14 days or 750 mg PO/IV once daily for 5 days

Nosocomial Pneumonia/ Skin/Skin Structure Infections: 750 mg PO/IV once daily for 7-14 days

Inhalational Anthrax Post-exposure therapy: 500 mg PO once daily for 60 days, beginning as soon as possible after exposure

Chronic Bacterial Prostatitis: 500 mg PO/IV once daily for 28 days

Children

Management of Drug-resistant TB

The following doses, based on body weight, may be given orally or intravenously for 60 days

< 50 kg: 8 mg/kg (maximum 250 mg) every 12 hours

50 kg or more: 500 mg once every 24 hours

Inhalational Anthrax Post-exposure therapy

≥6 months and <50 kg: 8 mg/kg PO 12hourly for 60 days beginning as soon as possible after exposure; individual dose not to exceed 250 mg

≥6 months and >50 kg: 500 mg PO once daily for 60 days, beginning as soon as possible after exposure

Safety in children for treatment duration >14 days has not been established

MOXIFLOXACIN

Presentation: Tablet containing 400mg, injectable solution containing 400mg/250ml

Indications: Drug resistance Tuberculosis, treatment and prophylaxis of pneumonic and scepticaemic plague;

Administration: *Adult; Treatment of drug-resistant tuberculosis*: 400mg OD for 18 to 20 months *Skin and Skin Structure Infections*

Complicated: 400 mg PO/IV once Daily for 7-21 days

Intra-abdominal Infections

Complicated: 400 mg PO/IV once Daily for 5-14 days

Pneumonic & Septicemic Plague: 400 mg PO/IV once Daily for 10-14 days

Children: Safety for children less than 18 years not established. To be prescribed under specialist care.

Side effects: Nausea, diarrhea , dizziness, decreased amylase , decreased basophils, eosinophils, hemoglobin, prothrombin time, red blood cells, neutrophils, decreased serum glucose, Increased serum chloride, Increased serum ionized calcium, Immune hypersensitivity reaction, prolonged QT interval, acute renal failure, agranulocytosis, anaphylactic reaction, aplastic anemia, extrinsic allergic alveolitis, hemolytic anemia, hepatic failure, hepatic necrosis, hepatitis, pancytopenia, seizure, serum sickness due to drug, stevens-johnson syndrome, tendon rupture, tendinitis, thrombocytopenia,torsades de pointes, toxic epidermal necrolysis

Contraindications: Hypersensitivity to moxifloxacin or any member of the quinolone class of antibacterials. Avoid in patients with previous history of serious side effects outlined in cautions above.

Cautions: Fluoroquinolones been associated with disabling and potentially irreversible serious adverse reactions from different body systems that can occur together in the same patient; adverse reactions include tendinitis,

tendon rupture, arthralgia, myalgia, peripheral neuropathy, and central nervous system effects (hallucinations, anxiety, depression, insomnia, severe headaches, and confusion); discontinue treatment immediately at the first signs or symptoms of any serious adverse reaction.

NORFLOXACIN

Presentation: Tablet containing 400mg Norfloxacin.

Indications: Urinary tract infections, chronic prostatitis.

Administration: *Urinary tract infections*; 400mg twice daily for 7 - 10 days (3 days for uncomplicated lower urinary tract infection).

Chronic relapsing urinary tract infection: 400mg twice daily for up to 12 weeks; may be reduced to 400mg once daily if adequate suppression within the first 4 weeks.

Chronic prostatitis; 400mg twice daily for 28 days.

Side effects: See notes above; also, euphoria, anxiety, tinnitus, polyneuropathy, exfoliative dermatitis, pancreatitis, vasculitis.

Contraindications: Hypersensitivity to 4-Quinolones or quinolone group of antibacterials.

Caution: See notes above. Renal impairment.

NOTE: may impair the performance of skilled tasks (e.g. driving).

4.1.6 Nitrofuran Medicines

These are synthetic Nitrofuran derivative antibacterial agents. They are bacteriostatic in action mainly at low concentration but bactericidal at higher concentrations. They are mostly used in the treatment of urinary tract infections caused by sensitive gram-negative bacilli and gram-positive cocci such as *Escherichia coli, Klebsiella, Enterobacter species, Enterococci* and *some strains of Staphylococci*.

They inhibit acetyl coenzyme A interfering with bacterial carbohydrate metabolism. The therapeutic concentration in the serum and tissue is very low after oral administration, hence they are rarely used for the treatment of systemic infections. High concentrations are excreted in the urine and antibacterial activity is greater in acidic urine. Acidic urine enhances tubular reabsorption of nitrofuran Medicines enhancing their antibacterial activity in the renal tissues. Antibacterial activity is reduced at higher pH.

The major side effects associated with the use of nitrofurans include anorexia, nausea, vomiting, acute and chronic pulmonary reactions, cholestatic hepatitis, jaundice, thrombocytopenia and aplastic anaemia. An example is a nitrofurantoin which occurs in two forms; the macrocrystalline form which is absorbed more slowly due to slower dissolution and causes less gastrointestinal distress and the microcrystalline form which has a higher dissolution rate and is more rapidly absorbed.

NITROFURANTOIN

Presentation: Tablets containing 50mg, 100mg Nitrofurantoin. A suspension containing 25mg/5ml Nitrofurantoin.

Indications: Urinary tract infections due to susceptible strains *of E. coli, Enterococci, Staphylococcus aureus* and certain strains of *Klebsiella, Enterobacteriaceae* and *Proteus* species.

Administration: *Adult*;

Acute uncomplicated infection: 50-100mg every 6 hours with food for 7 days.

Severe chronic recurrent infection; 100mg every 6 hours with food for 7 days.

Prophylaxis; 50 – 100mg at night.

Children:

Infection

Over 3 months; 3mg/kg body weight daily in 4 divided doses.

Prophylaxis

Over 3 months; 1mg/kg body weight at night.

Side effects: see notes above (4.1.6.). Also, peripheral neuropathy, angioedema, urticaria, rash and pruritis, exfoliative dermatitis, erythema multiforme, pancreatitis.

Contraindications: Impaired renal function, infants less than 3 months old, G6PD deficiency, porphyria, late pregnancy and breastfeeding.

Caution: Predisposing conditions such as renal impairment, anaemia, diabetes, electrolyte imbalance; vitamin B deficiency may enhance the peripheral neuropathy produced by nitrofurantoin. Monitor Liver Function Test (LFT).

4.1.7 Macrolides

These antibiotics contain many numbered lactone rings to which are attached one or more sugars. They bind irreversibly to the 50S ribosomal subunit and inhibit RNA dependent protein synthesis. They are weak bases and their activity increases in alkaline pH. They enter the pleural fluid, ascitic fluid, middle ear exudates and sputum. Penetration into the CSF is poor but increases in meningitis. They are bacteriostatic but may be bactericidal at higher concentrations. They are used in the treatment of respiratory, genital, gastrointestinal tract, skin and soft tissue infections especially when Beta-lactam antibiotics or tetracyclines are contra-indicated. They are effective against most strains of *Streptococcus, Haemophilus, Bordetella pertussis, Legionella pneumophila, Chlamydia species, Mycoplasma pneumonia and Ureaplasma urealyticum*. Examples include azithromycin, clarithromycin, erythromycin and troleandomycin.

The major side effects include cholestatic jaundice, hepatitis, pseudomembranous colitis and hypersensitivity reactions.

ERYTHROMYCIN

Presentation: Tablets or capsules containing 250mg, 500mg erythromycin. A suspension containing 125mg/5ml erythromycin ethyl succinate. Intravenous infusion (powder for reconstitution) containing 1g erythromycin lactobionate.

Indications: Alternative to penicillin in hypersensitive patients, alternative to tetracyclines in pregnant women; group-B streptococcus, campylobacter enteritis, pneumonia, legionnaires' disease, syphilis, non-gonococcal urethritis, chronic prostatitis, acne vulgaris, diphtheria.

Administration: Oral, adult and *child over 8 years old*; 250–500mg every 6 hours or 0.5g – 1g every 12 hours up to 4g daily in severe infections.

Children:

Up to 2 years; 125mg every 6 hours.

2–8 years; 250mg every 6 hours.

Doses may be doubled in severe infections. In mild infections where oral treatment is not possible; give injection at 25mg/kg body weight daily.

Side effects: Nausea, vomiting, abdominal discomfort, diarrhoea (pseudomonas colitis), urticaria, rashes, allergic reactions, reversible loss of hearing reported after large doses, cholestatic jaundice and cardiac effects.

Contraindications: Liver disease, hypersensitivity to erythromycin.

Caution: Renal or hepatic impairment, pregnancy and breastfeeding, porphyria and in cardiac arrhythmias.

AZITHROMYCIN

Presentation: Tablet containing 250mg azithromycin dihydrate. Film-coated tablet containing 500mg azithromycin dihydrate. An oral suspension containing 200mg/5ml azithromycin dihydrate.

Indications: Respiratory tract infections, otitis media, skin and soft tissue infections, uncomplicated genital chlamydial infections and non-gonococcal urethritis, as an alternative to tetracyclines in pregnancy.

Administration: *Adult*: 500mg once daily for 3 days.

Uncomplicated genital chlamydial infections and non-gonococcal urethritis: 1g as a single dose.

Children:

Over 6 months; 10mg/kg once daily for 3 days

Body weight 15-25kg: 200mg once daily for 3 days

Body weight 26-35kg: 300mg once daily for 3 days

Bodyweight 36-45kg: 400mg once daily for 3 days.

Side effects: Anorexia, dyspepsia, constipation, dizziness, headache, drowsiness, photosensitivity, hepatitis, interstitial nephritis, acute renal failure, asthenia, paraesthesia, convulsions and mild neutropenia, rarely tinnitus, hepatic necrosis, hepatic failure and taste disturbances.

Contraindications: See under erythromycin.

Caution: See under erythromycin

CLARITHROMYCIN

Presentation: Film-coated tablets containing 250mg, 500mg clarithromycin. A suspension containing 125mg/5ml clarithromycin powder for reconstitution with water.

Indications: Peptic Ulcer Disease, respiratory tract infections, mild to moderate skin and soft tissue infections, otitis media.

Administration: *Adult;* orally 250mg every 12 hours for 7 days increased in severe infections to 500mg every 12 hours for up to 14 days.

By intravenous infusion into larger proximal vein, 500mg twice daily.

Children:

Body weight under 8kg: 7.5mg/kg twice daily

8-11kg (1-2years): 62.5mg twice daily

12-19kg (3-6 years): 125mg twice daily

20 - 29kg (7-9 years): 187.5mg twice daily

30-40kg (10–12 years): 250mg twice daily

By intravenous infusion into larger proximal vein, 500mg twice daily

By intravenous infusion CHILD not recommended.

Side effects: see under Erythromycin; also reported, dyspepsia, headache, smell and taste disturbances, tooth and tongue discolouration, stomatitis, glossitis, pancreatitis, arthralgia, myalgia, dizziness, vertigo, tinnitus, anxiety, insomnia, nightmares, confusion, psychosis, convulsions, paraesthesia, hypoglycaemia, hepatitis, renal failure, leucopenia, and thrombocytopenia; on intravenous infusion, local tenderness, phlebitis.

Caution: See under Erythromycin.

4.1.8 Chloramphenicol

Chloramphenicol is a potent, potentially toxic, broad-spectrum antibiotic which should be reserved for the treatment of life-threatening infections, particularly those caused by *Salmonella* species and *Haemophilus influenza*. It inhibits protein synthesis and it is bacteriostatic in action. It exhibits high tissue penetration and reasonable concentration is achieved in the CSF even when the meninges are not inflamed. It is effective against a wide range of gram-positive and gram-negative bacteria and it is also active in-vitro against Rickettsiae, Lymphogranuloma psittacosis and Vibrio cholera. Chloramphenicol causes serious and sometimes fatal blood dyscrasias (aplastic anaemia, hypoplastic anaemia, thrombocytopenia). Chloramphenicol must not be used when less potentially toxic antibacterial agents are available. It must not be used to treat trivial infections such as influenza, colds, or throat infections, infections other than indicated or as prophylaxis for bacterial infections. Adequatedequate blood studies must be performed during treatment to detect blood disorders such as cytopenia before they become irreversible.

CHLORAMPHENICOL

Presentation: Capsules containing 250mg Chloramphenicol. A suspension containing 125mg/5ml Chloramphenicol palmitate. An injection containing 1g Chloramphenicol sodium succinate.

Indications: Potent, potentially toxic broad-spectrum antibiotic reserved for the treatment

of life-threatening infections for which less potentially toxic Medicines are ineffective or contraindicated, particularly for *Salmonella* infection and *Haemophilus influenzae*. It could also be used for the treatment of typhoid and life-threatening anaerobic infections, *Rickettsiae, Lymphogranulomapsitacosis* and bacterial infections due to susceptible microorganisms in which the benefit of use outweighs the serious side effects.

Administration: Oral or by intravenous injection or by intravenous infusion,

Adult: 50mg/kg body weight daily in 4 divided doses (exceptionally, can be doubled for severe infections such as septicaemia and meningitis. Providing high doses are reduced as soon as the clinical condition improves*).*

Children:

Neonate up to 14 days: 12.5 mg/kg twice daily

Neonate 14 days to 28 days: 12.5 mg/kg 2–4 times a day

Haemophilus epiglottis and pyogenic meningitis: 50–100mg/kg body weight daily in divided doses (high doses decreased as soon as the clinical condition improves).

Side effects: See notes above. Bone marrow depression, peripheral neuritis, optic neuritis, erythema multiforme, nausea, vomiting, diarrhoea.

Contraindications: Pregnancy, porphyria, trivial infections.

Caution: Avoid repeated courses and prolonged (beyond 7 days) treatment, reduce dose in hepatic or renal impairment, blood counts required before and periodically during treatment, avoid concurrent use with other medicines causing bone marrow depression, breastfeeding.

4.1.9 Cephalosporins

They are semi-synthetic derivatives of Cephalosporium C and belong to the beta-lactam antibiotics. They are composed of a 7-amino cephalosporins acid nucleus which is composed of a beta-lactam ring fused with a 6-member dihydrothiazine ring.

They are classified into the first, second and third generation. The classification is based on their spectrum of activity. In general progression from first to the third generation reveals broadening gram-negative activity, loss of efficacy on gram-positive organisms, greater efficacy against resistant organisms and increased cost.

They inhibit mucopeptide synthesis in the bacterial cell wall. They are broad-spectrum antibiotics which are used for the treatment of septicaemia, pneumonia, meningitis, biliary tract infections, peritonitis and urinary tract infections.

The pharmacology of the cephalosporins is similar to that of the penicillins. Excretion is principally through the renal route and is blocked by probenecid.

The principal side effect of the cephalosporins is hypersensitivity and about 10% of the penicillin-sensitive patients will also be allergic to cephalosporins. Haemorrhage due to interference with blood clotting factors has been associated with several cephalosporins. Examples of first-generation cephalosporins are cephradine and cephazolin; the second generation includes cefuroxime and cefamandole; the third generation is cefotaxime, ceftizoxime and cefodizime.

First Generation

CEPHALEXIN

Presentation: Tablets or capsules containing 250mg, 500mg Cephalexin. A suspension containing 125mg/5ml Cephalexin.

Indications: Respiratory tract infection due *to Streptococcus pneumonia and group A-B Haemolytic streptococci,* otitis media caused *by Streptococcus pneumonia, Haemophilus influenzae,* skin and skin structure infections caused by S*taphylococci or Streptococci species*, bone infections caused by *Staphylococci species* and genito-urinary infections including acute prostatitis.

Administration: 250mg every 6 hours OR 500mg every 8–12 hours increased to 1–1.5g every 6 – 8 hours for severe infections.

Children:

25mg/kg body weight daily in divided doses, doubled for severe infections, maximum 100mg/kg body weight daily;

Under 1 year: 125mg every 12 hours.

1–5 years: 125mg every 8 hours.

6–12 years: 250mg every 8 hours.

Side effects: see 4.1.9. above.

Contraindications: see 4.1.9. above

Caution: see 4.1.9. above.

Second Generation

CEFUROXIME

Presentation: Tablets containing, 250mg, 500mg cefuroxime axetil. Suspension containing 125mg/5ml cefuroxime axetil. An injection containing 250mg, 750mg, 1.5g cefuroxime sodium.

Indications: See 4.1.9. under Cefotaxime; but more active against *Haemophilus influenza* and *Neisseria gonorrhoeae.*

Administration: Oral; *Adult;* 250-500mg twice daily in most infections including mild to moderate lower respiratory tract infections. Doubled for more severe lower respiratory tract infections or if pneumonia is suspected.

By IM or IV injection or by intravenous infusion; 750mg every 6–8 hours: 1.5g every 6 – 8 hours in severe infections.

Surgical prophylaxis: 1.5g by IV injection at induction, may be supplemented with 750mg by IM injection 8–16 hours later (*abdominal, pelvic and orthopaedic operations*) OR followed by 750mg by IM injection every 8 hours for a further 24–48 hours (*cardiac, pulmonary, oesophageal and vascular operations*).

Children:

Urinary tract infections: 125mg twice daily, doubled in pyelonephritis.

Over 3 months: 125mg twice daily, if necessary doubled

Over 2 years with otitis media.

Child: usual dose 60mg/kg body weight daily (range of 30–100mg/kg daily) in 3 – 4 divided doses (2–3 divided doses in neonates).

Side effects: see 4.1.9. above.

Contraindications: see 4.1.9. above

Caution: see 4.1.9. above

Third Generation

CEFOTAXIME

Presentation: Injection containing 250mg, 1g Cefotaxime sodium powder.

Indications: Lower respiratory tract infections including pneumonia, urinary tract infections, gynaecological infections including pelvic inflammatory disease (PID), endometritis and pelvic cellulitis, septicaemia, skin and skin structure infections, intra-abdominal infections including peritonitis, bone or joint infections, CNS infections and pre-operative prophylaxis.

Administration: By intramuscular or intravenous injection or by intravenous infusion

Urinary tract and mild to moderate infections; 1g every 12 hours. In severe renal impairment, dose to be halved after the initial dose of 1g.

Moderate to serious infections; 1g every 8-hours.

Life-threatening infections: 2g every 8 hours. Especially, for life-threatening infections due to organisms less sensitive to cefotaxime, 6-hourly up to 12g daily.

By intravenous infusion; 1–2g over 20 – 60 minutes.

Children:

Neonate; 50mg/kg body weight daily in 2 – 4 divided doses; in severe infections 150–200mg/kg daily.

Child; 100–150mg/kg body weight daily in 2–4 divided doses; in severe infections, up to 200mg/kg daily.

Side effects: See notes above. Also, diarrhoea (rarely pseudo-membranous colitis), nausea and vomiting, allergic reactions including rashes, pruritis, urticaria, serum sickness-like reactions with rashes, fever and arthralgia, anaphylaxis, disturbance in liver enzymes, transient hepatitis, cholestatic jaundice, eosinophilia and blood disorders.

Contraindications: Cephalosporin hypersensitivity and porphyria.

Caution: Penicillin hypersensitivity, renal impairment, pregnancy and breastfeeding, false-positive urinary glucose may occur during treatment.

CEFTRIAXONE

Presentation: Injection powder, containing

250mg, 500mg and 1g ceftriaxone as sodium for reconstitution.

Indications: as for Cefotaxime, surgical prophylaxis, prophylaxis of meningococcal meningitis in post-exposure.

Administration: By deep intramuscular injection, or by intravenous injection over at least 2–4 minutes, or by intravenous infusion:

1 g daily; 2–4 g daily (in 1-2 divided doses) in severe infections

Early syphilis: by deep IM injection, 500 mg daily for 10 days.

Uncomplicated gonorrhoea and for post-exposure prophylaxis for neiserra by deep IM injection, 250 mg as a single dose. Surgical prophylaxis, by deep intramuscular injection or by intravenous injection over at least 2–4 minutes, 1 g at induction; colorectal surgery, by deep intramuscular injection or by intravenous infusion, 2 g at induction; intramuscular doses over 1 g divided between more than one site

Intramuscular doses over 1g divided between more than one site; single intravenous doses above 1g by intravenous infusion only.

Endocarditis caused by Haemophilus, actinobacillus, cardiobacterium, eikenella, and Kinsella species ('HACEK organisms') (in combination with another antibacterial) by intravenous infusion, 2–4 g daily.

Children:

Neonate: (by IV infusion over 60 minutes), 20–50 mg/kg daily (max. 50 mg/kg daily)

Infant and Child under 50 kg: by deep IM injection, or by IV injection over 2–4 minutes, or by IV infusion, 20–50 mg/kg daily; up to 80 mg/kg daily in severe infections; doses of 50 mg/kg and over by intravenous infusion only.

50 kg and over: adult dose

Side effects: Calcium ceftriaxone precipitates in urine (particularly in very young, dehydrated or those who are immobilised) or in gall bladder-consider discontinuation if symptomatic; rarely prolongation of prothrombin time, pancreatitis.

Contraindications: Neonates with jaundice, hypoalbuminaemia, acidosis or impaired bilirubin binding; concomitant treatment with calcium in children—the risk of precipitation in urine and lungs of neonates (and possibly infants and older children). **Cautions:** Severe renal impairment; hepatic impairment if accompanied by renal impairment, premature neonates; may displace bilirubin from serum albumin, administer over 60 minutes in neonates (see also Contraindications); treatment longer than 14 days, renal failure, dehydration— the risk of ceftriaxone precipitation in gall bladder.

CEFIXIME

Presentation: Tablet containing 200mg and 400mg; Suspension containing 100mg/5ml of Cefixime trihydrate.

Indications: Acute infections due to sensitive Gram-positive and Gram-negative bacteria, Uncomplicated anogenital gonorrhea

Administration: *Adult;*

Uncomplicated anogenital gonorrhoea, oral: 400 mg as a single dose

Acute infections due to sensitive Gram-positive and Gram-negative bacteria, oral: 200–400 mg daily given as a single dose or in 2 divided doses for 7 days, may be continued for up to 14 days if necessary, depending on the severity of infection.

Children:

Acute infections due to sensitive Gram-positive and *Gramnegative bacteria*

6–11 months: 75 mg daily

1–4 years: 100 mg daily

5–9 years: 200 mg daily

10–17 years: 200–400 mg daily, alternatively 100–200 mg twice daily

Uncomplicated gonorrhoea [anogenital and pharyngeal

infection—in combination with azithromycin]

13–17 years: 400 mg for 1 dose

Disseminated gonococcal infection [when sensitivity

confirmed]

16–17 years: 400 mg twice daily, following intravenous antibacterial treatment, starting 24–48 hours after symptoms improve, to give 7 days treatment in total.

Side effects: See above

Contraindications: Hypersensitivity to cefalosporins, penicillins or any beta-lactam antibiotics.

Cautions: Sensitivity to Beta Lactam antibacterials (avoid if history of immediate hypersensitivity reaction), moderate renal impairment, use may result in false positive urinary glucose and false positive Coombs' test.

Fourth Generation

CEFEPIME

Presentation: Powder for Injection (IV, Infusion, IM) containing 1g and 2g of Cefepime

Indications: Infections due to sensitive Gram-positive and Gram-negative bacteria, mild to moderate urinary tract infections.

Administration: *Adult and Child (body-weight 41 kg and above):*

Infections due to sensitive Gram-positive and Gram-negative bacteria: 50 mg/kg every 12 hours (max. per dose 2 g), increased if necessary to 50 mg/kg every 8 hours (max. per dose 2 g), increased dose used for severe infections, intravenous route preferred in severe infections.

Mild to moderate urinary tract infections: 0.5–1 g every 12 hours

Mild to moderate infections due to sensitive Gram-positive and Gram-negative bacteria: 1 g every 12 hours

Severe infections due to sensitive Gram-positive and Gram-negative bacteria: 2 g every 12 hours, increased if necessary to 2 g every 8 hours, increased dose used for very severe infections

Children:

Infections due to sensitive Gram-positive and Gram-negative bacteria

1 month: 30mg/kg every 8–12 hours; intravenous route preferred in severe infections

2 months–17 years (body-weight up to 41 kg): 50 mg/kg every 12 hours (max. per dose 2 g), increased if necessary to 50 mg/kg every 8 hours (max. per dose 2 g).

Side Effects: see 4.1.9. above

Contraindications: see 4.1.9. above

Caution: see 4.1.9. above

4.1.10 Tetracyclines

The tetracyclines are broad-spectrum antibiotics whose value has decreased owing to increasing bacterial resistance. They remain however the treatment of choice for infections caused by *Chlamydia* (trachoma, psittacosis, salpingitis, urethritis and Lymphogranuloma venereum),

Rickettsia (including Q-fever*), Mycoplasma* (respiratory and genital) infections. They are also used in acne, in destructive (refractory) periodontal disease, an exacerbation of chronic bronchitis and for leptospirosis. The tetracyclines are deposited in growing bones and teeth (being bound to calcium) causing dental staining and occasionally dental hypoplasia. They should therefore not be given to children under twelve years or pregnant or breastfeeding women. Most tetracyclines have a similar spectrum of activity but may have varying degrees of pharmacokinetics profile. However, minocycline has a broader spectrum of activity compared to the other tetracyclines.

Except for minocycline and doxycycline, the tetracyclines may exacerbate renal failure and should not be given to patients with kidney disease. Absorption of tetracyclines is decreased by milk (except doxycycline and minocycline), antacids, calcium, iron preparations and magnesium salts.

DOXYCYCLINE

Presentation: Tablets or capsules containing 50mg, 100mg Doxycycline hydrochloride.

Indications: Exacerbation of chronic bronchitis, brucellosis, gonorrhoea (if allergic or resistant to penicillins), syphilis, chlamydia, *Balantidum coli,* pelvic inflammatory disease, chronic prostatitis and sinusitis.

Administration: Usual dose: 200mg on day 1, then 100mg daily

Severe infections including chronic urinary tract infections: 200mg daily.

Acne: 100mg twice daily for 6–12 weeks or longer. Capsules should be swallowed whole with plenty of fluid during meals while sitting or standing.

Side effects: Nausea, vomiting, diarrhoea, headache and visual disturbances (may indicate benign intracranial hypertension), pancreatitis and pseudomembranous colitis on prolonged treatment.

Contraindications: Severe renal impairment, pregnancy, breastfeeding, children under 12 years and systemic lupus erythematosus.

Caution: Take with food; hepatic impairment and history of photosensitivity.

TETRACYCLINE

Presentation: Tablets or capsules containing 250mg and 500mg tetracycline hydrochloride. IM injection containing 100mg tetracycline hydrochloride. Intravenous infusion containing 250mg tetracycline hydrochloride.

Indications: see doxycycline above, also pleural effusion due to malignancy or cirrhosis, mycoplasma and rickettsia.

Administration: *Oral*; 250mg every 6 hours, increased in severe infections to 500mg every 6 – 8 hours.

Non-gonococcal urethritis: 500mg every 6 hours for 7–14 days (21 days if failure or relapse following the first course).

IM. injection; 100mg every 8 – 12 hours, or every 4 – 6 hours in severe infection.

By intravenous infusion; 500mg every 12 hours maximum 2g daily.

Side effects: Nausea, vomiting, diarrhoea, headache and visual disturbances (may indicate benign intracranial hypertension), pancreatitis and pseudomembranous colitis on prolonged treatment.

Contraindications: Severe renal impairment, pregnancy, breastfeeding, children under 12 years and systematic lupus erythematosus.

Caution: Hepatic impairment where it should not be administered intravenously, renal impairment (avoid if severe), history of photosensitivity, avoid giving with milk products and antacids since these products reduce the absorption of tetracycline.

4.1.11 5- Nitro imidazoles

The 5-nitro imidazole antimicrobial agents are active against various anaerobic bacteria and protozoa. Their mode of action is not well understood; however, they appear to enter the cells of microorganisms that contain nitro reductase where their nitro group is reduced to

intermediate compounds which bind to DNA leading to inhibition of synthesis of DNA and cell lysis.

They are active against many protozoa such *as Entamoeba histolytica, Giardia lamblia, Trichomonas vaginalis*, and most obligate anaerobes but generally not effective against facultative anaerobes or obligate anaerobes. They have a large apparent volume of distribution and are well distributed in the various tissues.

The common side effects associated with the use of 5-nitro imidazoles include nausea, vomiting, unpleasant taste, furred tongue, headache, dizziness, prolonged use may cause peripheral neuropathy, transient epileptiform seizures and leucopenia.

Tinidazole is similar to EYEdazole but has a longer duration of action and hence it is administered less frequently. Their major use is in the treatment of amoebiasis, giardiasis, trichomonas, bacterial vaginosis and systemic anaerobic infections. They should generally be used with caution in the first trimester of pregnancy, in breastfeeding and hepatic impairment.

METRONIDAZOLE

Presentation: Tablets containing 200mg, 400mg Metronidazole. A suspension containing 200mg/5ml Metronidazole benzoate. Intravenous infusion containing 5mg/ml Metronidazole. Suppositories containing 500mg Metronidazole; oral gel and skin cream.

Indications: Amoebic dysentery, trichomoniasis, giardiasis, systemic anaerobic infections particularly those due to *Bacteroides fragilis* and C*lostridium perfringens*, it is also useful in surgical and gynaecological sepsis in which its activity against colonic anaerobic bacteria is important. Useful in the treatment of antibiotic-associated colitis (pseudomembranous colitis) and anaerobic dental infections due to susceptible organisms.

Administration: *Adult*;

Anaerobic infections (usually treated for seven days): Oral, 800mg initially then 400mg every 8 hours. By IV infusion; 500mg every 8 hours.

Bacterial vaginosis; orally 400mg twice daily for 7 days or 2g as a single dose.

Acute ulcerative gingivitis; orally 200mg every 8 hours for 3 days.

Acute dental infections; orally, 200mg every 8 hours for 3 – 7 days.

Trichomoniasis: orally 2g as a single dose.

Giardiasis: orally 200mg every 8 hours for 7 days.

Amoebic dysentery; orally 400mg every 8 hours for 7 days.

Surgical prophylaxis; Oral; 400mg every 8 hours started 24 hours before surgery, then continued postoperatively by intravenous infusion or rectally until oral administration can be resumed.

By rectum; 1g every 8 hours or 125 – 250mg every 8 hours. By intravenous infusion; 500mg shortly before surgery then every 8 hours until oral administration can be resumed.

Children:

Anaerobic infections: Any route 7.5mg/kg body weight every 8 hours.

Acute ulcerative gingivitis;

1–3 years; 50mg every 8 hours.

3–7 years; 100mg every `12 hours.

7 – 10 years; 100mg every 8 hours all for 3 days.

Giardiasis:

Less than 5 years; 50mg every 8 hours, all for 7 days.

5 – 12 years; 100mg every 8 hours.

Amoebic dysentery;

Less than 9 years: 200mg every 8 hours for 7 days.

Surgical prophylaxis: 7.5mg/kg body weight every 8 hours.

Side effects: Nausea, vomiting, unpleasant taste and gastro-intestinal disturbances, rashes, urticaria and angioedema, rarely drowsiness, headache, dizziness, ataxia and darkening of urine. On prolonged or intensive therapy,

peripheral neuropathy, transient epileptiform seizures and leucopenia.

Contraindications: Hypersensitivity to metronidazole.

Caution: Disulfiram-like reactions with alcohol, hepatic impairment, pregnancy and breastfeeding.

TINIDAZOLE

Presentation: Tablets containing 500mg Tinidazole

Indications: See under Metronidazole. It is longer acting than Metronidazole.

Administration: *Anaerobic infections*; 2g stat followed by 1g daily for 5 – 6 days or 500mg twice daily for 5 – 6 days.

Bacterial vaginosis and acute ulcerative gingivitis; 2g as a single dose.

Abdominal surgery prophylaxis; 2g as a single dose approximately 12-hours before surgery.

Side effects: see under Metronidazole.

Contraindications: see under Metronidazole.

Caution: see under Metronidazole.

4.1.12 Carbapenems

MEROPENEM

Presentation: Powder for injection containing 500mg and 1g as meropenem trihydrate.

Indications: Aerobic and anaerobic Gram-positive and Gram-negative infections, hospital-acquired sepsis, Exacerbations of chronic lower respiratory-tract infection in cystic fibrosis, Meningitis, Endocarditis.

Administration: *Adult, Child body weight 50 kg and above*

Aerobic and anaerobic Gram-positive and Gram-negative infections, hospital-acquired sepsis*, by IV infusion or IV* injection: 0.5–1 g every 8 hours.

Exacerbations of chronic lower respiratory tract infection in cystic fibrosis; Meningitis; Endocarditis (in combination with another antibacterial) *by IV infusion or IV injection*: 2 g every 8 hours

Children: *by IV infusion or IV injection*:

Aerobic and anaerobic Gram-positive and Gram-negative

Infections; Hospital-acquired septicaemia

Neonate up to 7 days: 20 mg/kg every 12 hours.

Neonate 7 days to 28 days: 20 mg/kg every 8 hours.

1 month–11 years (body weight up to 50 kg): 10–20 mg/kg every 8 hours

Severe aerobic and anaerobic Gram-positive and Gramnegative infections

Neonate up to 7 days: 40 mg/kg every 12 hours.

Neonate 7 days to 28 days: 40 mg/kg every 8 hours.

Exacerbations of chronic lower respiratory-tract infection

in cystic fibrosis

By intravenous infusion

1 month–11 years (body weight up to 50 kg): 40 mg/kg every 8 hours

1 month–11 years (body weight 50 kg and above): 2 g every 8 hours

12–17 years: 2 g every 8 hours

Meningitis

By intravenous infusion

Neonate up to 7 days: 40 mg/kg every 12 hours.

Neonate 7 days to 28 days: 40 mg/kg every 8 hours.

1 month–11 years (body weight up to 50 kg): 40 mg/kg every 8 hours

1 month–11 years (body weight 50 kg and above): 2 g every 8 hours

12–17 years: 2 g every 8 hours

Side effects: Abdominal pain, diarrhoea, headache, inflammation, nausea, pain, skin reactions, thrombocytosis, vomiting, agranulocytosis, antibiotic associated colitis, eosinophilia, haemolytic anaemia, increased

risk of infection, leucopenia, neutropenia, paraesthesia, Severe cutaneous adverse reactions (SCARs), thrombocytopenia, thrombophlebitis.

Contraindication: Hypersensitivity

Cautions: Coadministration with valproic acid may increase risk of breakthrough seizures.

In renal impairment, adjust doses as follows:

- Use normal dose every 12 hours if EGFR 26–50ml/min/1.73 m2.
- Use half normal dose every 12 hours if EGFR 10–25 ml/min/1.73 m2.
- Use half normal dose every 24 hours if EGFR less than 10 ml/min/1.73 m2.

4.1.13 Glycopeptide

VANCOMYCIN

Presentation: Powder for injection containing 500 mg and 1g as Vancomycin Hydro-Chloride.

Indications: Treatment of infections with susceptible organisms including clostridium difficile, methicillin-resistant staphylococcal pneumonia, staphylococcal meningitis, antibiotic-associated colitis, sepsis, cellulitis, endocarditis treatment and prophylaxis;

Administration: *Adult*; by IV infusion

Adult: 15–20 mg/kg every 8–12 hours (max. per dose 2g) adjusted according to plasma-concentration monitoring

Serious staphylococcal infections: 500 mg over at least 60 minutes every 6 hours or 1 g over at least 100 minutes every 12 hours

Elderly; (over 65 years): 500 mg every 12 hours or 1 g once daily

Endocarditis prophylaxis (for procedures under general anaesthetic): 1 g over at least 100 minutes, then gentamicin 120 mg at induction or 15 minutes before procedure

Children:

Serious staphylococcal infections, by IV infusion

Neonate up to 1 week: 15 mg/kg initially, then 10 mg/kg every 12 hours

Neonate 1–4 weeks: 15 mg/kg initially, then 10 mg/kg every 8 hours

Child over 1 month: 10 mg/kg every 6 hours

Antibiotic-associated colitis, oral

Child 1 month–5 years: 5 mg/kg every 6 hours

Child over 5 years: 62.5 mg every 6 hours

Side effects: Nephrotoxicity including renal failure and interstitial nephritis; ototoxicity (discontinue if tinnitus occurs); blood disorders including neutropenia (usually after 1 week or cumulative dose of 25g), rarely agranulocytosis and thrombocytopenia; nausea; chills, fever; eosinophilia, anaphylaxis, rashes (including exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis, and vasculitis); phlebitis (irritant to tissue); on rapid infusion, severe hypotension (including shock and cardiac arrest), wheezing, dyspnoea, urticaria, pruritus, flushing of the upper body ('red man' syndrome), pain and muscle spasm of back and chest).

Caution: Avoid rapid infusion (risk of anaphylactoid reactions, see Side effects); rotate infusion sites; renal impairment; elderly; avoid if history of deafness; all patients require plasma vancomycin measurement (after 3 or 4 doses if renal function normal, earlier if renal impairment), blood counts, urinalysis, and renal function tests; monitor auditory function in elderly or if renal impairment; pregnancy and breastfeeding; systemic absorption may follow oral administration especially in inflammatory bowel disorders or following multiple doses.

4.2 Anti-fungals

These are medicines which are used in the treatment of fungal infections. Fungi are pathogenic microorganisms that possess a rigid chitinous cell wall. The treatment of fungal infections is generally more difficult and problematic compared to the treatment of bacterial infections because of the complex method of reproduction, their structure and metabolism.

The nature of therapy will depend on the type of fungus (whether it is a *mould, yeast* or *dimorphic*); the location of the infection, (whether it is on the skin, hair, nails, or within the system of the patient). Generally, systemic fungal infections are a warning sign of compromised body immunity.

In the treatment of superficial fungal infections, it is generally recommended that oral medication should be supplemented with topical antifungal cream or ointment to achieve better results. Generally, the duration of therapy will normally last for a minimum of four to six weeks.

Fungal infection of the meninges will normally present with severe complications due to immuno-depression and it is normally advisable to put the patients on parenteral antifungal Medicines for quicker action and clinical response. Systemic fungal infections such as candidiasis, blastomycosis, aspergillosis, plasmosis, cryptococcosis and mucormycosis will generally require parenteral or oral treatment depending on the severity of the infection and the condition of the patient. The duration of treatment will normally last two to three weeks. In general, antifungal Medicines are classified into the following broad groups:

4.2.1 Polyenes

This group includes nystatin (see also section 12 and 13) and amphotericin B. They are not absorbed from the gut and are active against most fungi and yeasts. However, nystatin is recommended principally for the treatment of candidiasis infections of the skin and mucous membranes. It is also used in the treatment of intestinal candidiasis.

AMPHOTERICIN

Presentation: Tablets containing 100mg Amphotericin B. Intravenous infusion containing 50mg Amphotericin sodium deoxycholate powder for reconstitution.

Indications: Intestinal candidiasis, systemic fungal infection

Administration: *Adult:* by intravenous infusion; *Systemic fungal infection*;

For deoxycholate form, Initial test dose, 1 mg over 20–30 minutes, followed by a 30-minute observation period. Dosing should start at 250 mcg/kg daily, gradually increased up to 1 mg/kg daily, or in severe infection, up to but not more than 1.5 mg/kg daily or on alternate days. Administration should be over 2–6 hours, where slower infusion may reduce adverse effects.

For liposomal form, initial test dose 1mg over 10 minutes, then 3mg/kg once daily, maximum 5mg/kg.

Children:
***Systemic fungal infections**, IV infusion*
Neonate, infant, or child: Initial test dose of 100 mcg/kg (maximum 1 mg) included as part of first dose, then 250 mcg/kg daily, gradually increased up to 1 mg/kg daily or in severe infection, up to maximum of 1.5 mg/kg daily.

For prolonged treatment, which is usually necessary, a higher dose (maximum 1.5 mg/kg) may be given on alternate days. If treatment is interrupted for longer than 7 days, recommence at 250 mcg/kg daily and increase gradually.

Side effects: Anorexia, nausea, vomiting, diarrhoea, epigastric pain, febrile reactions, renal toxicity, blood disorders, neurological disorders including hearing loss, abnormal liver function (discontinue treatment). **Caution:** Toxicity common when given parenterally, pregnancy, breastfeeding, monitor plasma electrolytes, hepatic and renal functions, concurrent administration with corticosteroids and other nephrotoxic Medicines.

NYSTATIN

Presentation: Sugar-coated tablets containing 500,000 units nystatin. Suspension containing 100,000 units/ml nystatin. Vaginal pessaries containing 100,000 i.u. nystatin

Indications: Candidiasis

Administration: *Oral candidiasis*, oral: 100,000 units after food four times daily usually for 7 days, continue for 48 hours after lesions have resolved

Intestinal and esophageal candidiasis, oral: 500,000 units four times daily, doubled in severe infections, continue for 48 hours after clinical cure

Vaginal candidiasis; insert 1-2 pessaries at night for at least 14 nights.

Children

***Oral candidiasis**, oral*

Neonate; 100,000 units as a single dose

Child over 1 month: 100,000 units four times daily after feeds; treatment is usually given for 7 days and continued for 2 days after lesions have healed.

***Intestinal and esophageal candidiasis**, oral*

Child over 1 month: 100,000 units four times daily after feeds; immunocompromised children may require 500,000 units four times daily.

Side effects: Nausea, vomiting diarrhoea at high doses, local irritation, sensitization, a rash may occur.

Contraindications: History of hypersensitivity to nystatin

4.2.2 Imidazoles

This group includes clotrimazole, econazole, isoconazole, ketoconazole and tioconazole (see also Section 13). They are active against a wide range of fungi and yeasts. Their major indication is in the treatment of vaginal candidiasis and dermatophyte infections.

CLOTRIMAZOLE

Presentation: Pessaries containing 100mg, 500mg Clotrimazole. Cream 1%, Topical 505, vaginal cream 1 %, Lotions1 % and Solutions 1%.

Indications: Vaginal and vulval candidiasis; oral, topical/scalp fungal infections.

Administration: insert 2 pessaries at night for 3 nights or 1 pessary for 6 nights. For oral 20 drops after meals 3 times and for fungal dermatosis apply twice a day.

Side effects: Occasional local irritation

Contraindications: Hypersensitivity to imidazole and other antifungal Medicines.

Caution: Antibiotic therapy, oral contraceptives, pregnancy and diabetes mellitus may affect the clinical effectiveness of clotrimazole.

KETOCONAZOLE CREAM

See **Section 13** Under Medicines acting on the Skin

MICONAZOLE CREAM

See **Section 13** Under Medicines acting on the Skin

4.2.3 Triazoles

This group includes fluconazole and itraconazole which are absorbed by mouth. They are indicated for the treatment of local and systemic candidiasis and cryptococcal infections. They are also indicated in aspergillosis *and* histoplasmosis.

FLUCONAZOLE

Presentation: Capsules containing 50mg, 150mg, 200mg Fluconazole. Suspension containing 50mg/5ml, 200mg/5ml Fluconazole. Intravenous infusion containing 2mg/ml Fluconazole.

Indications: Acute or recurrent vaginal candidiasis, mucosal candidiasis, tinea pedis, corporis, cruris, Versicolor and dermal candidiasis, systemic mycoses, systemic candidiasis, cryptococcal infections including meningitis.

Administration:

Acute or recurrent vaginal candidiasis; an oral single dose of 150mg.

Mucosal candidiasis; oral, 50 – 100mg daily for 7 – 14 days.

Tinea pedis, corporis, cruris, Versicolor and dermal candidiasis; oral, 50mg daily for 2 – 4 weeks (up to 6 weeks for tinea pedis).

Systemic mycoses, oral or By IV infusion*:* Initial dose 800mg, then maintenance at 400 mg until 2 weeks after negative blood cultures (200 mg daily for at least 6 months)

Systemic candidiasis; oral or IV infusion, 400mg initially then 200mg daily and continued according to patient response.

Cryptococcal meningitis: by IV infusion; 800 mg daily for 2 weeks, followed by 400 mg daily for 8 weeks.

Prevention of relapse of cryptococcal meningitis in AIDS patients after completion of primary therapy, oral or IV infusion: 100-200mg daily.

Prevention of fungal infections in immunocompromised patients following cytotoxic chemotherapy or radiotherapy oral or IV infusion: 50–400mg daily adjusted according to risk; 400mg daily if high risk or systemic infections e.g. following bone marrow transplantation; commence treatment before the anticipated onset of neutropenia and continue for 7 days after the neutrophil count in desirable range.

Children:

over 1 year; oral or IV infusion: 1-2mg/kg body weight daily.

Systemic and life-threatening infections; 3–6mg/kg body weight daily. Can be increased up to 12mg/kg body weight daily in a child aged 5 - 13 years.

Prevention of fungal infections in immunocompromised patients following cytotoxic chemotherapy or radiotherapy (according to extent and duration of neutropenia):

Neonate up to 2 weeks old: 3-12 mg/kg daily every 72 hours

Neonate 2-4 weeks old: 3-12 mg/kg daily every 48 hours, max. 400mg daily.

Side effects: Vestibular and auditory damage, nephrotoxicity, rarely, hypomagnesaemia on prolonged therapy, antibiotic-associated colitis; also reported, nausea, vomiting, rash.

Contraindications: Acute porphyria.

Caution: Renal impairment, pregnancy, breastfeeding, children (use only if no alternative treatment), raised liver enzymes.

ITRACONAZOLE

Presentation: Capsule containing 100mg of Itraconazole.

Indications: Oropharyngeal candidiasis, Vulvovaginal candidiasis, Pityriasis versicolor, Dermatophytosis, Nail infections, Systemic infections, Tinea pedis, Tinea manuum, Tinea corporis, Tinea cruris, Tinea capitis, Onychomycosis, Systemic aspergillosis where other antifungal drugs inappropriate or ineffective, Histoplasmosis, Systemic cryptococcosis including cryptococcal meningitis where other antifungal drugs inappropriate or ineffective.

Administration: *Adult*

Oropharyngeal candidiasis, oral: 100 mg (or 200 mg in patients with AIDS or neutropenia) daily for 15 days *Vulvovaginal candidiasis*, oral*:* 200 mg twice daily for 1 day

Pityriasis versicolor, oral: 200 mg daily for 7 days

Dermatophytosis, oral: 100 mg daily for 15 days or 200 mg daily for 7 days in tinea corporis or tinea cruris; doses are 100 mg daily for 30 days or 200 mg twice daily for 7 days in tinea pedis or tinea manuum

Nail infections, oral: 200 mg daily for 3 months or pulse therapy with 200 mg twice daily for 7 days repeated once (for fingernails) or twice (for toenails) after drug-free intervals of 21 days

Systemic infections, oral: Given in usual doses of 100-200 mg once daily, increased to 200 mg twice daily for invasive or disseminated infections, including cryptococcal meningitis

Children

3-5mg/kg 1-2 times daily, for 7-30 days; maximum 200mg/dose. Dose and duration to be titrated according to indication and severity of infection.

Contraindications: Acute porphyrias, hypersensitivity, co-administration with Colchicine and venetoclax, pregnancy.

Cautions: Active liver disease, elderly, history of hepatotoxicity with other drugs, susceptibility to congestive heart failure.

4.2.4 Penicillin Derivatives

These include Griseofulvin. This drug is selectively concentrated in keratin and is the drug of choice for widespread or intractable dermatophyte infection. It is well absorbed by mouth but inactive when applied topically.

GRISEOFULVIN

Presentation: Tablets containing 125mg, 250mg, 500mg Griseofulvin. Suspension containing 125mg/5ml griseofulvin.

Indications: Treatment of ringworm infection of the skin, hair, nails namely tinea corporis, tinea pedis, tinea cruris, tinea barbae, tinea capitis when caused by one or more of the following fungi, *Tinea rubrum, Tinea tonsurans, Tinea mentagrophytes, Tinea interdigitalis, Tinea verrucosum, Tinea megnini, Tinea schueleini, Microsporum audouini, M. canis, M. gypseum* and *Epidermophyton floccosum.*

Administration: *adult*; 500mg–1 g (10 mg/kg) daily with fatty food in single or divided doses.

Duration of treatment depends on the infection and severity: at least 4 weeks for skin and hair, at least 6 weeks for scalp ringworm. In severe infection, duration is up to 3 months, up to 6 months for fingernails, and up to 12 months or more for toenails.

Children:

Infant or child: 10–20 mg/kg (maximum 1 g) once daily or in divided doses, use divided doses if treatment is failing; up to 25 mg/kg/day for 6–8 weeks may be required for the treatment of tinea capitis. Duration of treatment is as guide:

2–4 weeks: Tinea corporis

4–8 weeks: Tinea pedis and tinea capitis

6–12 weeks: Tinea ungium.

Side effects: Headache, nausea, vomiting, rashes, photosensitivity, dizziness, fatigue, agranulocytosis and leucopenia, lupus erythematosus, erythema multiforme, toxic epidermal necrolysis, peripheral neuropathy, confusion and impaired co-ordination.

Contraindications: Hypersensitivity to griseofulvin, porphyria, hepatocellular failure, lupus erythematosus and related conditions, pregnancy (avoid pregnancy for one month after treatment).

Caution: Breastfeeding, enhances the effect of alcohol, may impair the performance of skilled tasks e.g. driving

4.2.5 Fluorinated Pyrimidine derivatives

These include Flucytosine. This is a synthetic antifungal drug which is only active against yeasts and has been used for the treatment of systemic candidiasis, cryptococcosis and torulopsosis. Side effects are uncommon but bone marrow depression can occur.

FLUCYTOSINE

Presentation: Tablet containing 250mg Flucytosine, Solution for injection 10mg/ml.

Indications: Systemic yeast and fungal infections; adjunct to Amphotericin (or Fluconazole) in cryptococcal meningitis, an adjunct to amphotericin in severe systemic candidiasis and other severe or long-standing infections.

Administration: *Adult*: Oral: 50–150 mg/kg daily in 4 divided doses.

By intravenous infusion over 20-40 minutes, 200mg/kg daily in 4 divided doses usually for not more than 7 days; extremely sensitive organisms, 100-150mg/kg daily may be sufficient; treat for at least 4 months in cryptococcal meningitis.

Children:

Neonate: 50mg/kg every 12 hours

Child: 50 mg/kg every 6 hours usually for not more than 7 days, alternatively 25–37.5 mg/kg every 6 hours; usually for not more than 7 days

Oral:

Child: 50 mg/kg every 6 hours. In infections due to extremely sensitive organisms, 25–37.5 mg/kg every 6 hours may be sufficient. Treatment does not usually extend beyond 7 days. Continue for at least 4 months in cryptococcal meningitis.

Caution: Renal impairment; elderly; blood disorders; liver and kidney function test and blood counts required (weekly in renal impairment or blood disorders); pregnancy, breastfeeding.

Side effects: Nausea, vomiting, diarrhoea, rashes; less frequently confusion, hallucinations, convulsions, headache, sedation, vertigo, alterations in liver function tests (hepatitis and hepatic necrosis reported); blood disorders including thrombocytopenia, leucopenia, and aplastic anaemia

4.2.6 Allylamines

TERBINAFINE TABLETS AND CREAM

See **Section 13** Under Medicines acting on the Skin

4.2.7 Other Antifungals

These include Gentian violet, Benzoic acid, Undecanoic acid, Salicylic acid and Sulphur. These agents have weak antifungal activity and are used only topically in the treatment of superficial fungal skin infection. However, resistance easily develops. They are mostly used in form of ointments or creams and applied topically to infected surfaces. (See section 12).

4.3 Antiprotozoals

4.3.1 Antimalarials

High Plasmodium falciparum resistance to chloroquine necessitated the Zambian Government to change the malaria treatment policy. The first-line drug of choice for treatment of uncomplicated malaria should be an Artemisinin-based Combination Therapy (ACT). Artemether-Lumefantrine has been selected for this purpose. However, wherever Artemether-Lumefantrine is contraindicated or is not available, Sulphadoxine-pyrimethamine is the drug of choice.

For all cases of severe malaria, quinine is the drug of choice. The use of artemisinin or its derivatives as a monotherapy is not preferred as the possibility and potential for the development of parasites resistance and failure for treatment adherence is high.

Wherever monotherapy of artemisinin or its group of compounds isis unavoidable, the doses recommended in this formulary should be used. The dose for artemether-lumefantrine is determined by body weight to avoid or overdosing. It is recommended that the first dose, wherever possible, should possible, should be given by observed Drug Therapy (DOTS).

ARTEMETHER+LUMEFANTRINE (AL)

Presentation: Tablets containing 20mg/120mg, 80mg/480mg of Artemether/Lumefantrine.

Indications: Treatment of uncomplicated malaria in both adults and children above 10 kg body weight.

Administration: Doses to be given at 0, 8, 24, 36, 48, and 60 hours from first dose

Adult

Uncomplicated falciparum malaria, oral: Initially 80mg/480mg of Artemether/ Lumefantrine followed by 5 further doses of 80mg/480mg of Artemether/Lumefantrine at 8, 24, 36, 48, and 60 hours.

Children: *using 20/120mg tablets*

Uncomplicated P. falciparum and other Plasmodium malaria, oral

*Infant or child 5–14 kg***:** Initially 1 tablet followed by 5 further doses of 1 tablet each at 8, 24, 36, 48, and 60 hours (total 6 tablets over 60 hours)

Child 15–24 kg: Initially 2 tablets followed by 5 further doses of 2 tablets each at 8, 24, 36, 48, and 60 hours (total 12 tablets over 60 hours)

Child 25–34 kg: Initially 3 tablets followed by 5 further doses of 3 tablets each at 8, 24, 36, 48, and 60 hours (total 18 tablets over 60 hours)

Child over 34 kg: Initially 4 tablets followed by 5 further doses of 4 tablets each at 8, 24, 36, 48, and 60 hours (total 24 tablets over 60 hours

Artemether + lumefantrine is not recommended for children below 10kg bodyweight (1 year).

To increase bioavailability, absorption can be enhanced if it is administered after meals (preferably containing fatty foods). See schedule for recommended doses.

Wt (Kg)	Age (yrs)	No. of tablets per dose. Give twice daily	(Arte-mether + Lume-fantrin dose dose (mg)	Total no. tablets to be given over 3 days
<10	<1	Not recom-mended	N/A	N/A
10-14	1-5	1	20 + 120	6
15-24	6-8	2	40 + 240	12
25-34	9-12	3	60 + 360	18
>35	>12	4	80 + 480	24

Side effects: Sleep disorders, headache, dizziness, palpitations, abdominal pain, anorexia, diarrhoea, vomiting, nausea, pruritis, rash, cough, arthralgia, myalgia.

Contraindications: History of arrhythmias, clinical bradycardia, congestive heart failure accompanied by reduced left ventricular ejection fraction, family history of sudden death or congenital QT interval prolongation, breastfeeding

Caution: electrolyte imbalance, use with other medicines known to cause QT interval prolongation, hepatic impairment, renal impairment, pregnancy, patients unable to take food (ris of recrudescence), concomitant use of other drugs that are metabolized by enzyme cytochrome P450.

ARTESUNATE

Presentation: vial containing 30mg, 60mg and 120mg anhydrous artesunic acid with a separate 1ml amp of sodium bicarbonate solution, and 5ml of Sodium Chloride; Injection (IM/IV); and suppository 100 mg.

Indications: Severe malaria

Administration: *Adult (20kg and above);* 2.4 mg/kg

The recommended dosing schedule for artesunate is as follows:

- On admission (time = 0).
- After 12 hours.
- 24 hours after the initial dose.
- After the 3 initial doses in 24 hours, if the patient is able to tolerate oral medication, switch to Artemether/Lumefantrine for a full course of 3 days.

If the patient can not tolerate oral medication, Give IV dose once daily for a maximum of 6 days.

Give a full course of artemisinin-based combination therapy (see artemether + lumefantrine above) or oral quinine (in 1st trimester pregnancy) after initial parenteral artesunate.

Children *<20kg*: 3.0 mg/kg

>20kg: 2.4 mg/kg given at 0, 12, and 24 hours, then once daily until oral treatment is possible

Rectal suppository

2 months–3 years(5-14kg): 100mg suppository

>3–6 years: 200mg (two 100mg suppositories) suppositories

Side effects: Anaemia, increased transaminase enzymes, thrombocytopaenia, and hyperbilirubinaemia.

Contraindications: Known serious hypersensitivity

Caution: Hypersensitivity – consider discontinuing in hypotension, dyspnoea, urticaria or generalised rash.

DAPSONE+PYRIMETHAMINE

Presentation: Tablet containing a combination of 100 mg of dapsone and 25 mg of pyrimethamine.

Indications: Malaria prophylaxis in children with sickle cell disease and patients allergic to sulphur drugs.

Administration: 25mg pyrimethamine and 100mg dapsone tablet taken once per week, preferably in the morning.

Side effects: GI irritation, photosensitivity, haemolysis, methaemoglobinaemia, allergic dermatitis (rarely including toxic epidermal necrolysis and SJS), hepatitis, agranulocytosis, "dapsone syndrome" resembling mononucleosis (rare hypersensitivity reaction with symptoms including rash, fever, jaundice, and eosinophilia).

Contraindications: Severe anaemia, porphyria, severe G6PD deficiency.

Caution: Increased risk of bleeding following recent surgery.

SULFADOXINE + PYRIMETHAMINE (SP)

Presentation: Tablets containing 500mg Sulfadoxine and 25mg Pyrimethamine.

Indications:

(1) Treatment of uncomplicated malaria in both adults and children First treatment in the following

- Children 5-10kg bodyweight
- The second and third trimester of pregnancy
- When artemether-lumefantrine is not available
- Hypersensitivity to artemether-lumefantrine.

(2) Intermittent Presumptive Treatment (IPT) in pregnancy.

Administration: Single-dose adult treatment containing 25mg/kg body weight Sulfadoxine plus 75mg/kg body weight Pyrimethamine. Recommended single adult dose is 1500mg sulfadoxine plus 75mg pyrimethamine (i.e. 3 tablets).

Intermittent Presumptive Treatment (IPT) in pregnancy: from second trimester; 1500mg sulfadoxine plus 75mg pyrimethamine (i.e. 3 tablets) every 4 weeks for at least 3 doses.

(See dosage schedule below):

Sulphadoxine-pyrimethamine dosage schedule

Weight (kg)	Age (years)	No. of Tablets
5-10	2-11 months	0.5
10-14	1-2	0.75
15-20	3-5	1
21-30	6-8	1.5
31-40	9-11	2
41-50	12-13	2.5
>50	14 and above	3

Side Effects: Serious adverse reactions to sulfa medicines are rare. When they occur, they include severe cutaneous reactions, such as Stevenson Johnson syndrome and toxic epidermal necrolysis. Gastrointestinal disturbances include nausea, vomiting and stomatitis.

Contraindications: Hypersensitive to sulfa Medicines or pyrimethamine and in hepatic renal dysfunction.

PRIMAQUINE

Presentation: Tablets containing 7.5mg, 15mg and 30mg of Primaquine base.

Indications: Adjunct in the treatment to eliminate the liver stages of infestation. Gametocytocidal treatment of P. falciparum malaria (after standard blood schizontocide therapy). Recommended for radical cure of plasmodium ovale and plasmodium vivax in endemic areas.

Administration: *Adult*; 15mg daily for 14 – 21 days OR 750 mcg/kg once a week for 8 weeks.

Gametocytocidal treatment of P. falciparum malaria (after standard blood schizontocide therapy), oral: 250–500 mcg/kg as a single dose.

Children:
0.25mg/kg body weight daily for 14 – 21 days.
In mild to moderate G6PD deficiency, use 500–750 mcg/kg once a week for 8 weeks.

Side effects: Nausea, vomiting, abdominal pain, less commonly methaemoglobinaemia, haemolytic anaemia especially in G6PD deficiency.

Contraindications: Patients undergoing quinacrine therapy, acutely ill patients suffering from systemic disease manifested by the tendency of granulocytopenia (e.g. rheumatoid arthritis, lupus erythema).

Caution: G6PD deficiency, pregnancy, breastfeeding.

QUININE DIHYDROCHLORIDE

Presentation: Tablets (coated) containing 200mg and 300mg Quinine dihydrochloride base, injection containing 150mg, 300mg/ml Quinine dihydrochloride in 2 ml ampoules.

Indications: Treatment of severe and complicated malaria; First-line treatment for uncomplicated malaria during the first trimester of pregnancy; Second-line treatment in case of treatment failure with first-line treatment.

Administration: *Adult:*

Severe and complicated malaria: by slow IV infusion (over 4 hours): Initially 20 mg/kg followed by 10 mg/kg every 8 hours until the patient can take oral quinine given at 10

mg/kg every 8 hours to complete a total of 7 days.

By IM injection; 10mg/kg body weight diluted in saline or water for injection (to a concentration of 60-100mg salt/ml), repeated after 4 hours and then 8 hourly.

Uncomplicated malaria in pregnancy in the first trimester;

oral: 10mg/kg (to a maximum of 600mg) 3 times a day for 7 days

Children;

by intramuscular injection: 10mg/kg body weight diluted in saline or water for injection (to a concentration of 60-100mg salt/ml), repeated after 4 hours and then 8 hourly. A loading dose is not recommended by this route.

Infants up to 1 year: 250mg daily in divided doses for 5–7 days.

1 – 3 years: 400mg daily in divided doses for 5–7 days.

3–6 years: 650mg daily in divided doses every 4 – 6 hours for 5–7 days.

6–12 years; 1000mg (1g) daily every 4–6 hours for 5–7 days.

If a patient with chloroquine-resistant malaria is seriously ill, quinine should be given by intravenous infusion over 4 hours in a loading dose of 30mg/kg body weight followed by a maintenance dose of 10mg/kg body weight in 500ml 5% glucose over 4 hours every 8 hours until the patient can swallow tablets to complete the course.

Side effects: Tinnitus, headache, hot and flushed skin, nausea, abdominal pain, rashes visual disturbances (including temporal blindness), confusion, hypersensitivity reactions including angioedema, blood disorders (including thrombocytopenia and intravascular coagulation), acute renal failure, cardiovascular effects and hypoglycaemia (especially after parenteral administration.

Contraindications: Hypersensitivity to quinine, G6PD deficiency, optic neuritis, tinnitus, thrombocytopenic purpura, haemoglobinuria.

Caution: Atrial fibrillation, conduction defects, heart block, blood glucose concentrations should be monitored, G6PD deficiency.

4.3.2 Amoebicides

METRONIDAZOLE

Presentation: Tablets containing 200mg, 400mg Metronidazole. A suspension containing 200mg/5ml metronidazole benzoate. Intravenous infusion containing 5mg/ml (100ml) metronidazole.

Indications: Acute invasive intestinal amoebiasis, extra-intestinal amoebiasis (including liver abscess) and symptomless amoebic cyst passers.

Administration: oral:

Intestinal infection: 800 mg every 8 hours for 5 days

Extra-intestinal infection: 400–800 mg for 5–10 days. Alternatively, 35–50 mg/kg daily in 3 divided doses for

5–10 days. Max: 2,400 mg daily.

Children:

1–3 years; 200mg every 8 hours.

3–7 years; 200mg every 6 hours.

7–10 years; 400mg every 8 hours.

Side effects: See under 4.1.11.

Caution, contraindications: See under 4.1.11.

TINIDAZOLE

Presentation: Tablets containing 500mg Tinidazole

Indications: Same as for 4.3.2.

Administration: *Intestinal amoebiasis*; 2g daily for 2 – 3 days.

Amoebic involvement of the liver; 1.5 – 2g daily for 3 – 5 days.

Urogenital tract trichomoniasis and giardiasis; single 2g dose (repeat once if necessary).

Children:

Intestinal amoebiasis: 50–60mg/kg body weight daily for 3 days.

Amoebic involvement of the liver: 50 – 60mg/kg body weight daily for 5 days.

Urogenital tract trichomoniasis and giardiasis; a single dose of 50–70mg/kg body weight.

Side effects: See under 4.1.11

Caution, contraindications: See under 4.1.11

4.3.3 Trypanocides

MELARSOPROL

Presentation: Injection containing 3.6% Melarsoprol (5ml amp)

Indications: Meningo-encephalitic stage of African trypanosomiasis. It is effective in both Gambian and Rhodesian strains of the disease. It is also effective in the early stage of the disease.

Administration: by slow IV injection through a fine needle and avoid leakage to tissue.

Adult, 50kg or more; 3.5mg/kg daily for 3 – 4 days. The course is repeated after 7 days. A third course of the same dose can be given if required after 10 – 21 days. Reduce dose accordingly in children and underweight patients.

Children: 2.2 mg/kg per day (maximum: 5 ml) once daily for 10 days

Side effects: Pyrexia, reactive encephalopathy, haemorrhagic encephalopathy, hypersensitivity reaction, hepatic damage, vomiting, agranulocytosis, dermatitis.

Contraindications: G6PD deficiency, hypersensitivity to the drug.

Caution: Leprosy patients, the administration should be under close supervision to monitor response, the initial dose should be based on the clinical assessment of the patient rather than on the body weight.

SURAMIN

Presentation: Injection containing 1g suramin powder for reconstitution.

Indications: Treatment of early stages of both Gambian and Rhodesian strains of trypanosomiasis. Also, in the prophylaxis of Gambian and Rhodesian trypanosomiasis. In the treatment of late stages of the disease involving the central nervous system, it should be given in combination with Melarsoprol.

Administration: Due to its toxicity, it is advisable to give initial test doses of between 100–200mg before initiation of treatment for Anaphlaxas reactions to the drug.

Early stages of African trypanosomiasis: 5mg/kg body weight on 1st day. 10mg/kg body weight on 3rd day, then 20mg/kg body weight on days 5, 11, 17, 23 and 30. Alternatively, it can be given as follows; 5 doses of 1g given over 3 weeks.

In late-stage infections of T. rhodesiense: 2–3 injections (5,10, and 20mg respectively) are often given before starting treatment with melarsoprol.

Children:
All ages: 5 mg/kg on day 1 (as a test dose), followed by 20 mg/kg on day 3, 10, 17, 24, and 31.

Side effects: Nausea, vomiting, loss of consciousness are the most common side effects. Colic and acute urticaria are the immediate side effects, later side effects include papular eruptions, parenthesis, photophobia, hyperaesthesia of the palms of the hands and soles of the feet, prolonged use may result in albuminuria, haematuria and crystalluria.

Contraindications: Known hypersensitivity to the drug

Caution: Renal insufficiency, occurrence of palmer-planter hyperaesthesia necessitates caution since it may lead to peripheral neuritis.

PENTAMIDINE ISETIONATE

Presentation: Powder for injection containing 300mg of Pentamidine Isetionate

Indication: Treatment and prophylaxis of Pneumocystis jirovecii (Pneumocystis carinii) pneumonia (specialist use only), Visceral and cutaneous leishmaniasis, Trypanosomiasis.

Administration: *Haemolymphatic first-stage of rhodesiense and gambiense HAT, by IM injection:* 4 mg/kg daily for 7 days or on alternate days for a total of 7–10 doses

Children:

By intravenous infusion

Treatment and Prophylaxis of Pneumocystis jirovecii (Pneumocystis carinii) pneumonia (specialist use only): 4 mg/kg once daily for at least 7–10 days

Visceral leishmaniasis (specialist use only)

By deep intramuscular injection

1–17 years: 3–4 mg/kg once daily on alternate days, maximum total of 10 injections, course may be repeated if necessary.

Cutaneous leishmaniasis (specialist use only)

By deep intramuscular injection

1–17 years: 3–4 mg/kg 1–2 times a week until condition resolves

Trypanosomiasis (specialist use only)

By deep intramuscular injection, or by intravenous infusion

Adult and Child 1–17 years: 4 mg/kg once daily or on alternate days for a total of 7–10 injections

Side effects: Dizziness, hypoglycaemia (can be severe and sometimes fatal), hypotension (can be severe and sometimes fatal), local reaction, nausea, rash, taste altered.

Cautions: Anaemia, bradycardia, cardiac disease, history of ventricular arrhythmias, hyperglycaemia, hypertension, hypoglycaemia, hypokalaemia, hypomagnesaemia, hypotension, leucopenia, risk of severe hypotension following administration, thrombocytopenia.

FEXINIDAZOLE

Presentation: Tablet and injection containing 600mg of fexinidazole.

Indications: Rhodesiense HAT, trypanosomes, gambiense HAT

Administration: Dosage of fexinidazole in adults and children aged ≥ 6 years

Body weight	No. of tablets (600 mg) to be taken once daily with food		Duration
≥ 35 kg	Loading phase	3 tablets (1800 mg)	4 days
	Main-tenance phase	2 tablets (1200 mg)	6 days
20–34 kg	Loading phase	2 tablets (1200 mg)	4 days
	Main-tenance phase	1 tablet (600 mg)	6 days

Side effects: vomiting, nausea, asthenia, decreased appetite, headache, insomnia, tremor and dizziness, hypokalemia. Vomiting is more frequent in children than in adults.

Neuropsychiatric adverse-reactions: insomnia, hallucination, agitation, logorrhea, abnormal behavior, anxiety, psychotic disorder, suicidal ideation QT interval prolongation, increase risk for ventricular arrhythmias in conditions coexisting with neutropenia.

Contraindications: Hypersensitivity, jaundice, generalized oedema, bleeding, hepatic insulfficiency, severe congestive cardiac failure, hypomagnesaemia, cockapne syndrome, patients taking imidazole derivatives (disulfram like reactions)

Caution: Psychiatric disorders, blood dyscrasia, neutropenia.

4.4 Anthelmintics

4.1.1 Intestinal Anthelmintics

MEBENDAZOLE

Presentation: Tablets containing 100mg and 500mg mebendazole. A suspension containing 500mg/5ml mebendazole.

Indications: For the treatment of *Ttrichuris Trichur* (whipworm), E*nterobius vermicularis* (pinworm), threadworms, A*scaris lumbricoides* (roundworm*), Ancytoma duodenal* (common hookworm), or *Nector erythema* (American hookworm), in single or mixed infections.

Administration: *Adult:*

For mass treatment control programmes, oral: 500 mg as a single dose 4 times a year

Threadworm: 100mg as a single dose. If reinfection occurs, a second dose may be given after 2–3 weeks.

Whipworm: 100mg twice daily for 3 days or 500mg as a single dose.

Roundworms: 100mg twice daily for 3 days.

H*ookworm*: 100mg twice daily for 3 days.

Children:
Under 2 years: Not yet recommended.
Over 2 years: Adult doses as above

Side effects: Abdominal pain, diarrhoea, hypersensitivity reactions including erythema, rash, urticaria and angioedema.

Contraindications: Hypersensitivity to mebendazole. **Caution:** Pregnancy especially the first trimester, breastfeeding, safety for use has not been established in children less than 2 years of age. Use only if the benefit outweighs the risk.

ALBENDAZOLE

Presentation: Tablet containing 400mg Albendazole and Suspension containing 100 mg/5 ml.

Indications: Chronic Strongyloides infection, Hydatid disease, Neurocysticercosis, Ascaris Lumbricoides, Ancylostomiasis, taenia Solium Tapeworm, Echinococcus Tapeworm

Administration: *Adult*: oral: 400 mg twice daily for 3 days, dose may be repeated after 3 weeks if necessary

Hydatid disease (cystic echinococcosis, dog tapeworm):

15 mg/kg (max. 800 mg) daily in 2 divided doses (maximum daily dose, 800 mg) for 28 days followed by 14 tablet-free days, up to 3 courses may be given.

Neurocysticercosis (pork tapeworm, taenia solium), parenchymal disease: 15 mg/kg daily in 2 divided doses (maximum daily dose, 800 mg) for 8–30 days.

Hookworm infections: 400 mg for 1 dose, may be repeated in 3 weeks.

Children:

Hydatid disease *(cystic echinococcosis, dog tapeworm)*

2–17 years: 7.5 mg/kg twice daily (max. per dose 400 mg twice daily) for 28 days followed by 14-day break, repeated for up to 2–3 cycles

Ascariasis, hookworm infections, enterobiasis, and trichostrongyloidiasis

12 months–2 years: 200 mg as a single dose (may be repeated in 3 weeks)

over 2 years: 400 mg as a single dose (may be repeated in 3 weeks)

Whipworms (trichuriasis)

12 months–2 years: 200 mg as a single dose (for moderate infections) or 200 mg initially then 100 mg twice daily for 3 days (severe infections).

over 2 years: 400 mg as a single dose (for moderate infections) or 400 mg daily for 3 days (severe infections).

Strongyloidiasis

over 2 years: 400 mg once or twice daily for 3–7 days; dose may be repeated after 3 weeks if necessary

Capillariasis

over 2 years: 400 mg daily for 10 days.

Side effects: Headache, abnormal LFTs, abdominal pain, nausea, vomiting, dizziness, vertigo, increased intracranial pressure, rash, urticaria, acute renal failure, aplastic anaemia

Contraindications: Hypersensitivity to albendazole or benzymidazoles

Caution: Monitor theophylline levels if used concomitantly, and in pregnancy.

NICLOSAMIDE

Presentation: Tablets (chewable) containing 500mg Niclosamide.

Indications: *Taenia saginata* (beef tapeworm*), Diphyllobothrium latum* (fish tapeworm*), Hymenolepis nana* (dwarf tapeworm) and *Taenia solium*.

Administration: *Adult and child over 6 years old*

Taenia solium; 2g as a single dose after a light breakfast followed by a purgative after 2 hours.

Taenia saginata and Diphyllobothrium Latium; as for *Taenia solium* but half the dose may be taken after breakfast and the remainder one hour later followed by a purgative 2 hours after the last dose.

Hymenolepis nana: 2g as a single dose on the first day then 1 g daily for 6 days.

Tablets should be chewed thoroughly or crushed before washing it down with water.

Children:

Taenia solium/Taenia saginata and Diphyllobothrium Latium

under 2 years; 500mg.

2–6 years; 1g.

6 years and above: adult dose

Hymenolepis nana

under 2 years; 500mg on the first day then 250mg daily for 6 days.

2–6 years; 1g on the first day then 500mg daily for 6 days.

6 years and above: adult dose

Side effects: Nausea, retching, abdominal pains, lightheadedness, and pruritis.

Contraindications: Hypersensitivity to niclosamide or any of its components.

Caution: Use with caution in pregnancy, breastfeeding and children under 2 years of age. Use only when benefit outweighs the potential risk.

PYRANTEL

Presentation: Tablets containing 125mg Pyrantel pamoate. Suspension containing 250mg/5ml pyrantel pamoate.

Indications: Ascaris, threadworm and hookworm infestation.

Administration: *Adult and child over 6 months*;

Ascaris lumbricoides alone; a single dose of 5mg/kg body weight.

Mixed infections involving A*scaris lumbricoides*; a single dose of 10mg/kg body weight.

Hookworm: 10mg/kg body weight (maximum 1g) given as a single dose for light infestations, heavy infestations may need single daily doses for 3 days.

Threadworm; A single dose of 10mg/kg body weight (maximum 1g); cure rates are improved if one or two further doses are given at intervals of 2 weeks.

Side effects: Anorexia, abdominal cramps, nausea, vomiting, diarrhoea, headache, dizziness, sleep disturbance, rash.

Contraindications: Hepatic disease and pregnancy.

Caution: Safety for use in children under 2 years has not been established.

4.2.2 Schistosomicides

PRAZIQUANTEL

Presentation: Tablets containing 600mg Praziquantel.

Indications*:* *Schistosoma japonicum, Schistosoma haematobium, Schistosoma mansoni* and all other types of bilharziasis infestation. It is also useful in the treatment of taenia saginata, solium and hymenolepis nana.

Administration: *Schistosoma haematobium, Schistosoma mansoni*; 40mg/kg body weight as a single dose,

Schistosoma japonicum; 60mg/kg body weight divided into 3 doses in one day.

Distomiasis; 75mg/kg body weight divided into 3 doses in one day.

Children:
Below 4 years: Not recommended
4 years and above: 5-25 mg/kg as a single dose OR 25-75mg/kg daily in 3 divided doses up to 6 days.

Side effects: Praziquantel is well tolerated and side effects are usually mild and transient, but more frequent or serious in patients with heavy worm burden. These include malaise, headache, dizziness, abdominal discomfort (with or without nausea), pyrexia, rarely urticaria.

Contraindications: Previous hypersensitivity reaction to praziquantel, since parasitic destruction in the eye may cause lesions.

Caution: Safety for use in children under 4 years is not yet established. May produce drowsiness, observe caution when driving or performing functions requiring a high level of concentration during treatment.

4.4.3 Antifilarials

DIETHYLCARBAMAZINE

Presentation: Tablets containing 100mg diethylcarbamazine.

Indications: Bancrofti filariasis, topical eosinophilia, loasis.

Administration: *For mass treatment program:* 6 mg/kg in divided doses over 24 hours, once a year.

Filariasis; to minimise reactions, treatment is commenced with a dose of 1mg/kg body weight on the 1st day and increased gradually over 3 days to 6mg/kg body weight in divided doses. This dosage is maintained for 21 days.

Topical eosinophilia; 13mg/kg body weight per day for 4 – 7 days.

Children:
Under 10 years: half the dose of children over 10 years
Over 10 years: adult doses as above.

Side effects: Allergic reaction including pruritis, risk of lethal encephalitis, drowsiness, malaise, headache, nausea and vomiting.

Caution: Pregnancy and breastfeeding, administer carefully to avoid or control allergic reactions.

SURAMIN

Presentation: See 4.3.3.

Indications: Eradication of adult filaria in onchocerciasis

Administration: Normal adult dose is 1g given on days 1,3,7,14, and 21. Weekly doses can be given for an additional 5 weeks.

Children:
Infants; 10–11mg/kg body weight.
less than 12 years; 15-20mg/kg body weight.

Side effects: See 4.3.3.

Caution, and contraindications: See 4.3.3.

4.5 Antituberculosis

Treatment for sputum positive TB, TB meningitis, massive pleural effusion and TB pericarditis new and relapse cases is in two phases**:** Intensive (initial) phase and the continuation phase using. The total duration of treatment of the two phases is eight months.

Intensive phase (Initial): Concurrent use of four Medicines during the initial phase is designed to reduce the population of viable bacteria as rapidly as possible and to prevent the emergence of drug-resistance bacteria. This will include the daily use of isoniazid, rifampicin and pyrazinamide and ethambutol under supervision for 2 months.

Continuation phase: After the intensive phase, treatment is continued for 6 months with isoniazid, ethambutol (Longer treatment may be necessary for bone and joint T.B. infections, for T.B. meningitis or resistant organisms).

a) Recommended dosage for sputum positive Tuberculosis, Tuberculosis meningitis, massive pleural effusion and Tuberculosis pericarditis new cases

2-month regimen:	
Isoniazid	*Adult:* 300mg daily.
Ethambutol	*Adult under 50kg: 6*00mg daily *50kg and over:* 800mg daily.
Pyrazinamide	*Adult under 50kg:* 1.5g daily *50kg and over:* 2g daily
Rifampicin	*Adult under 50kg:* 450mg daily *50kg and over:* 600mg daily
Followed by a 6-month regimen:	
Isoniazid:	*Adult:* 300mg daily.
Ethambutol	*Adult under 50kg:* 600mg daily *50kg and over:* 800mg daily.

b) Recommended dosage for new cases sputum negative, extrapulmonary Tuberculosis new cases

2-month regimen:	
Isoniazid	*Adult:* 300mg daily
Rifampicin	*Adult under 50kg:* 450mg daily. *50kg and over:* 600mg
Pyrazinamide	*Adult under 50kg:* 1.5g daily *50kg and over:* 2g daily.
Followed by a 6-month regimen	
Isoniazid	*Adult*: 300mg daily.
Ethambutol	*Adult under 50kg:* 600mg daily *50kg and over:* 800mg daily

c) Recommended dosage for relapse cases sputum negative and sputum positive

2-month regimen:	
Streptomycin	*Adult:* 1g daily
Isoniazid	*Adult:* 300mg daily
Rifampicin	*Adult under 50kg:* 450mg daily *50kg and over:* 600mg
Pyrazinamide	*Adult under 50kg*: 1.5g daily *50kg and over*: 2g daily.
Ethambutol	*Adult under 50kg*: 600mg daily. *50kg and over*: 800mg daily.
Followed by a 1-month regimen:	
Isoniazid	*Adult*: 300mg daily
Rifampicin	*Adult under 50kg:* 450mg daily *50kg and over:* 600mg
Pyrazinamide	*Adult under 50kg:* 1.5g daily *50kg and over:* 2g daily.
Ethambutol	*Adult:* 800mg daily
Followed by a 5-month regimen:	
Isoniazid	*Adult:* 300mg daily
Rifampicin	*Adult under 50kg:* 450mg daily *50kg and over:* 600mg
Ethambutol	*Adult:* 800mg daily.

Pregnancy and Breast-Feeding: The standard regimen (above) may be used during pregnancy and breast-feeding; pyridoxine supplements are advisable. Streptomycin should not be given in pregnancy.

Children: As for adults, children are given Isoniazid, Rifampicin, and Pyrazinamide for the first 2 months followed by isoniazid and rifampicin during the next 4 months. If Pyrazinamide is omitted from the initial phase, then treatment with Isoniazid and Rifampicin should be given for 9 months**.**

Except in exceptional circumstances (e.g. drug resistance), Ethambutol should be avoided in young children because of the difficulty in testing eyesight and in obtaining reports of visual symptoms (see below).

The recommended dosage for children

2-month regimen:	
Rifampicin	75mg – 300mg daily
Isoniazid	50mg – 100mg daily
Pyrazinamide	250mg – 500mg daily
4-month regimen:	
Rifampicin	75mg – 300mg daily
Isoniazid	50mg – 100mg daily

Doses in children depend very much on the age, weight and nutritional status of the child.

Immunocompromised Patients:

Immunocompromised patients may develop tuberculosis owing to reactivation of previously

latent disease or due to new infection. Multi-resistant Mycobacterium tuberculosis may be present or the infection may be caused by other mycobacteria e.g. *M avium* complex in which case specialist advice is needed. Culture should always be carried out and the type of organism and its sensitivity confirmed. The minimum duration of treatment of 9 months is currently recommended for *M. tuberculosis* infection.

Monitoring: Since isoniazid, rifampicin and pyrazinamide are associated with liver toxicity hepatic function should be checked before and during treatment with these Medicines; those dependent on alcohol or who have pre-existing liver disease require special care.

Renal function: This should be checked before treatment with antituberculous Medicines and appropriate dosage adjustments made. Streptomycin or ethambutol should preferably be avoided in patients with renal impairment, but if users require dose reduction and possibly drug concentration monitoring.

Visual acuity should be tested before ethambutol is used.

Rifampicin is a key component of any antituberculous regimen. Like isoniazid, it should always be included unless there is a specific contraindication.

Caution: Rifampicin induces hepatic enzymes, which accelerate the metabolism of several Medicines including oestrogens, corticosteroids, phenytoin, sulphonylureas, and anticoagulants.

Important: the effectiveness of oral contraceptives is reduced and alternative family planning advice should be offered.

Ethambutol is included in a treatment regimen if resistance is suspected; it can be omitted if the risk of resistance is low. For unsupervised treatment, ethambutol is given in a dose of 25 mg/kg daily in the initial phase followed by 15 mg/kg daily in the continuation phase (or 15 mg/kg daily throughout).

Side effects: are largely confined to visual disturbances in the form of loss of acuity, colour blindness, and restrictions of visual fields. The earliest features of ocular toxicity are subjective and patients should be advised to discontinue therapy immediately if they develop deterioration in vision and promptly seek further advice. Early discontinuation of the drug is almost always followed by recovery of eyesight. Patients who cannot understand warnings about visual side effects should, if possible, be given an alternative drug, in particular, **Ethambutol should be avoided in children until they are at least 6 years old and capable of reporting symptomatic visual changes accurately.**

An ophthalmic examination should be performed before, and at intervals during, treatment.

Streptomycin is now used for resistant organisms and relapses. It is given intramuscularly in a *Standard dose* of 1 g daily reduced to 500-750 mg in patients under 50 kg or those over 40 years of age. Children are given streptomycin in a dose of 15-20mg/kg daily. Plasma drug concentrations should be measured, particularly in-patients with impaired renal function in which streptomycin must be used with great care.

Side effects increase after a cumulative dose of 100g, which should only be exceeded in exceptional circumstances.

Pyrazinamide is a bactericidal drug only active against intracellular dividing forms of mycobacterium tuberculosis; it exerts its main effect only in the first two or three months. It is particularly useful in tuberculous meningitis because of good meningeal penetration. It is not active against *M. Bovis*. Serious liver toxicity may occasionally occur.

ETHAMBUTOL HYDROCHLORIDE

Presentation: Tablets containing 400mg Ethambutol hydrochloride

Indications: Tuberculosis, in combination with other Medicines in the intensive and the continuation phase.

Administration: Adult and child over 6 years, see notes above (4.5).

Side effects: optic neuritis, red/green colour blindness, and peripheral neuritis.

Contraindications: Young children, optic neuritis, and poor vision.

Caution: Reduce dose in renal impairment; elderly; pregnancy; warn patients to report visual changes – see above notes.

PYRAZINAMIDE

Presentation: Tablets containing 500mg Pyrazinamide

Indications: Tuberculosis in combination with other Medicines in intensive phase

Administration: See notes above (4.5.)

Side effects: Hepatotoxicity including fever, anorexia, hepatomegaly, jaundice, liver failure, nausea, vomiting, arthralgia, sideroblastic anaemia, urticaria.

Contraindications: Liver damage, porphyria.

Caution: Hepatic impairment (monitor hepatic function, see also below), renal impairment, diabetes, gout

*Hepatic disorders***.** Patients or their carers should be told how to recognize signs of liver disorders and advised to discontinue treatment and seek immediate medical attention if symptoms such as persistent nausea, vomiting, malaise or jaundice develop.

RIFAMPICIN + ISONIAZID

Presentation: Tablets containing 150 mg + 75 mg, 150+100 mg, 300+150 mg, 75 mg + 50 mg (children) of Rifampicin + Isoniazid

Indication: Tuberculosis intensive phase

Dose: See notes above (4.5.)

Side effects: Anorexia, nausea, vomiting diarrhoea, a flu-like syndrome characterized by fever, malaise headache, chills skin rashes

Contraindications: See notes above (4.5.)

Caution: See notes above (4.5.)

ISONIAZID

Presentation: Tablets containing 50mg, 100mg Isoniazid.

Indications: Tuberculosis, in combination with other Medicines; intensive and continuation phase.

Prophylaxis.

Administration: Oral; *See notes above*

Side effects: Nausea, vomiting; peripheral neuritis with high doses (pyridoxine prophylaxis, see notes above), optic neuritis, convulsions, psychotic episodes; hypersensitivity reactions including fever, erythema multiforme, purpura; agranulocytosis; hepatitis (especially over the age of 15); systemic lupus erythematosus-like syndrome, pellagra, hyperglycaemia, and gynaecomastia reported.

Contraindications: Drug-induced liver disease; anaesthetic, potentiated by isoflurane; antacids reduce absorption; increases toxicity of cycloserine, metabolism of carbamazepine, phenytoin inhibited.

Caution: Hepatic impairment (monitor hepatic function, see also below); renal impairment; slow acetylation status (increased risk of side-effects); epilepsy; history of psychosis; alcoholism; pregnancy and breast-feeding; porphyria.

Hepatic disorders: Patients or their carers should be told how to recognize signs of liver disorders and advised to discontinue treatment and seek immediate medical attention if symptoms such as persistent nausea, vomiting, malaise or jaundice develop.

ETHAMBUTOL + ISONIAZID

Presentation: Tablets containing 400mg ethambutol, 150mg isoniazid.

Indication: Tuberculosis continuation phase.

Administration: *See notes above*

Side effects: peripheral neuritis is the most common adverse effect when higher dosages are used, skin rashes, ataxia dizziness, optic neuritis and hepatic damage.

Contraindications: See notes above (ethambutol and isoniazid)

Caution: See notes above (ethambutol and isoniazid).

Drugs for Resistance Tuberculosis

BEDAQUILINE

Presentation: Tablets containing 200 mg of Bedaquiline.

Indication: Only use in combination with at least 3 drugs to which the patients TB isolate is susceptible

Administration: First 2 weeks, 400 mg per day then 200 mg 3 times a week, at least 48hrs in between the doses

Side effects: QTc prolongation (56-61%), nausea, arthralgia, vomiting, transaminases increased, headaches, abdominal pain.

Contraindications: QTc interval more than 500 milliseconds.

Caution: QTc prolongation can occur, coadministration with other drugs known to cause QTc prolongation may augment this side effect.

CYCLOSERINE

Presentation: Tablet/capsule containing 250mg of Cycloserine

Indications: Treatment of drug resistance TB in combination with other drugs.

Administration: Adults - 250 mg twice a day for 2 weeks, then 500mg- 1000mg/day but not to exceed 1000mg/day.

Side effects: Confusion, restlessness, drowsiness, vertigo, cardiac arrhythmia, headache.

Contraindications: Alcohol dependence, depression; epilepsy, severe anxiety.

Caution: Should be excised in patients with renal dysfunction, history of seizures, depression, alcohol users and severe anxiety. Watch out for hypersensitivity reactions.

DELAMANID

Presentation: Oral formulated tablets containing 50 mg

Indications: Treatment of drug resistance TB in combination with other drugs.

Administration: *Adult (12 years and above)* 100 mg twice daily.

Children:
6-11 years 50mg twice a day for 6 months,

Side effects: Anxiety, chest pain, cough, depression; dyslipidaemia, ear pain, electrolytes imbalances, psychotic disorder, QTc prolongation

Contraindications: QTc interval more than 500 milliseconds

Caution: Those on ART, risk of QTc prolongation, myocardial infarction, heart failure with reduced ejection fraction.

ETHIONAMIDE

Presentation: Tablet containing 250mg Ethionamide

Indications: Treatment of drug resistance tuberculosis in combination with other drugs.

Administration: 250mg/day then increase 250mg twice daily for 1-2 days then gradual increase to tolerated doses of 750mg/day. Not to exceed 1000mg in 3 divided doses.

Side effects: Postural hypotension, headache, dizziness, drowsiness, headache, psychosis, photosensitivity, peripheral neuropathy.

Contraindications: Hypersensitivity reactions, severe hepatic dysfunction.

Caution: Use with caution in diabetes mellitus patients, thyroid diseases, hepatic impairment.

PROTHIONAMIDE

Presentation: Tablet containing 250 mg Prothionamide.

Indications: It is indicated in the management of drug-resistant Tuberculosis in combination with other drugs.

Administration: For both adults and paediatrics – 15 to 20 mg/kg once daily. Maximum should be 1g in a day. Consider twice daily if the patient is unable to tolerate once daily regimen.

Side effects: Nausea, vomiting, diarrhoea, metallic taste, and abdominal pain. Rarely patients may present with serious acute hepatitis, psychotic disturbances, optic neuritis, hypothyroidism and gynaecomastia (in men).

Contraindications: Severe liver disease, pregnancy, porphyria, and hypersensitivity to Ethionamide.

Caution: Reduce dose in renal disease and use with caution in breastfeeding mothers.

PARA-AMINO-SALICYLIC ACID

Presentation: Powder containing 5g.

Indications: It is indicated in the management of drug-resistant Tuberculosis in combination with other drugs.

Administration: *Adults* - 4g every 8-hourly (three times a day); not to exceed 12 g per day.

Children:
200–300 mg/kg per day in 2–4 divided doses; maximum 10 g daily

Side effects: Diarrhoea, dizziness, gastrointestinal discomfort, hypersensitivity, and skin rashes.

Contraindications: History of hypersensitivity.

Caution: Glucose-6-phosphate dehydrogenase (G6PD) deficiency (risk of haemolysis), hepatic impairment, peptic ulcer disease, renal impairment, congestive heart failure, patients on therapy of more than 1 month should be considered for maintenance vitamin B12. Pregnancy, breastfeeding, sodium salt in heart failure, gastric ulcer. Monitor patient closely for 1st 3 months of treatment and counsel to report: sore throat, fever, unusual bleeding or bruising, persistent nausea or vomiting, or abdominal pain.

4.6 Antileprotics

The World Health Organization has made recommendations to overcome this problem of dapsone resistance and to prevent the emergence of resistance to other antileprotic Medicines. These recommendations are based on the same principles as for the chemotherapy of tuberculosis. Medicines recommended are **dapsone, rifampicin and clofazimine.**

A three-drug regimen is recommended for multibacillary leprosy (lepromatous, borderline lepromatous, and borderline leprosy) and a two-drug regimen for those suffering from paucibacillary leprosy (borderline tuberculoid, tuberculoid, and indeterminate). These regimens, which are widely applicable throughout the world (with minor local variations), are as follows:

Multibacillary leprosy (3-drug regimen): Rifampicin 600mg once-monthly, supervised (450mg for adults weighing less than 35kg and children 10 to 14 years of age). 10mg/kg once a month for children below 10 years or less than 40kg). Dapsone 100mg daily in adults is adminsitered. Child <10 years old or <40kg: 2mg/kg daily in leprosy. Child >10 to 14 years 50mg dail. Clofazimine 300mg once monthly (supervised) OR 50mg daily (or 100mg on alternate days), self-administered.

Children 10-14 years: 150mg once a month OR 50mg daily. Children <10 years of age (less than 40kg): 100 mg and 50 mg twice a week. Lepromatous lepra reactions, dosage increased to 300mg daily for a maximum of 3 months.

Treatment for multibacillary leprosy should be given for at least 2 years and be continued, if possible, up to smear negativity. It should be continued unchanged during both type 1 (reversal) or type II (erythema nodosum leprosum) reactions which, if severe, should receive their specific treatment (e.g.

prednisolone or increased clofazimine dosage). Paucibacillary leprosy (2-drug regimen), Rifampicin 600mg once monthly supervised (450mg for adults weighing less than 35kg and children 10 to 14 years of age. 10mg/kg once a month for children below 10 years or less than 40kg), Dapsone 100mg daily, self-administered. Child <10 years old or <40kg 2mg/kg daily in leprosy. Child >10 to 14 years 50mg daily. Treatment for paucibacillary leprosy should be given for 6 months. If treatment is interrupted the regimen should be recommenced where it was left off to complete the full course.

Neither the multibacillary nor the paucibacillary antileprosy regimen is sufficient to treat tuberculosis, therefore patients who also have tuberculosis should be given appropriate antituberculosis medicines in addition to the antileprosy regimen.

CLOFAZIMINE

Presentation: Capsules containing 50mg, 100mg Clofazimine

Indications: Multibacillary leprosy, in combination with Dapsone, chronic leprae type 2 (ENL) reactions **Administration:** Leprosy, see notes above.

Adult: 300mg once monthly (supervised) OR 50mg daily (or 100mg on alternate days), self-administered.

Children

10-14 years: 150mg once a month OR 50mg daily.

<10 years of age (less than 40kg): 100 mg and 50 mg twice a week.

Lepromatous lepra reactions, dosage increased to 300mg daily for a maximum of 3 months.

Side effects: Nausea, vomiting (hospitalise if persistent), abdominal pain; headache, tiredness; brownish-black discolouration of lesions and skin including areas exposed to light; reversible hair discolouration; dry skin; red discolouration of faeces, urine and other body fluids; also, rash, pruritus, photosensitivity. Acne-like Eruptions, anorexia, eosinophilic enteropathy, bowel obstruction, dry eyes, dimmed vision, macular and subepithelial corneal pigmentation; elevation of blood sugar, weight loss, splenic infraction lymphadenopathy.

Caution: Hepatic and renal impairment; pregnancy and breast-feeding; may discolour soft contact lenses; avoid if persistent abdominal pain and diarrhoea.

DAPSONE (DDS-Diamino Diphenyl Sulphone)

Presentation: Tablets containing 10mg, 25mg, 100mg

Indications: Leprosy, dermatitis herpetiformis.

Administration: 6-10mg/kg/week divided into a single daily dose.

Adult; 50-100mg daily in a single dose.

Therapy is generally continued for 3 years after the disease has been inactive in Tuberculoid leprosy; 5 to 10 years in borderline leprosy; and for life in lepromatous leprosy.

Children:

<10 years old or <40kg: 2mg/kg daily in leprosy.

>10 to 14 years: 50mg daily

prophylaxis of leprosy

under 2 years: 5mg weekly

over 2 years: 10 mg weekly.

Side effects: Nausea, vomiting (hospitalise if persistent, abdominal pain, headache, tiredness: brownish-black discolouration of lesions and skin including areas exposed to light; reversible hair discolouration; dry skin; red discolouration of faeces, urine and other body fluids; also rash, pruritus, photosensitivity, acne-like eruptions, anorexia, eosinophilic enteropathy, bowel obstruction, dry eyes, dimmed vision, muscular and subepithelial corneal pigmentation; elevation of blood sugar, weight loss, splenic infraction lymphadenopathy.

Caution: Cardiac or pulmonary disease; anaemia (treat severe anaemia before starting); G6PD deficiency (including breastfeeding of affected children, pregnancy; avoid in porphyria.

RIFAMPICIN

Presentation: Capsules containing 150mg, 300mg Rifampicin

Indications: In combination with Dapsone in the treatment of multibacillary and paucibacillary leprosy. Tuberculosis, in combination with other medicines.

Administration:

Brucellosis, legionnaires' disease and serious staphylococcal infections, (in combination with other Medicines), by mouth or by intravenous infusion: 0.6-1.2g daily (in 2-4 divided doses).

Tuberculosis, in combination with other Medicines, see notes above (4.5).

Side effects: Gastro-intestinal symptoms including anorexia, nausea, vomiting, diarrhoea (pseudomembranous colitis reported); those influenzal syndromes (with chills, fever, dizziness, bone pain), respiratory symptoms (including shortness of breath), collapse and shock, haemolytic anaemia, acute renal failure, and thrombocytopenic purpura; alterations of liver function, jaundice, flushing, urticaria, and rashes; other side-effects reported include oedema.

Contraindications: Liver failure.

Caution: Reduce dose in hepatic impairment (liver function tests and blood counts in hepatic disorders and on prolonged therapy); renal impairment (if above 600mg daily); pregnancy and breast-feeding (see notes above)

Important: advise patients on oral contraceptives to use additional means, discolours soft contact lenses; see also notes above.

Note: If treatment is interrupted re-introduce with a low dosage and increase gradually; discontinue permanently if serious side effects develop.

	Dapsone	100 mg daily		
Children (10-14 years)	Rifampicin	450 mg once a month	12	6
	Clofazimine	150 mg once a month and 50mg daily		
	Clofazimine	50 mg daily		
Children <10 years old or <40kg	Rifampicin	10 mg/kg once month	12	6
	Clofazimine	100mg once a month, 50mg twice weekly		
	Dopsone	2mg/kg daily		

Hepatic disorders: Patients or their carers should be told how to recognise signs of liver disorder and advised to discontinue treatment and seek immediate medical attention if symptoms such as persistent nausea, vomiting, malaise or jaundice, porphyria muscular weakness and myopathy, leucopenia, eosinophilia, menstrual disturbances; urine, saliva, and other body secretions coloured orange-red; thrombophlebitis reported if infusion used for a prolonged period.

Th table below summarises the recommended leprosy treatment regimens

Age group	**Drug**	**Dosage and Frequency**	**Duration (months)**	
			MB	**PB**
Adult	Rifampicin	600mg once a month	12	6
	Clofazimine	300mg once a month and 50mg daily		

Treatment for drug-resistant leprosy
The World Health Organization Guidelines Development Group recommends for leprosy patients with rifampicin resistance to be treated using at least two of the following second-line drugs: clarithromycin, minocycline, or a quinolone (ofloxacin, levofloxacin or moxifloxacin), plus clofazimine daily for 6 months, followed by clofazimine plus one of the second-line drugs daily for an additional 18 months. In case of rifampicin plus ofloxacin resistance, a quinolone should not be chosen; therefore, the recommended regimen is clarithromycin, minocycline and clofazimine for 6 months followed by clarithromycin or minocycline plus clofazimine for an additional 18 months. the table below shows the recomended drug resistant leprosy regimens.

Resistance type	Treatment	
	First 6 months (daily)	Next 18 months (daily)
Rifampicin resistance	Ofloxacin 400mg*+minocycline 100mg +clofazimine 50 mg	Ofloxacin 400mg*OR minocycline 100mg +clofazimine 50 mg
	Ofloxacin 400mg*+clarithromycin 500mg +clofazimine 50 mg	Ofloxacin 400mg*+clofazimine 50 mg
Rifampicin and Ofloxacin resistance	Ofloxacin 500mg+minocycline 100mg +clofazimine 50 mg	Ofloxacin 400mg*OR minocycline 100mg +clofazimine 50 mg

*Ofloxacin can be replaced by Levofloxacin or moxifloxacin.

4.7 Antivirals

The majority of viral infections resolve spontaneously and do not need specific therapy. Treatment is primarily symptomatic.

4.7.1 Medicines used in Herpes Simplex and Varicella Zoster Infections

Acyclovir is active against herpes viruses but does not eradicate them. It is effective only if started at the onset of infection. Acyclovir can be used either systemically or topically (including the eye) for the treatment of *Herpes simplex* infections of the skin and mucous membranes (including genital herpes) or systemically for the treatment of *Varicella-zoster*. It may be given by mouth to immunocompetent adults and older adolescents for the treatment of chickenpox but not to immunocompetent children in whom the disease is milder. In immunocompromised patients with *Herpes simplex* and *Varicella-zoster* infection, it can also be used prophylactically to prevent a recurrence.

Valaciclovir, a product of acyclovir, is licensed for use in herpes zoster and *herpes simplex* infections of the skin and mucous membranes (including genital herpes).

Idoxuridine is only used topically because of its systemic toxicity. It is only effective if used at the onset of infection. It is indicated for use in the treatment of *herpes simplex* lesions of the skin and external genitalia. It is less effective in herpes zoster infection.

ACYCLOVIR

Presentation: Tablets containing aciclovir 200mg, 400mg, 800mg. IV infusion vial containing 250mg, 500mg powder for reconstitution. Sugarfree suspension containing aciclovir 200mg/5ml (125ml), 400mg/5ml (50ml); Cream containing aciclovir 5%, 2g, 10g tube. Eye ointment containing aciclovir 3%, 4.5g tube.

Indications: *Herpes simplex* and *Varicella-zoster*

Administration: *Oral*;

Genital Herpes: initial treatment: 200mg PO every 4 hours (5 times daily) for 10 days or 400mg PO 8 hourly for 7-10 days.

*Herpes simplex virus encephalitis:*10 -15mg/kg IV 8hr for 10 days.

Mucocutaneaus Herpes simplex Virus infection: Treatment in immunocompromised patients;5mg/kg IV,8hr for 7 days.

Herpes Zoster(shingles): Acute treatment; 800mg PO 4hr for 7-days, in immunocompromised 10mg/kg IV 8hr for 7 days.

Children:

***Neonatal herpes simplex Virus infection*;**

≥ *34 weeks:* 20mg/kg IV every 8 hr for 21 days

<34 weeks: 20mg/kg IV 12 hr for 21 days.

Mucocutaneous Herpes simplex virus infection;

<12 years: 10-15mg/kg IV 8hr for 7 days

≥ *12 years:* 5-10mg/kg IV 8hr 5-7 days.

Herpes Zoster (chickenpox)*:*

<12 years (immunocompromised): 20mg/kg IV 8hr for 7 day

≥ *12 years* (immunocompetent): 800mg PO evrery 4hr for 7-days.

≥ *12 years* (Immunocompromised): 30mg/kg/day IV every 8hr for 7-10 day.

Side effects*:* Rashes; gastro-intestinal disturbances; rises in bilirubin and liver enzymes, increases in blood urea and creatinine, decreases in haematological indices, headache, neurological reactions (including dizziness), fatigue; on iv infusion, sever local inflammation (sometimes leading to ulceration), also confusion, hallucinations, agitation, tremors, drowsiness, psychosis, convulsions and coma. **Contraindications*:*** Hypersensitivity.

Caution*:* Maintain adequate hydration; renal impairment; pregnancy and breast-feeding. Avoid rapid infusion because of risk of renal damage.

VALACYCLOVIR

Presentation: Tablets containing Valacyclovir hydrochloride 500mg and 1000mg

Indications*:* Treatment of *Herpes zoster* and herpes simplex infections of the skin and mucous membranes including initial and recurrent genital herpes.

Administration: *Herpes zoster:* 1g 3 times daily for 7 days

Herpes simplex: the first episode, 500mg twice daily for 5 days (up to ten days if severe); Recurrent infection, 500mg twice daily for 5 days

Herpes labialis: 2g every 12 hr for 1 day.

Genital herpes; 1g PO every 12 hr for 10 days, recurrent episodes: 500mg PO every 12hr for 3 days.

Children:

<2 years; safety and efficacy not established

Chickenpox

>2 years: 20mg/kg PO 8hr for 5 days; not exceed 1 g 8hr. ***Herpes labialis***

<12 years safety and efficacy not established

>12 years: 2g PO every 12hr for 1 day.

Side effects*:* As for acyclovir; nausea and headache, neutropenia, elevated aspartate transaminase, elevated ALT.

Contra indications: Hypersensitivity to Valacyclovir or acyclovir

Caution*:* Maintain adequate hydration; renal impairment; pregnancy and breastfeeding.

IDOXURIDINE

Presentation*:* Application (with applicator) containing Idoxuridine 5% in dimethyl sulphoxide 5ml

Indications*:* *Herpes simplex* and *herpes zoster*

Administration: Apply to lesions 4 times daily for 4 days, starting at the first sign of attack

Children under 12 years, not recommended.

Side effects: Stinging on the application, changes in taste; overuse may cause maceration

Contraindications: Pregnancy (toxicity in animal studies); not to be used in the mouth.

Caution: Avoid contact with eyes, mucous membranes, and textiles; breast-feeding (may taste unpleasant).

4.7.2 Medicines used in Cytomegalovirus (CMV) infections

Ganciclovir is related to aciclovir but is more active against cytomegalovirus and is also more toxic. It should therefore only be given when the potential benefit outweighs the risks. It is usually given by intravenous infusion, but capsules are available for maintenance treatment of CMV retinitis in AIDS patients following IV therapy if the condition is stable. Ganciclovir should not be given together with zidovudine as the combination causes severe myelosuppression.

GANCYCLOVIR

Presentation: Capsules containing gancyclovir 250mg. IV infusion powder for reconstitution containing ganciclovir sodium 500mg per vial.

Indications: Life-threatening or sight-threatening cytomegalovirus infections in immunocompromised patients; prevention of cytomegalovirus disease during immunosuppressive therapy following organ transplantation.

Administration: *by IV infusion* over one hour, initial

(Induction treatment), 5mg/kg every 12 hours for 14 - 21 days for treatment or 7-14 days for prevention; maintenance (for patients at risk of relapse of retinitis) 6mg/kg daily on 5 days per week or 5mg/kg daily every day; if retinitis progresses, initial induction treatment may be repeated.

Maintenance in AIDS patients where retinitis is stable (following at least three weeks of iv gancyclovir), *by mouth*, 1g 4 times daily with food or 500mg 6 times daily with food.

In renal impairment, consult product literature.

Children:

Initially 5 mg/kg every 12 hours for 14–21 days, then maintenance 6 mg/kg once daily, on 5 days of the week;

Alternatively, maintenance 5 mg/kg once daily; maintenance only for patients at risk of relapse; if disease progresses initial induction treatment may be repeated.

Side effects: Most frequent, leucopenia and thrombocytopenia; less frequent, includes anaemia, fever, rash, infections, gastrointestinal haemorrhage, dizziness, mood disturbances, disturbances in taste and vision, local inflammation, pain, phlebitis at the injection site (see product literature for full list).

Contraindications: Hypersensitivity to ganciclovir or aciclovir, pregnancy (effective contraception should be used during treatment and barrier contraception for men during and for 90 days after treatment); breastfeeding (until 72 hours after the last dose); abnormally low neutrophil or platelet counts.

Caution: Close monitoring of blood counts; a history of cytopenia; low platelet count; concomitant use of myelosuppressants or Medicines which inhibit rapid cell replication; potential carcinogen and teratogen; renal impairment; ensure adequate hydration during administration; vesicant-infuse into the vein with adequate flow preferably via a plastic cannula; limited experience in children-not for neonatal or congenital cytomegalovirus.

VALGANCICLOVIR

Presentation: Available in 450 mg tablets and 50mg/ml solution for injection.

Indications: Treatment of Cytomegalovirus retinitis, CMV colitis or Esophagitis in HIV-infected patients.

Administration: *Cytomegalovirus Retinitis*; induction dose; 900mg PO every 12 hr for 21 days, then maintenance 900mg PO, OD.

CMV colitis or esophagitis in HIV-infected patients(off-label); Ganciclovir 5mg/kg/dose every 12hr once therapy is tolerated, change to valganciclovir 900mg 12 hr for 21-42 days.

Children:

CMV prevention in kidney and heart Transplant

<4 months: safety and efficacy not established

4 months -16 years: Daily dose(mg)= 7 x BSA x CrCl;

Not to exceed 900mg/day. Begin within 10 days

Side effects: Abdominal pain, anaemia, diarrhoea, fever, granulocytopenia, headache, vomiting.

Contraindications: History of clinically significant hypersensitivity reaction to valganciclovir, ganciclovir or excipients.

Caution: Hematological toxicity; severe leucopenia, anaemia, thrombocytopenia, pancytopenia and born marrow suppression, impaired fertility, fetal toxicity and carcinogenic.

4.7.3 Medicines used in human immunodeficiency virus (HIV) infection

While there is currently no known cure for HIV infection, there is evidence that treating HIV infected patients with antiretroviral Medicines does have benefits in terms of improved health and quality of life. The use of antiretroviral medicines to treat HIV infected patient should only be undertaken by those experienced in their use.

Monitoring HIV infection/therapy

CD4 count

The CD4 count is useful for staging HIV disease and for timing the initiation of prophylaxis against opportunistic infections.

Viral load count

Viral load test measures the amount of HIV RNA in the blood. Right now, if CD4 count and viral loads are not available, there is no other way to define failure of therapy with laboratory tests. The level of HIV in the blood indicates a person's risk of getting sick. The lower the load the less likely the patient to get sick and the longer they will live. It is expected that after 6 months of therapy there should be low viral RNA detectable in the plasma if treatment is optimal.

Initiating

Clinical decisions on initiating or changing therapy should be guided by a combination of CD4 count and viral load count monitoring and consideration of the clinical condition of the patient. It is proposed that initiation of treatment be considered when viral load counts are > 10,000 to 50,000 copies/ml with falling CD4 count (<200-300 cells/ mm^3).

Special considerations for starting ARV therapy should be given to patients with:

- **TB-** Start with CD4< 200 or total lymphocyte count < 1200/mm3 or other HIV-related stages 2 or 3 conditions currently or in past 12 months.
- **Kaposi's Sarcoma** – is considered an AIDS-defining condition; start on ARV therapy. A total lymphocyte count of < 1,200-cells/ mm3 can be substituted for the CD4 **count if HIV-related symptoms exist** (WHO stage II and III). An absolute lymphocyte count is less useful in the patient without symptoms. If there is no CD4 testing, HIV-infected patients with no symptoms (WHO stage I) should be treated; observe for the development of early symptoms and refer for further evaluation (e.g. CD4 and Viral load testing) if feasible.

Response to treatment

Change in viral load 8-12 weeks after starting treatment is considered the best single marker of therapeutic effect, with the predictive value being increased when viral load and CD4 counts are combined. Treatment aims to reduce the level of virus in the blood as low as possible and preferably to undetectable levels and to prevent the emergence of resistance. However, therapy goals set should be realistic and will depend on the stage at which the patient is started on treatment, the baseline viral load and CD4 counts, previous exposure to treatment Medicines and presence and extent of drug resistance.

Choice of Medicines

Failure of Medicines to work has been most frequently associated with the emergence of resistance. Using a combination of Medicines delays the emergence of resistance.

It is generally accepted that triple therapy with two nucleoside analogues and one NNRTI or protease inhibitor is the preferred regimen. Monotherapy is not recommended due to the rapid emergence of resistance and poor response.

When to change therapy

Decisions to change therapy will depend on several factors - clinical eg. intolerance due to side effects or adverse events; virological eg. rising viral load count; and immunological eg. falling CD4 count. Occurrences of pregnancy T.B, New effective Medicines

The choice of whether to change all the Medicines or to change just one or some of the Medicines will depend on previous exposure to treatment Medicines, the toxicity profile of alternative Medicines, availability of viral sensitivity assays, availability of testing facilities for CD4 and viral load counts.

The current practice appears to lean towards changing treatment after 3 months if there is little or no clinical improvement or if CD4 remains the same as dropping or if virus levels are rising after initially falling.

It is preferable, in general, to change at least one class of most likely affected Medicines (e.g. NRTIs) and even better to use an entirely new regimen when there is treatment failure due to drug failure as opposed to drug toxicity. Where drug toxicity is the problem a different drug or Medicines of equivalent potency from the same class of agents can be substituted.

4.7.3.1 Nucleoside reverse transcriptase inhibitors

Abacavir: Hypersensitivity Reactions: Life-threatening hypersensitivity reactions characterized most commonly by fever or rash and possibly nausea, vomiting, diarrhoea, abdominal pain, dyspnoea, cough, lethargy, malaise, headache, and myalgia, less frequently by mouth ulceration, oedema, hypotension, sore throat, adult respiratory distress syndrome, paraesthesia, arthralgia, conjunctivitis, lymphadenopathy, lymphocytopenia, renal failure, and anaphylaxis and rarely by myol6sis have been reported. Laboratory abnormalities may include raised liver enzymes (see Hepatic disease below) and creatine kinase. Symptoms usually appear in the first 6 weeks, but may occur at any time; monitor patients for symptoms every 2 weeks for 2 months; discontinue immediately if any symptom of hypersensitivity develops and do not rechallenge (risk of a more severe hypersensitivity reaction); also discontinue if hypersensitivity cannot be ruled out, even when other diagnoses possible (if rechallenge is necessary, it must be carried out in a hospital setting). If abacavir is stopped for any reason other than hypersensitivity, exclude hypersensitivity reaction as the cause and rechallenge only if medical assistance is readily available; care is needed with concomitant use of drugs which are known to cause skin toxicity.

Patient advice: Patients should be told about the importance of regular dosing (intermittent therapy may increase sensitization), how to recognize signs of hypersensitivity, and advised to seek immediate medical attention if symptoms develop or before restarting treatment.

Hepatic disease: Potentially life-threatening lactic acidosis and severe hepatomegaly with steatosis have been reported. Exercise caution in patients (particularly obese women) with hepatomegaly, hepatitis, liver enzyme abnormalities or risk factors for liver disease and hepatic steatosis (including alcohol abuse) and discontinue if the rapid deterioration in liver function tests, symptomatic hyperlactatemia, progressive hepatomegaly, or lactic acidosis occurs.

ABACAVIR (ABC)

Presentation: Oral liquid containing 100mg/5ml (as sulfate); Tablet containing 300 mg (as sulfate).

Indications: HIV infection in combination with at least two other antiretroviral medicines.

Administration: HIV infection in combination with at least two other antiretroviral medicines, by mouth, Adult, 300 mg twice daily

Children:
3 months – 16 years: 8 mg/kg twice daily (maximum, 600 mg daily).

Side effects: Hypersensitivity reactions including rash, nausea, vomiting, diarrhoea, anorexia, lethargy, fatigue, fever, headache, insomnia, and dizziness (see also note on Hypersensitivity reactions above); pancreatitis, liver damage and lactic acidosis (see note on Hepatic disease above; very rarely Stevens-Johnson syndrome and toxic epidermal necrolysis, rash and gastrointestinal disturbances more common in children.

Cautions: Chronic hepatitis B or C, hepatic impairment.

TENOFOVIR DISOPROXIL FUMARATE (TDF)

Presentation: Tablet containing 300 mg Tenofovir disoproxil fumarate – equivalent to 245 mg tenofovir disoproxil.

Indications: HIV infection in combination with other antiretroviral medicines.

Administration: by mouth*, Adult,* 245 mg (1 tablet) once daily.

Side effects: Nausea, vomiting, abdominal pain, flatulence, diarrhoea, anorexia; hypophosphataemia; dizziness, peripheral neuropathy, headache, dyspnoea, insomnia, depression, asthenia, sweating, myalgia, rash, hypertriglyceridaemia, hyperglycaemia, neutropenia; nephritis, nephrogenic diabetes insipidus, renal impairment, effects on renal proximal tubules (including Fanconi syndrome), proteinuria, polyuria, reduced bone density; pancreatitis, hepatitis, lactic acidosis, raised liver enzymes, creatinine and serum amylase reported. **Cautions:** Renal impairment hepatic disease, pregnancy, breastfeeding. Hepatic disease. Potentially life-threatening lactic acidosis and severe hepatomegaly with steatosis have been reported. Exercise caution in patients (particularly obese women) with hepatomegaly, hepatitis (especially hepatitis C treated with interferon alfa and ribavirin), liver enzyme abnormalities, or risk factors for liver disease and hepatic steatosis (including alcohol abuse). Discontinue if rapid deterioration in liver function tests, symptomatic hyperlactatemia, progressive hepatomegaly, or lactic acidosis occurs. Exacerbation of hepatitis in patients with chronic hepatitis B may occur on discontinuation of tenofovir.

Patient advice: Tablets can be dispersed in at least 100 ml water, orange juice or grape juice for patients with difficulty swallowing.

TENOFOVIR ALAFENAMIDE (TAF)

Presentation: Tablet containing 25 mg Tenofovir alafenamide.

Uses: HIV infection in combination with other antiretroviral medicines. Chronic Hepatitis-B.

Administration: *by mouth*, Adult: 25mg once daily.

Side effects: See Tenofovir disoproxil fumarate. **Contraindications:** Similar to Tenofovir disoproxil fumarate.

Cautions: Decompensated liver disease, HIV co-infection.

LAMIVUDINE (3TC)

Presentation: Tablets (film-coated) containing 150mg lamivudine. An oral solution containing 10mg/ml lamivudine.

Indications: Advanced HIV infection, in combination with other antiretroviral medicines.

Administration: Adolescent/adult; Bodyweight > or = 50kg; 150mg twice daily. Bodyweight < 50kg 2mg/kg body weight twice daily.

Children:

Neonates (<30 days); 2mg/kg body weight twice daily.

Child; 4mg/kg body weight twice daily.

Side effects: Most frequent ones include headache, anaemia fatigue, nausea, diarrhoea, skin rash and abdominal pain, fever, alopecia, lactic acidosis.

Caution: Renal impairment, hepatic disease due to chronic hepatitis B infection (risk of rebound hepatitis on discontinuation); pregnancy (avoid in the first trimester), Breast-feeding.

ZIDOVUDINE (AZT)

Presentation: Tablets containing 300mg zidovudine, capsules containing 100mg zidovudine. Syrup containing 10mg/ml zidovudine. Injection containing 10mg/ml zidovudine.

Indications: Management of advanced HIV infection such AIDS in combination or AIDS-related complex; early symptomatic or asymptomatic HIV infection with markers indicating risk of disease progression; symptomatic or asymptomatic HIV-infected children with markers indicating significant immune suppression; consider for prevention of maternal-fetal HIV transmission (by treating pregnant women and their newborn infants in combination with other medicines.

Administration: *Adolescent/adult*; 200mg every 8 hours or 300mg twice a day.

Children:

Infant, below 3 months, orally; 2mg/kg body weight every 6 hours. intravenously 1.5mg/kg body weight every 6 hours.

Usual dose: 90mg – 180mg/m^2 of body surface area every 6 hours.

Side effects: Frequent side effects include headache, hematologic toxicity, granulocytopenia and anaemia.

Contra-indications: Abnormally low neutrophil counts or haemoglobin values (see datasheet); neonates with hyperbilirubinaemia requiring treatment other than phototherapy, or with raised transaminase.

Caution: Haematological toxicity (blood tests at least every 2 weeks for first 3 months then at least once a month); vitamin B12 deficiency; renal impairment; hepatic impairment; risk of lactic acidosis; elderly; pregnancy; breastfeeding not recommended during treatment.

EMTRICITABINE (FTC)

Presentation: Capsule containing 200mg, Oral solution containing 10mg/ml Emtricitabine.

Indications: Management of HIV infection in combination with other antiretroviral drugs.

Administration: *Adult:* 200mg capsule once daily OR 240mg solution once daily (Dose equivalence and conversion 240mg oral solution = 200mg Capsule).

Side effects: Abnormal dreams, hyperpigmentation, pruritus.

Contraindications: Hypersensitivity

Caution: Lactic Acidosis, hepatic and renal impairment; chronic hepatitis B.

4.7.3.2 Non-nucleoside reverse transcriptase inhibitors

EFAVIRENZ (EFV)

Presentation: Capsule containing 50mg; 100mg; 200 mg; Oral liquid containing 150mg/5 ml. Tablet containing 600 mg Efavirenz.

Indications: HIV infection in combination with at least two other antiretroviral medicines.

Administration: *Adult*: 600 mg once daily

Children: 3 months–17 years
Body-weight 3.5–4 kg: 100 mg once daily
Body-weight 5–7.4 kg: 150 mg once daily
Body-weight 7.5–14 kg: 200 mg once daily
Body-weight 15–19 kg: 250 mg once daily
Body-weight 20–24 kg: 300 mg once daily
Body-weight 25–32.4 kg: 350 mg once daily
Body-weight 32.5–39 kg: 400 mg once daily
Body-weight 40 kg and above: 600 mg once daily

Note: The bioavailability of efavirenz from the oral solution is lower than that from the capsules and tablets; the oral solution is therefore not interchangeable with either the capsules or tablets on a milligram-for-milligram basis.

Side effects: Rash, usually occurring in the first 2 weeks, is the most common adverse effect; discontinue if the rash is severe or if the rash is accompanied by blistering, desquamation, mucosal involvement or fever; if the rash is mild or moderate, continue without interruption (rash usually resolves whin 1 month).

Psychiatric disorders: patients should be advised to seek medical attention if severe, depression, psychosis or suicidal ideation occur.

Contraindications: Pregnancy, especially in the first trimester (substitute nevirapine for efavirenz in pregnant women or women for whom effective contraception cannot be assured).

Cautions: Chronic hepatitis B or C; hepatic impairment (avoid if severe; renal impairment. Breastfeeding; the elderly; a history of mental illness or seizures.

NEVIRAPINE (NVP)

Presentation: Oral liquid: 50 mg/5 ml. Tablet: 200 mg.

Indication: HIV infection in combination with at least two other antiretroviral medicines; prevention of mother-to-child HIV transmission.

Administration: HIV infection (in combination with other antiretroviral medicines), *by mouth*, Adult, 200 mg once daily for first 14 days, then (if no rash present) 200 mg twice daily

Children:
Infant 15-30 days old: 5 mg/kg once daily for 14 days, then (if no rash present) 120 mg/m^2 twice daily for 14 days, then 200 mg/m^2 twice daily.
1 month-13 years: 120 mg/m^2 once daily for first 14 days, then (if no rash present) 120-200 mg/m^2 twice daily.
Prevention of mother-to-child transmission *by mouth*
Neonate: 2mg/kg OR as per HEI protocol according to weight bands, in combination with AZT/3TC.

NOTE: In adults, if treatment is interrupted for more than 7 days, reintroduce at a dose of 200 mg daily (Infant 15-30 days old, 5mg/kg; Child over 1 month, 120 mg/m^2) and increase dose cautiously.

Side effects: Rash, usually occurring in the first 6 weeks, is the most common side-effect; incidence can be reduced if introduced at a low dose and dose increased gradually. Monitor closely for skin reactions during first 18 weeks; discontinue permanently if the rash is severe or if the rash is accompanied by blistering oral lesions, conjunctivitis, facial oedema, general malaise, or hypersensitivity reactions; if the rash is mild or moderate, continue without interruption but the dose should not be increased until rash resolves.

Patient advice: Patients should be told how to recognize hypersensitivity reactions and advised to discontinue treatment and seek immediate medical attention if symptoms of hepatitis, severe skin reaction or hypersensitivity reactions develop; severe hepatic impairment, headache, nausea.

Caution: hepatic impairment; chronic hepatitis B or C, high CD4 cell count, and women (greater risk of hepatic side effects preferably avoid in women with a CD4 cell count greater than 250 cells/mm^3 and in men with a CD4 cell count greater than 400 cells/mm^3; pregnancy breastfeeding.

Hepatic disease: Potentially life-threatening hepatotoxicity, including fatal fulminant hepatitis, reported usually occurring in the first 6 weeks. Close monitoring is required during the first 18 weeks; assess liver function before treatment then every 2 weeks for 2 months, then after 1 month, and then regularly. Discontinue permanently if liver abnormalities are accompanied by hypersensitivity reactions, for example, rash, fever, arthralgia, myalgia, lymphadenopathy, hepatitis, renal impairment, eosinophilia, and granulocytopenia). If severe liver abnormalities occur without hypersensitivity reactions, suspend, but discontinue permanently if significant liver function abnormalities recur. Monitor patient closely if there is mild to moderate liver abnormalities with no hypersensitivity reactions.

ETRAVIRINE (ETR)

Presentation: Tablet containing 25mg, 100mg or 200mg of Etravirine

Indications: HIV infection resistant to other non-nucleoside reverse transcriptase inhibitor and protease inhibitors in combination with other antiretroviral drugs (including a boosted protease inhibitor).

Administration: *Adult*: 200 mg twice daily, to be taken after food.

Children:

16 to <20 kg: 100 mg twice daily;

20 to <25 kg: 125 mg twice daily;

25 to <30 kg: 150 mg twice daily;

At least 30 kg: 200 mg twice daily (maximum dose)

Side effects: Rash, nausea, vomiting, hyperglycaemia, headache, diarrhea, peripheral neuropathy, angioedema, dry mouth, gynaecomastia, hyperhidrosis, hypersomnia, pancreatitis, angina, myocardial infarction.

Contraindication: Acute porphyrias

Cautions: hepatic impairment, SJS

4.7.3.3 Protease inhibitors

Presentation: Oral suspension containing 80mg Lopinavir and 20mg Ritonavir, Tablets 100mg/25mg.

Indications: Progressive or advanced HIV infection, in combination with other ARVs.

Administration: *Adult*: 800mg/200mg tablet once daily or 400mg/100mg orally twice daily.

Children:

Less than 15kg: 12mg/kg (Lopinavir component) orally twice daily

15-40kg: 10mg/kg (Lopinavir component) orally twice daily;

Greater than 40kg: Lopinavir 400mg/100mg Ritonavir twice daily.

under 6 months: 16mg/kg (Lopinavir component) orally twice daily.

Side effects: More frequent include diarrhoea, nausea, vomiting, abdominal pain, headache, dizziness and asymptomatic hypercholesterolemia.

Caution: Hepatic impairment; ensure adequate hydration to reduce risk of nephrolithiasis; haemophilia (possible increased bleeding); pregnancy; metabolism of many Medicines inhibited if administered concomitantly (consult product literature), breast-feeding.

RITONAVIR (RTV)

Presentation: Tablet containing 100 mg Ritonavir.

Indications: HIV infection, as a pharmacological booster to increase other protease inhibitors, in combination with other antiretroviral drugs; Non-severe covid-19 in patients with high risk progression to severe disease, used in combination with Nirmatrevir, for patients presenting within 5 days of symptomatology.

Administration: *Adult:* 100 mg twice daily.

It is given for 5 days when indicated for Covid-19.

Children:
7–14.9 kg: 3 mg/kg twice daily
15–40 kg: 2.5 mg/kg twice daily (maximum 100 mg twice daily)

Side effects: Most frequent side effects include nausea, vomiting, diarrhoea, headache, abdominal pain, and anorexia. Rarely spontaneous bleeding in haemophiliacs, pancreatitis, increased levels of triglycerides and cholesterol, hyperglycaemia, ketoacidosis, diabetes, and hepatitis.

Contraindications: Severe hepatic impairment, hypersensitivity, drugs highly dependent on CYP3 for clearance such as Amiodarone, Colchicine, Rifampin, Carbamazepine, Phenobarbitone, Phenytoin, Simvastatin, Midazolam, Sildenafil.

Cautions: Cardiac conduction disorders, pancreatitis, hepatitis, hypersensitivity, haemophilia (possible increased bleeding); pregnancy; metabolism of many medicines inhibited, and toxicity increased if administered concomitantly (consult product literature), breastfeeding.

ATAZANAVIR + RITONAVIR (ATV-r)

Presentation: Tablet containing 300 mg + 100 mg of Atazanavir+Ritonavir

Indications: HIV infection in combination with other antiretroviral drugs

Administration: Adult: 300 mg+100mg once daily.

Children: *Oral*
Over 6 years (15 kg up to 25 kg): 150 mg atazanavir and 80 mg ritonavir once daily
25–30 kg: 200 mg atazanavir and 100 mg ritonavir once daily
30 kg and over: 300 mg atazanavir and 100 mg ritonavir once daily (maximum dose)
Recommended for patients from 6 years of age; currently insufficient data for patients under 6 years of age.

Side effects: Jaundice, nausea, diarrhea, vomiting, anorexia, abdominal pain, taste disturbances, peripheral neuropathy, fever, rash, cough, increase in cholesterol.

Containdications: Severe hepatic impairment, hypersensitivity.

Cautions: Cardiac conduction disorders, electrolyte disturbances, predisposition to QT prolongation, concormitant use with PPIs.

DARUNAVIR + RITONAVIR (DRV-r)

Presentation: Tablet containing 400/50mg or 600/100mg of Darunavir/Ritonavir

Indications: HIV infection in combination with other antiretroviral drugs in patients previously treated with antiretroviral therapy

Administration: *Adult:* 800/100mg once daily for second line therapy, and 600/100 mg twice daily for third line therapy.

Children:
15-29kg: 375mg twice daily
30-39kg: 450mg twice daily
40kgs and above: 600mg twice daily
12–17 years: 800mg once daily

Once daily dose only to be used if no resistance to darunavir, if plasma HIVRNA concentration less than 100 000 copies/ml, and if CD4 cell count greater than 100 cells×106 / liter)

Side effects: Increased cholesterol and triglycerides, nausea, vomiting, diarrhea, rash, fever, headache, hyperglycaemia, osteonecrosis, fat redistribution, acute hepatitis, bad dreams.

Contraindications: Hypersensitivity to darunavir, patients with severe hepatic impairment, combination with strong CYP3A inducers such as rifampicin. Contraindicated in patients with hemophilia type A and B, Statins such as Simvastatin, Colchicine.

Caution: Must be taken with food, people with hepatitis B and C, risk of severe skin reactions, hyperglycaemia.

4.7.3.4 HIV-Integrase Inhibitors

DOLUTEGRAVIR (DTG)

Presentation: Tablets containing 10mg, 20mg, 50mg Dolutetravir sodium. Tablet for oral suspension 5mg.

Indications: HIV infection without resistance to other inhibitors of HIV integrase, in combination with other antiretroviral drugs; Integrase strand transfer inhibitor (INSTI)-associated resistance.

Administration: *Adult:* 50mg once daily; *Suspected INSTI resistance:* 50 mg twice daily.

Children: >4weeks
3-5.9kg: 5mg once daily
6-9.9kg: 15mg once daily
10-13.9kg: 20mg once daily
14-19.9kg: 25mg once daily
>20kg: 50mg once daily
12–17 years (body weight 40 kg and above): 50 mg once daily

Side effects: Diarrhoea, abdominal discomfort, abnormal dreams, dizziness, flatulence, headache, fatigue, insomnia, skin rashes and pruritus. Less common: exacerbation of chronic liver disease, hypersensitivity reactions.

Contraindications: Hypersensitivity.

Caution: Hypersensitivity reactions reported; Severe hepatic or renal impairment; pregnancy

RALTEGRAVIR (RAL)

Presentation: Tablet (film-coated) containing 400mg Raltegravir.

Indications: HIV infection without resistance to other inhibitors of HIV integrase, in combination with other antiretroviral drugs.

Administration: *Adult:* 400mg twice daily. Alternatively: 1200 mg once daily.

Once daily dosing for use in patients who are treatment naive or virologically suppressed on an initial regimen of 400mg twice daily.

Children:
Initiated by a specialist

Side effects: Diarrhoea, abdominal discomfort, abnormal dreams, dizziness, flatulence, headache, fatigue, insomnia, skin rashes and pruritus, hypersensitivity, hyperlipidemia. Less common: acne, alopecia, chronic liver disease, gynaecomastia, erectile dysfunction, hypertension.

Contraindications: Hypersensitivity

Caution: Psychiatric illness, myopathy, Hypersensitivity reactions.

CABOTEGRAVIR (CAB)

Presentation: Injection containing 600mg/3ml of Cabotegravir

Indications: Pre-exposure prophylaxis for HIV

Administration: Initiation injections: 600 mg Intramuscular (IM) x 2 doses given 1 month apart (the second initiation injection can be given up to 7 days before or after the date scheduled to receive injection); then Continuation injections: 600 mg IM every 2 months.

Side effects: Injection site reaction, rhabdomyolysis, headache, renal dysfunction, diarrhea, nausea, upper RTIs, hepatitis, pancreatitis, depression.

Contraindications: Hypersensitivity to cabotegravir, coadministration with carbamazepine, phenobarbitone, phenytoin, rifampicin and rifapentine, administration in unknown or positive HIV status.

Cautions: Hepatotoxicity, hypersensitivity, depressive disorders.

4.7.4 Medicines Used in Covid-19

NIRMATRELVIR (NMV)

Presentation: Tablet containing 150mg of Nirmatrelvir

Indications: Non-severe covid-19 in patients with high risk progression to severe disease, used in combination with ritonavir, for patients presenting within 5 days of symptomatology.

Administration: *Adult and children ≥12years and 40kg*: 300mg twice daily for 5 days. Reduce the dose to 150mg for eGFR ≥30 ml/min and <60 ml/min.

Side effects: Altered taste, diarrhoea, headache, nausea, vomiting.

Contraindications: Severe renal impairment, hypersensitivity, drugs highly dependent on CYP3 for clearance such as Amiodarone, Colchicine, Eplerenone, Simvastatin, Midazolam, Sildenafil, Ivabradine.

Cautions: Renal impairment, hypersensitivity, hepatic impairment, pregnancy and breastfeeding.

RITONAVIR

(Refer to section on HIV: 4.7.3.3)

REMDESIVIR (RDV)

Presentation: Injection containing 100mg/vial of Remdesivir

Indication: Non-severe and severe covid-19 infection, for patients presenting within 7 days of symptomatology.

Administration: *Adult and Children ≥ 40kg:* 200mg on day 1 and 100mg on subsequent days. Duration 3-10 days depending on severity.

Children:

≥3kg to <40kg: 5mg/kg on day 1 and 2.5mg/kg on subsequent days. Duration 3-10 days depending on severity.

Side effects: Renal impairment, hyperglycaemia, anaemia, increased transaminases, lymphopaenia, increased prothrombin time, headache, nausea, rash.

Contraindications: Hypersensitivity.

Cautions: Hypersensitivity, hepatic impairment, renal impairment, coadministration with hydroxy/chloroquine.

MOLNUPIRAVIR (MOV)

Presentation: Capsule containing 200mg of Molnupiravir.

Indications: Non-severe covid-19 infection, for patients presenting within 5 days of symptomatology.

Administration: *Adults ≥18years*: 800mg twice daily for 5 days

Side effects: Diarrhoea, nausea, vomiting, dizziness, skin reactions.

Contraindications: Pregnancy.

5 Medicines acting on the Endocrine System

5.1 Medicines used in diabetes

5.1.1 Insulin preparations

A polypeptide hormone found naturally in the body which plays an important role in the metabolism of carbohydrates, fats and proteins. It is used for the management of insulin-dependent diabetes mellitus (IDDM) or type 1 diabetes. IDDM is due to a deficiency in insulin synthesis and secretion.

Insulin used for treatment is extracted mainly from pork pancreas and purified by crystallization. Also available are beef/pork and human varieties and biosynthetically made and semisynthetic human varieties. Immunological resistance to insulin is uncommon. Antigenic (immune) response occurs in some individuals. It is inactivated by gastrointestinal enzymes, so it is given by injection, mainly subcutaneously. It can also be given continuously by subcutaneous infusion although this is not the preferred route as it requires expert supervision at all times.

Insulin is the drug of choice in patients with a rapid onset of symptoms and most children require insulin from the onset.

Blood glucose concentrations must be monitored for patients receiving insulin treatment. Variations in lifestyles, infection, corticosteroids and oral contraceptives may affect insulin requirements. In pregnancy, insulin requirements must be assessed frequently.

Insulin is available in three types of preparations:

A polypeptide hormone that is synthesised and secreted from the pancreatic beta cells. It plays an important role in the metabolism of carbohydrates, fats and proteins. It is used for the management of Diabetes mellitus. Two types of insulins are available in Zambia, human insulin and human insulin analogues. Human insulin which is used for treatment is manufactured using recombinant DNA technique.

Human insulin analogues are produced in the same way but the insulin is modified to produce a desired kinetic characteristic such as extended duration or faster absorption and onset of action.

Insulin administration: Insulin, being a protein, is inactivated by gastrointestinal enzymes. It is thus administered by injection, the subcutaneous route is ideal most of the times. The injection should be given in a body area with plenty of subcutaneous fat such as the abdomen, thigh or buttock.

Absorption from a limb site can vary considerably (by as much as 20–40%) day-to-day, particularly in children. Local tissue reactions, changes in insulin sensitivity, injection site, blood flow, depth of injection, and the amount of insulin injected can all affect the rate of absorption. Exercise can also increase insulin absorption so can massage of the injectionsite.

Lipohypertrophy can occur due to repeatedly injecting into the same small area, and can impair the absorption of insulin, and contribute

to poor glycaemic control. Patients should be advised not to use affected areas for further injection until the skin has recovered. Lipohypertrophy can be minimised by using different injection sites in rotation. Injection sites should be checked for signs of infection, swelling, bruising, and lipohypertrophy before administration.

Insulin preparations: Insulin preparations can be broadly categorised into three groups based on their time-action profiles: short-acting insulins (including soluble insulin and rapid-acting insulins), intermediate-acting insulins and long-acting insulins.

Short-acting insulins: Short-acting insulins have a relative rapid onset of action and a short duration to mimick physiological insulin production after a glucose meal. These are available as soluble or regular human Insulin, and the rapid-acting insulin analogues (insulin aspart insulin glulisine and insulin lispro.

Soluble insulin: Soluble insulin is usually given subcutaneously but some preparations can be given intravenously and intramuscularly. For maintenance regimens, it is usual toinject the insulin 15 to 30 minutes before meals, depending on the insulin preparation used. When injected subcutaneously, soluble insulin has a rapid onset of action (30 to 60 minutes), a peak action between 1and 4 hours, and aduration of action of up to 8 hours. When injected intravenously, soluble insulin has a short half-life of only a few minutes and its onset of action is instantaneous. Soluble insulin administered intravenously is the most appropriate form of insulin for use in diabetic emergencies e.g. Diabetic ketoacidosis and peri-operatively.

Rapid-acting Insulins: Insulin aspart, insulin glulisine, and insulin lispro have a faster onset of action (within 15 minutes) and shorter duration of action (approximately 2–5 hours) than soluble insulin and are usually given by subcutaneous injection. For maintenance regimens, these insulins should ideally be injected immediately before meals. Rapid-acting insulin, administered before meals, has an advantage over short-acting soluble insulin in terms of improved glucose control, reduction of HbA1c, and reduction in the incidence of severe hypoglycaemia, including nocturnal hypoglycaemia.

Intermediate-acting insulin: Intermediate-acting insulins (isophane insulin/NPH have an intermediate duration of action, designed to mimic the effect of endogenous basal insulin. When given by subcutaneous injection, they have an onset of action of approximately 1–2 hours, a maximal effect at 3–12 hours, and a duration of action of 11–24 hours. Isophane insulin is a suspension of insulin with protamine; it may be given as one or more daily injections alongside separate meal-time short-acting insulin injections, or mixed with a short-acting (soluble or rapid-acting) insulin in the same syringe—Isophane insulin may be mixed with a short-acting insulin by the patient, or a pre-mixed biphasic insulin can be supplied (biphasic isophane insulin, biphasicinsulin aspart and biphasic insulin lispro. Biphasic insulins (biphasic isophane insulin, biphasic insulin aspart, biphasic insulin lispro) are pre-mixed insulin preparations containing various combinations of short-acting insulin (soluble insulin or rapid-acting analogue insulin) and an intermediate-acting insulin. The percentage of short-acting insulin varies from 15% to 50%. These preparations should be administered by subcutaneous injection immediately before a meal.

Long-acting insulin: Like intermediate-acting insulins, the long-acting insulins (insulin detemir, insulin glargine insulin degludec) mimic endogenous basal insulin secretion, but their duration of action may last up to 36 hours. They achieve a steady-state level after 2–4 days to produce a constant level of insulin. Insulin glargine and insulin degludec are given once daily and insulin detemir is given once or twice daily according to individual requirements.

Loss of warning of hypoglycaemia is a common problem with insulin-treated patients. The cause is unknown, but patients should be warned of the hazard. Beta-blockers and change to human insulin may blunt hypoglycaemic awareness. Patients especially drivers and those operating machinery should be strongly advised about the dangers of hypoglycaemia.

Insulin handling: Insulin vials should be stored under refrigeration at 2 – 8º Celsius. Exposure to direct sunlight can accelerate the degradation of insulin. Discolouration, turbidity or unusual viscosity in soluble insulin indicates deterioration or contamination. Insulin suspensions (intermediate and long-acting) should be discarded if the sediment cannot be suspended, if a clumped, granular precipitate is apparent, or if a deposit of solid particles is seen on the wall of the vial. To resuspend insulin suspension, gently roll the vial/pen between the hands and avoid vigorous shaking.

5.1.1.1 Rapid-acting Insulin

Insulin aspart, insulin glulisine, and insulin lispro are used for initial stabilization of diabetes mellitus. Rapidacting

insulins have a faster onset of action (within 15 minutes) and shorter duration of action (approximately 2–5 hours) than soluble insulin and are usually given by SC injection. For maintenance regimens, these insulins should ideally be injected immediately before meals. Often used in combination with intermediate or long-acting insulin.

INSULIN LISPRO, ASPART, GLULISINE

Presentation: Injection 100units/ml; Prefill pen 100units/ml

Indications: Diabetes mellitus, diabetic ketoacidosis, diabetes during surgery

Administration: *Diabetic emergencies (eg DKA or in surgery)*, IV/Infusion: *Adult*: 0.1 units/kg/hour.

Adult: According to requirements, total daily dose 0.5–1 unit/kg/day. Starting doses are often low and titrated based on individual patient insulin requirements. During intensifcation of insulin therapy it is used in combination with basal insulin, where 50% of total daily dose is calculated at 0.3–0.5 units/kg and given in 3 pre-meal doses.

Children:

1 to 17 years: 0.05 units/kg/hour. Dosing is according to individual insulin requirements. Initiate treatment by calculating total daily dose of 0.5–0.75 units/kg/day; give 60% of total daily dose in 3–4 pre-meal boluses. Used in combination with long acting insulin.

Prepubertal age: 0.5–1 unit/kg/day

Pubertal age: 1–2 units/kg/day, overlapped with intermediate or long-acting insulin at 0.3 units/kg with IV insulin for 2 hours.

Side effects: Hypoglycemia, hypokalemia, and skin changes at injection site (lipoatrophy or lipohypertrophy), refraction disorder, swollen joints, diabetic neuropathy and local allergic reactions at site of injection.

Contraindications: During episode of hypoglycaemia.

Caution: Decreased insulin requirements: diarrhea, vomiting, hypothyroidism, renal impairment.

5.1.1.2 Short-acting Insulin

This is the only type of insulin that can be administered intravenously during the treatment of diabetic emergencies, ketoacidosis, during surgery or intravenous feeding. It can also be administered intramuscularly when the intravenous route is not available. When injected subcutaneously, it has a rapid onset of action (after 30 to 60 minutes) a peak action of 2 to 4 hours, and a duration of action of up to 8 hours.

When injected intravenous, it has a very short half-life of only about 5 minutes and its effect disappears within 30 minutes.

SOLUBLE INSULIN

Presentation: Injection containing 100 units/ml of soluble insulin human or analogue.

Indications: Diabetes mellitus, diabetic emergencies and at surgery, diabetic ketoacidosis or coma, hyperglycaemiaia.

Administration: *Adult:* Subcutaneous, intramuscular, or intravenous injection or infusion according to individual requirement. For maintenance regimens, it is usual to inject 15 to 30 minutes before meals.

Children*: Diabetes Mellitus SC:*

Neonate, infant or child: According to requirements; used in combination with intermediate- or longacting insulin in which the total daily dose is initiated at 0.5 units/kg/day;

***Diabetic ketoacidosis or coma**, IV infusion*

Infant or child: 0.05–0.1 units/kg/hour (maximum 0.2 units/kg/hour), depending on the rate of reduction of serum glucose.

Side effects: Fat hypertrophy at the injection site, hypoglycaemia in overdose, see notes above.

Caution: See notes above. Reduce dose in renal impairment.

Biphasic insulin aspart, Pre-mixed/Biphasic Insulin Isophane (30/70) (30% Rapid/regular plus 70% Intermediate-acting)

5.1.1.3 Intermediate Acting Insulin

Presentation: Injection containing 100 units/ml and 300iu/3ml Pen set

Indications: Diabetes mellitus

Administration: By subcutaneous injection 0.3 and 1.0 IU per kg body weight 30 minutes before the meal

Side effects: See under Soluble insulin and Isophane insulin

Caution: See notes above

ISOPHANE INSULIN

(Isophane Insulin Injection; Isophane Protamine Insulin Injection; Isophane Insulin (NPH); intermediate acting)

Presentation: Injection containing 100 units/ml of isophane insulin

Indications: Diabetes mellitus

Administration: By subcutaneous injections according to the patient's requirements.

Side effects: Hypoglycaemia, lipodystrophy and lipohypertrophy, hypokalemia, muscle weakness, itchness, parasthesia

Caution: See soluble insulin

5.1.1.4 Long Acting Insulins

INSULIN DETEMIR

Presentation: Injection containing 100units/ml (10ml vial); Prefilled syringe:100units/ml (3ml) pen

Indications: Type 1 or 2 diabetes mellitus

Administration: once daily dose: subcutaneously with evening meal or at bedtime

Twice daily dosage: SC with morning meal and either with evening meal or at bedtime.

Side effects: Hypoglycaemia, headache, mental confusion, urticarial, local allergic reaction blurred vision, lipodystrophy, lipohypertrophy, hypokalemia

Contraindications: Systemic allergic reactions; during episode of hypoglycaemia.

Caution: Lower dose when used with GLP-1 receptor agonist. Use with caution in patients with decreased insulin requirements such as diarhea, vomiting, hypothyroidism, renal or hepatic impairment.

INSULIN GLARGINE

Presentation: Iinjection containing 100units/ml (10ml vial); 100units/ml (3ml prefilled pen)

Indications: Type1 and 2 Diabetes mellitus

Administration: subcutaneously, 1/3 of daily dose of insulin with the remaining 2/3of total daily dose given as premeal short-acting insulin.

Type 1 0.2-0.4units/kg

Type 2: 0.2units/kg once daily

Optimal glucose lowering effect may take 5 days to fully manifest.

Side effects: headache, influenza like symptoms, diarhea, pharyngitis, lipodystrophy and lipohypertrophy, altered taste, fluid retention, hypokalemia, local allergic reaction.

Contraindications: documented hypersensitivity; Use during hypoglycaemia.

Caution: Evidence of safety in pregnancy is limited, use insulin Isophane when long-acting insulin is required.

INSULIN DEGLUDEC

Presentation: Injection containing 100units/ml; 200units/ml prefilled pen.

Indications: Type1 or 2 Diabetes Mellitus

Administration: *Type1*: 0.2-0.4units/kg

Type 2: insulin naïve patients start at 10units SC per day

Side effects: Nasopharyngitis, hypoglycaemia, headache, diarrhea, injection site reaction, peripheral edema, lipodystrophy.

Contraindications: During hypoglycaemia, and hypersensitivity.

Caution: Risk of anaphylaxis

5.1.1.5 Premixed Insulin

Rapid-Acting+Intermediate Acting

Presentation: Injection containing 100units/ml (10ml vial)

Indications: Diabetes mellitus

Administration: by SC injection*: Adult and Child:* According to individual requirements

Side effects: See above

Short-Acting+Intermediate Acting

Presentation: Injection containing 100units/ml (10ml vial)

Indications: Diabetes mellitus

Administration: Adults and Children: *by SC injection:* According to individual requirements, administered at or near meals.

Individual insulin requirement ranges at 0.3-1 IU/kg/day, adjusted according to physical activity, diet, or concomitant illness.

Side effects: see above

5.1.2 Oral hypoglycaemics Medicines

They are used in the management of diabetes mellitus type 2. They are indicated for people who fail to achieve control after a two to three month trial of diet and exercises. They should not be considered as a replacement for but rather as complementary to diet.

5.1.2.1 Sulphonylureas

There are several sulphonylureas. There is no evidence of any difference in their effectiveness. Chlorpropamide had more side effects mainly because of its long duration of action and potential for accumulation and therefore the increased risk of hypoglycaemia.

The choice of drug depends on the age and renal function of the patient. Elderly patients are prone to hypoglycaemia when a long-acting drug is used. In this category of patient chlorpropamide and glibenclamide should be avoided.

Caution: These Medicines encourage weight gain. Caution should be exercised when used in the elderly and hepatic and renal insufficiency because of the risk of hypoglycaemia. Avoid use in porphyria.

Contraindications: Pregnancy, breastfeeding, ketoacidosis, intercurrent illness (e.g. myocardial infarction, coma, infection and trauma) and in surgery. Insulin therapy should be administered in these conditions.

GLIBENCLAMIDE

Presentation: Tablet containing 2.5mg, 5mg Glibenclamide.

Indications: Diabetes mellitus type 2

Administration: Initially 5mg daily adjusted according to response. Maximum dose 15mg daily taken with breakfast

Side effects: Hypoglycaemia, rarely gastrointestinal disturbances and headaches.

Caution and Contra-indications: See notes above.

GLICLAZIDE

Presentation: Tablets containing 80mg gliclazide

Indications: Diabetes mellitus Type 2.

Administration: Initially 40 mg – 80mg daily, adjusted according to response up to 160mg as a single dose with breakfast. Higher doses should be divided. Maximum 320mg daily.

Side effects: Hypoglycaemia, rarely gastrointestinal disturbances, headache.

Caution and contraindications: See notes above

GLIPIZIDE

Presentation: Tablet containing 2.5mg, 5mg glipizide.

Indication: Diabetes mellitus Type 2.

Administration: Initially 2.5mg – 5mg daily adjusted according to response, maximum 40mg daily. Up to 15mg may be given as a single dose before breakfast. Higher doses should be divided.

Side effects: Hypoglycaemia, gastrointestinal disturbances, headache

Caution and contraindications: See notes above.

GLIMEPIRIDE

Presentation: Tablet containing 1mg, 2mg and 4mg Glimepiride

Indications: Diabetes mellitus Type 2

Administration: Initially 1mg daily adjusted according to response maximum dose 8mg/day

Side effects: Rare hypersensitivity, vasculitis.

Caution: See Sulphonylureas

5.1.2.2 Biguanides

These are only effective in diabetics with some residual functioning pancreatic islet cells as they only act in the presence of endogenous insulin. They are used in type II diabetes when dieting and exercise have failed to achieve adequate control of hyperglycaemia. They can be used alone or with a sulphonylurea.

METFORMIN HYDROCHLORIDE

Presentation: Tablets containing 500mg, 850mg Metformin hydrochloride.

Indications: Diabetes mellitus type 2

Administration: 500mg every 8 hours or 850mg every 12 hours with or after food. Maximum 3g daily in divided doses.

Children:

8–10 years: Initially 200 mg once daily adjusted according to response at intervals of at least a week; maximum 2 g daily in 2–3 divided doses

Over 10 years: Initially 500 mg once daily adjusted according to response at intervals of at least a week; maximum 2 g daily in 2–3 divided doses.

Side effects: Metallic taste, nausea, anorexia, vomiting, abdominal pain, diarrhoea, lactic acidosis (withdraw treatment), decreased vitamin B_{12} absorption.

Contraindications: Hepatic or renal impairment, predisposition to lactic acidosis, heart failure, severe infection or trauma, dehydration, alcohol dependence, pregnancy, breastfeeding.

Caution: See notes above.

5.1.2.3 Dipeptidyl Peptidase (DPP) 4 Inhibitors

VILDAGLIPTIN

Presentation: Tablet containing 5mg of Vildagliptin

Indications: Type 2 diabetes mellitus as monotherapy (if metformin inappropriate), or in combination with other antidiabetic drugs (including insulin) if existing treatment fails to achieve adequate glycaemic control

Administration: by mouth

Adult: 50 mg twice daily, reduce dose to 50 mg once daily in the morning when used in dual combination with a sulfonylurea.

Side effects: Dizziness, uncommon, arthralgia, constipation, headache, hypoglycaemia, peripheral oedema. Rare: Increased risk of infection, hepatitis, myalgia, pancreatitis, skin reactions.

Contraindications: Ketoacidosis

Caution: Avoid in severe heart failure.

SITAGLIPTIN

Presentation: Tablet containing 25mg or 50mg Sitagliptin

Indications: Type 2 diabetes

Administration: by mouth*: Adult:* 50mg once daily, to a maximum of 100 mg once daily

Side effects: Common: Headache, hypoglycaemia. Uncommon: Constipation, dizziness, skin reactions, angioedema, back pain, cutaneous, vasculitis, interstitial lung disease, joint disorders, myalgia, pancreatitis acute, renal impairment, Stevens-Johnson syndrome, vomiting.

Contraindications: Serious hypersensitivity, Ketoacidosis.

Caution: Pregnancy (avoid), acute pancreatitis, acute kidney injury.

5.1.2.4 Thiazolidinediones

PIOGLITAZONE

Presentation: Tablet containing 15mg, 30mg or 45mg of Pioglitazone.

Indications: Type 2 diabetes

Administration: Adults: 15-30mg once daily with a meal. Maximum dose is 45mg daily.

Side effects: Hypoglycaemia, oedema when used in combination with sulphonylureas or insulin, upper respiratory infection, headache, heart failure, myalgia, bone fracture, weight gain, numbness, visual impairment, bladder cancer and insomia

Contraindications: History of heart failure, previous or active bladder cancer, uninvestigated macroscopic hematuria, hepatic impairment, Diabetic ketoacidosis

Caution: Concomitant use with insulin (risk of heart attack), Elderly: increased risk of heart failure, fractures and bladder cancer; increased risk of bone fractures especially in women; Pregnancy and breastfeeding: avoid.

5.1.2.5 Sodium-Glucose Co-Transporter 2 (SGLT-2) Inhibitors

DAPAGLIFLOZIN

Presentation: Tablet containing either 5mg or 10mg Dapagliflozin.

Indications: Type 2 diabetes, heart failure (to reduce risk of cardiovascular death and hospitalization), chronic kidney disease (to reduce the progression, hospitalization and cardiovascular death associated with CKD)

Administration: by mouth, 5-10mg daily

Side effects: Genital fungal infections, UTIs, nasopharyngitis, back pain, increased urination, nausea, dyslipidaemia, constipation, ketoacidosis, hypoglycaemia, rash.

Contraindications: Serious hypersensitivity e.g. anaphylaxis and angioedema.

Caution: Genital micotic infections, UTI, necrotizing fasciitis of the perineum; do not initiate in eGFR<25ml/min/1.73m^2

5.1.2.6 Glucagon Like Polypeptide 1 Receptor Agonists

SEMAGLUTIDE

Presentation: Injection as 0.25mg/0.5ml, or 2mg/1.5ml, or 4mg/3ml, or 8mblet 3mg, 7mg or 14mg of Semaglutide.

Indications: Type 2 diabetes mellitus [monotherapy (if metformin inappropriate) or in combination with other antidiabetic drugs], Obesity.

Administration: mouth: 3mg once daily for 30 days, then increase to 7mg once daily for 1 month. Maximum dose is 14mg daily.

By subcutaneous injection

Adult: Initially 0.25 mg once weekly for 4 weeks, then

increased to 0.5 mg once weekly for at least 4 weeks, then increased if necessary to 1 mg once weekly

Side effects: Common or very common: Appetite decreased, burping, cholelithiasis, constipation, diarrhoea, dizziness, fatigue, gastrointestinal discomfort, gastrointestinal disorders, hypoglycaemia (in combination with insulin or sulfonylurea), nausea, vomiting, weight decreased.

Uncommon: Taste altered

Contraindications: Diabetic ketoacidosis.

Caution: patients treated with insulin, history of pancreatitis

5.1.3 Treatment of hypoglycaemia

Hypoglycemia is a potentially fatal condition requiring immediate treatment. 3 to 4 teaspoons of sugar, with a little water, should be taken. This can be repeated if necessary in 10 to 15 minutes. Up to 50 ml of 50% glucose intravenous infusion should be administered in case of unconsciousness.

Alternatively, glucagon, a natural hormone, can be given instead of parenteral glucose. It can be administered subcutaneously, intramuscularly or intravenously. If it is not effective within 20 minutes intravenous glucose should be given.

Chronic hypoglycaemia resulting from the excess endogenous secretion of insulin is managed using diazoxide.

GLUCAGON

Presentation: Injection available as a powder for reconstruction containing 1mg/ml glucagon hydrochloride with lactose.

Indications: Acute hypoglycaemia

Administration: By SC or IM injection

Adult: 1mg, if no response within 10 minutes give dextrose IV. If the patient

does not respond within 10 minutes, intravenous glucose should be given

Children:

1 month–8 years (body weight up to 25kg): 500 mcg, if no response within 10minutes, intravenous glucose should be given.

9–17 years (body weight 25 kg and above): 1 mg, if no response within 10minutes, intravenous glucose should be given.

Side effects: Nausea, vomiting, hypocalcaemia rarely hypersensitivity reaction.

Contraindications: Insulinoma, phaeochromocytoma, glucagonoma.

DIAZOXIDE

Presentation: Tablets containing 50mg Diazoxide

Indications: Chronic intractable hypoglycaemia.

Administration: *Children and adults;* 5mg/kg body weight daily in 2 – 3 divided doses.

Side effects: Anorexia, nausea, vomiting, hyperuricaemia, hypotension, oedema, tachycardia, arrhythmias, extrapyramidal effects, hypertrichosis on prolonged treatment.

Caution: Ischaemic heart disease, pregnancy, labour, impaired renal function, haematological examinations and blood pressure monitoring required during prolonged treatment, growth, bone and developmental checks required in children.

5.2 Medicines acting on the thyroid

5.2.1 Thyroid Hormones

They are used in hypothyroidism (myxoedema) and also in diffuse non-toxic goitre and carcinoma. Neonatal thyroidism requires prompt treatment for normal development.

THYROXINE SODIUM

Presentation: Tablets containing 25mcg, 50mcg and 100mcg thyroxine sodium.

Indications: Hypothyroidism, Hyperthyroidism (blocking-replacement regimen) in combination with carbimazole.

Administration: *Adult 18–49 years:* Initially 50–100mcg once daily, adjusted in steps of 25–50mcg every 3–4 weeks, adjusted according to response; maintenance 100–200mcg once daily, dose to be taken preferably at least 30 minutes before breakfast or other medication.

Adult 50 years and over: Initially 25 mcg once daily, adjusted in steps of 25 mcg every 4 weeks, adjusted according to response; maintenance 50–200 mcg once daily, dose to be taken preferably at least 30 minutes

before breakfast, caffeine-containing liquids (e.g., coffee, tea), or other medication.

Hyperthyroidism (blocking-replacement regimen) in combination with carbimazole, oral: *Adult:* 50–150mcg daily therapy usually given for 18 months

Children:

Infants: 10mcg/kg daily up to a maximum of 50mcg daily. Subsequent therapy to reach 100mcg daily by 5 years and adult doses by 12 years, guided by clinical response, growth assessment and measurement of plasma thyroxine (T3 & T4) and thyroid-stimulating hormone (TSH).

Side effects: Arrhythmias, anginal pain, tachycardia, cramps in skeletal muscles, headache, restlessness, excitability, flushing, sweating, diarrhoea, excessive weight loss.

Caution: Cardiovascular disorders, prolonged myxoedema, adrenal insufficiency.

5.2.2 Antithyroid Medicines

CARBIMAZOLE

Antithyroid medicines are used to prepare patients for thyroidectomy and inducing life-long remission.

Presentation: Tablets containing 5mg, 20mg Carbimazole.

Indications: Hyperthyroidism.

Administration: 30 – 60mg daily as a single dose until the patient becomes euthyroid (4 – 8 weeks) then progressively reduce dose to a maintenance dose of 5-15mg daily for 112-18 months.

Children

0.5-0.7mg/kg daily or in 3 divided doses, 0.2mg/kg daily maintenance dose, adjusted according to response, but not to exceed 30mg daily.

Higher doses should be prescribed under specialist supervision only.

Side effects: Pruritis, nausea, headache, arthralgia, jaundice, neutropenia and agranulocytosis, alopecia, hepatotoxicity

Caution: May cause bone marrow suppression, withdraw treatment if signs of infection especially sore throat appear, white blood cell counts should be performed if there is evidence of infection, pregnancy and breastfeeding.

PROPYLTHIOURACIL

Presentation: Tablet containing 50mg Propylthiouracil

Indications: Hyperthyroidism and thyroid storm

Administration: By mouth; *Adult:*

Thyrotoxic crisis/storm, thyrotoxicosis: Loading dose of 500- 1,000 mg followed by 250 mg every 4 hours.

Hyperthyroidism (including Graves disease): Initial 50-150 mg (depending on severity) 3 times daily to restore euthyroidism; maintenance dose of 50 mg 2 to 3 times daily for a total of 12 to 18 months.

Children:

Hyperthyroidism, oral

Neonate - 12 years: Initially 2.5–5 mg/kg 2-3 times daily until euthyroid.

Maintenance dosage to maintain euthyroid state is commonly 30–60% of the initial dose.

Side effects: Agranulocytosis, bone marrow disorders, glomerulonephritis, acute hearing impairment, leucopenia, thrombocytopenia, vomiting, alopecia, arthralgia, arthritis, encephalopathy, fever, gastrointestinal disorder, haemorrhage, headache, hepatic disorders, hypoprothrombinaemia, interstitial pneumonitis, lupus like syndrome, lymphadenopathy, myopathy, nausea, nephritis, skin reactions, taste altered, vasculitis.

Caution: Hepatic impairment – risk of life-threatening hepatotoxicity

IODINE AND IODIDE

Presentation: Aqueous solution containing iodine 5%, potassium iodide 10%. Total iodine 130mg/ml.

Indications: Thyrotoxicosis (pre-operative), Subacute and chronic thyroiditis, and radiation emergency

Administration: 0.1 – 0.3ml three times daily well diluted with milk or water.

Side effects: Hypersensitivity reactions, headache, lachrymation, conjunctivitis, pain in salivary glands, laryngitis, bronchitis, rashes; prolonged use depression, insomnia, impotence, goitre in infants of mothers taking iodides.

Caution: pregnancy and breastfeeding (avoid).

5.3 Corticosteroids

Corticosteroids permit many biochemical reactions in the body to proceed at optimal rates. They are therefore used as replacement therapy in adrenocortical insufficiency. Their clinical use is dependant on the anti-inflammatory, antiallergic and lymphocytic properties of each active substance.

Corticosteroids have both glucocorticoid and mineralocorticoid properties in varying proportions. Generally, anti-inflammatory agents have high glucocorticoid and low mineralocorticoid effects and those with high mineralocorticoid effects are more suitable for adrenal replacement therapy and topical management of inflammatory skin conditions.

Glucocorticoid effects are responsible for the control of sodium, potassium, protein, carbohydrate and lipid metabolism and also increase haemoglobin and red and white cells in the blood. Betamethasone, dexamethasone, methylprednisolone and prednisolone have high glucocorticoid activity.

Mineralocorticoid effects influence electrolyte and water metabolism. Fludrocortisone, hydrocortisone, cortisone and aldosterone have high mineralocorticoid activity hence their low or moderate anti-inflammatory activity. Their fluid retention property renders them unsuitable for long term use in inflammatory disease suppression.

Betamethasone and dexamethasone, because of their high glucocorticoid and insignificant mineralocorticoid activity are the most suitable for long term administration. Cortisone and hydrocortisone are suitable for adrenal replacement therapy.

Corticosteroids have a poor side effect profile. Their use should only be considered after serious consideration of the risk-benefit factors. Prolonged use should only be considered in life-saving or life-prolonging situations and only after other therapeutic measures have proved ineffective.

The dosage should be carefully determined and varies from one condition to another and from patient to patient. High doses are associated with necrosis of the femoral head and they may also cause mental disturbances, depression, euphoria and muscle wasting. They may also worsen the infection and suppress clinical signs. Infections like TB, septicaemia may be masked until they reach an advanced stage. They may also cause peptic ulcer disease and Cushing's syndrome-like features with moon face, striae and acne.

High dosage or prolonged use may exaggerate normal physiological actions of corticosteroids. These include sodium and water retention, potassium loss (mineralocorticoid), hyperglycaemia and osteoporosis.

The risks in children are even greater and prolonged use is rarely justified. Corticosteroid use in children may result in the suppression of growth. High doses during pregnancy may affect adrenal development in the child.

It is preferable to use local treatment using creams, intra-articular injections, inhalations, eye drops or enemas to systemic treatment. It is preferable to administer the dose in the morning. The prescriber should consider an alternate day dose regimen e.g. prednisone 40mg orally on alternate days instead of 20mg per day. The lowest dose for the shortest possible course of treatment should be considered.

Withdrawal of treatment should be gradual. The length of withdrawal depends on the dosage and duration of therapy. Too rapid withdrawal can lead to acute adrenal insufficiency, hypertension and death. Withdrawal symptoms like rhinitis, conjunctivitis, loss of weight, arthralgia and painful itchy skin may be experienced.

Patients who have received doses of 50mg or more per day of cortisone for periods of more than 1 month should be considered potential cases of pituitary/adrenal suppression for at least one year after corticosteroid withdrawal.

Anaesthetists must be informed of corticosteroid therapy to avoid precipitous fall in BP during anaesthesia or in the immediate -post-operative period. If an acute infection, trauma or surgery occurs during a course of corticosteroid treatment, increase rather than reduce the dose, giving it parenterally if necessary.

Side effects: Electrolyte imbalance leading to sodium retention, oedema, hypertension and increased potassium retention, Cushing's syndrome, with hirsutism, acne, moon face and striae, increased appetite, muscle weakness, osteoporosis, peptic ulcer and gastric upsets, skin thinning. Glucose tolerance may be diminished and diabetes precipitated.

Growth retardation in children, inactivity or atrophy of adrenal cortex, impairment of the immune process, delayed wound healing, increased risk of infection and thrombosis, pancreatitis, glaucoma, cataract, mental disorder.

Contraindications: TB (combine with anti TB treatment if unavoidable), local and systemic infections if not controlled by chemotherapy,

active peptic ulcer, psychoses, osteoporosis, renal dysfunction, diabetes mellitus, glaucoma, hypertension, myasthenia gravis, thromboembolic disorders, congestive heart failure, pregnancy and herpes infections.

Caution: Concomitant use with cardiac glycosides, thiazide diuretics, antidiabetic Medicines, coumarins, rifampicin, phenytoin, barbiturates and NSAIDs. Perform routine ophthalmic checks with long-term use.

Patients should carry "steroid cards" where available.

Replacement therapy

This is necessary for situations where the adrenal cortex does not secrete adequate hydrocortisone. Physiological replacement is best achieved with a combination of fludrocortisone and hydrocortisone (mineralocorticoid).

FLUDROCORTISONE ACETATE

Presentation: Tablets containing 100mcg fludrocortisone acetate.

Indications: Mineralocorticoid replacement in adrenocortical insufficiency (see 5.3. above); Congenital adrenal hyperplasia

Administration: Adult: 50–100mcg daily. *Addison's disease or adrenalectomy:* 50 to 300mcg daily.

Children:
5mcg/kg body weight daily.
Congenital adrenal hyperplasia; Addison's disease or adrenalectomy
50 to 300mcg daily.

Side effects, Contraindications, and Cautions: See 5.3 above on corticosteroids.

HYDROCORTISONE

Presentation: Tablets containing 10mg, 20mg hydrocortisone; Injection: powder for reconstitution containing 100mg hydrocortisone as sodium succinate.

Indications: Adrenocortical insufficiency (See 5.3.), Addison's disease or following adrenalectomy, suppression of inflammatory and allergic disorders, shock.

Administration: *Adult*

Replacement therapy; 20 to 30mg daily orally in 2 divided doses. Larger dose in the morning and smaller in the evening. Optimal dose determined according to clinical response.

In acute adrenocortical insufficiency; 100mg every 6 to 8 hours intravenous in 9% sodium chloride infusion.

In the suppression of inflammatory and allergic disorders; IM or slow IV injection or infusion, 100 – 500mg given 3 to 4 times in 24 hours or as required.

In anaphylactic shock; as an adjunct to adrenaline 100 to 300mg intravenous injection.

Children: By slow iv injection
Up to 1 year; 25mg.
1–5 years: 50mg.
6–12 years; 100mg.
Alternative: 1 – 2mg/kg IV bolus, then 150 – 250mg/day in divided doses every 6 to 8 hours

Side effects, Contraindications, and Cautions: See 5.3 above on corticosteroids; also, perineal irritation may follow intravenous administration of phosphate ester.

BETAMETHASONE

Presentation: Tablets containing 500mcg betamethasone; injection containing 4mg/ml betamethasone as sodium phosphate.

Indications: Suppression of inflammatory and allergic disorders, congenital adrenal hyperplasia, cerebral oedema, foetal lung maturation.

Administration: Oral; 0.5–5mg daily. Injection; intramuscular or slow intravenous or infusion; 4–20mg repeated up to 4 times in 24 hours.

Children: By slow intravenous injection
up to 1 year; 1mg.
1 – 5 years; 2mg.
6- 12 years; 4 mg.

Side effects, Caution, Contraindications: see notes above.

DEXAMETHASONE

Presentation: Tablets containing 500mcg, 2mg dexamethasone, injection containing 4mg/ml, 20mg/ml dexamethasone sodium phosphate. **Indications:** Suppression of inflammatory and allergic disorders; shock, diagnosis of Cushing's disease; congenital adrenal hyperplasia, cerebral oedema, foetal lung maturation.

Administration: Oral; 0.5 – 9mg daily. By intramuscular, slow intravenous injection or infusion; initially 0.5 – 20mg.

Cerebral oedema; intravenous injection 10mg initially then 4 mg every 6 hours as required for 2 – 10 days.

Foetal Lung Maturation: IM 6mg twice daily for 2 days between 24-34 weeks of Gestation age.

Children:
200 – 500mcg/kg body weight daily

Side effects, contraindications, Caution: See notes above. Perineal irritation may follow intravenous administration of the phosphate ester.

METHYLPREDNISOLONE

Presentation: Tablets containing 2mg, 4mg, 16mg methylprednisolone; Injection – powder for reconstitution containing methylprednisolone as sodium succinate 125mg, 500mg and 1 g.

Indications: Suppression of inflammatory and allergic disorders, cerebral oedema.

Administration: Oral; 2–40mg daily. IM or slow IV injection or infusion; initially 10–500mg.

Graft rejection; up to 1g daily by intravenous infusion up to 3 days.

Children:
Infants and child <12 years: 1 to 2 mg/kg/day in 1 or 2 divided doses, maximum daily dose: 60mg/day
Child> 12years: 1 g/day infused over 1 hour
Systemic onset juvenile idiopathic arthritis BY IV infusion:
10–30 mg/kg once daily or on alternate days (max. per dose 1 g) for up to 3 doses.

Side effects, Contraindications, Caution: See notes above, rapid intravenous administration of large doses has been associated with cardiovascular collapse.

PREDNISOLONE

Presentation: Tablets containing 1mg, 2.5mg, 5mg, 25mg Prednisolone.

Indications: Suppression of anti-inflammatory and allergic disorders.

Administration: Oral; initially up to 10–20mg daily (severe condition up to 60mg daily) preferably after breakfast. Can be reduced within a few days but may need to be continued for several weeks or months. Maintenance dose 2.5 – 15mg daily.

Alternatively: 1mg/kg. Consider steroid taper as soon as clinical condition allows.

Side effects, Contraindications, Caution: See notes above

TRIAMCINOLONE

Presentation: Tablets containing 2mg, 4mg Triamcinolone; injection (aqueous suspension) containing 40mg/ml triamcinolone acetonide intramuscular/intra-articular

Indications: Suppression of inflammatory and allergic disorders, Rheumatic and Arthritic Disorders.

Administration: *Oral*; 2 – 24 mg daily.

By deep IV injection into gluteal muscle 40mg of acetonide for depot effect, repeated at intervals according to patient's response. Maximum single dose 100mg.

Side effects: See notes above. In high dosage, may cause proximal myopathy.

Contraindications: See notes.

Caution: Avoid in chronic therapy.

5.4 Androgens and anti-androgens

TESTOSTERONE

Presentation: Capsules containing 40mg testosterone undecanoate; injection containing 20mg, 50mg testosterone propionate, 40mg testosterone phenylpropionate, 250mg testosterone enanthate, implant 100mg testosterone.

Indications: Androgen deficiency, delayed puberty, breast cancer, male hypogonadism.

Administration:

Hypogonadism (males), by slow IM injection: Initially 250 mg every 2–3 weeks, usual maintenance dose, 250 mg every 3–6 weeks.

Children:
Hypogonadism, IM
Children over 12: 25–75 mg every 3–4 weeks

Alternatively: according to the manufacturer's preparations.

Side effects: Prostate abnormalities and cancer, headache, depression, cholestatic jaundice, electrolyte disturbances, increased bone growth, androgenic effects.

Contraindications: Breast cancer in men, prostate cancer, liver tumours, hypercalcaemia, pregnancy, breastfeeding, nephrosis.

Caution: Cardiac, renal, hepatic impairment, Ischaemic heart disease, elderly, migraine, hypertension.

CYPROTERONE ACETATE

Cyproterone acetate is an anti-androgen used in the treatment of severe hypersexuality and sexual deviation in male is also used as an adjunct in prostate cancer and treatment of acne and hirsutism in women.

Presentation: Tablets containing 50mg Cyproterone acetate.

Indications: (see notes above); prostate cancer

Administration: 50mg twice daily after food.

Side effects: Fatigue, breathlessness, weight changes.

Contraindications: Hepatic disease, severe diabetes, sickle cell anaemia, severe depression, thrombo-embolic disorders; youth under 18 years.

Caution: Chronic alcoholism, monitor blood count, hepatic function, adrenocortical function, diabetes mellitus.

SILDENAFIL

Presentation: Tablets containing 25mg Sildenafil.

Indications: Erectile dysfunction

Administration: Initially 50mg (elderly 25mg) approximately 1 hour before sexual activity, subsequent doses adjusted according to response to 25 – 100mg as a single dose as needed; max 1 doze in 24 hours, (max. single dose 100mg).

Side Effects: Dyspepsia, headache, flushing, dizziness, visual disturbances, priapism.

Contraindication: Treatment with nitrates, recent stroke and myocardial infarction, hypertension, hereditary degenerative retinal disorders.

Caution: Cardiovascular disease, predisposition to prolonged erection, renal impairment.

TADALAFIL

Presentation: Tablets containing 10mg or 20mg Tadalafil.

Indications: Erectile dysfunction, Benign prostatic hyperplasia, Pulmonary arterial hypertension (initiated under specialist supervision).

Administration: Adult:

Erectile dysfunction: Initially 10 mg (max. per dose 20 mg), to be taken at least 30 minutes before sexual activity, subsequent doses adjusted according to response, the effect of intermittent dosing may persist for longer than 24 hours, continuous daily use not recommended; maximum 1 dose per day.

Erectile dysfunction; for patients who anticipate sexual activity at least twice a week: 5 mg once daily, reduced to 2.5 mg once daily, adjusted according to response.

Pulmonary arterial hypertension (initiated under specialist supervision): 40 mg once daily.

Benign prostatic hyperplasia: 5 mg once daily.

Side effects: Hypotension, headache, myalgia, nasal congestion, gastroesophageal reflux disease.

Contraindications: Mild to severe heart failure, patients in whom vasodilation or sexual activity are inadvisable, uncontrolled hypertension, unstable angina, stroke, arrhythmias, aortic and mitral valve disease, left ventricular dysfunction, life-threatening arrhythmias, pericardial congestive cardiomyopathy, coronary artery disease.

Caution: Cardiovascular disease, predisposition to prolonged erection, renal impairment.

5.5 Other Endocrine Medicines

See Under Medicines used in Obstetrics and Gynaecology

6 Medicines used in Obstetrics and Gynaecology

6.1 Prostaglandins and Oxytocics

These medicines are used to induce abortion or induce or augment labour, in management of incomplete abortion and to prevent postpartum haemorrhage in the third stage of labour. They include Oxytocin, Ergometrine, Ergometrine + Oxytocin and Prostaglandins such as Misoprostol.

CARBETOCIN

Presentation: Injection containing 100mcg/ml

Indications: Prevention of uterine atony after delivery of the baby

Administration: by slow intravenous injection: 100 mcg for 1 dose, to be given over 1 minute, administer as soon as possible after delivery, preferably before removal of placenta

Side effects: Chest pain, chills, dizziness, dyspnoea, feeling hot, flushing, headache, hypotension, nausea, pain, pruritus, taste metallic, tremor, vomiting, hyperhidrosis, tachycardia.

Contraindications: Eclampsia, epilepsy, pre-eclampsia

Caution: Asthma, cardiovascular disease (avoid if severe), hyponatraemia, migraine.

OXYTOCIN

Presentation: Injection containing 5 units, 10 units per ml of Oxytocin

Indications: Induction or augmentation of labour, management of the third stage of labour, prevention and treatment of postpartum haemorrhage, Incomplete, inevitable, or missed abortion.

Administration: *Induction of labour, by* slow intravenous infusion: 1 – 3 milli units per minute adjusting according to the uterine response.

Augmentation of labour, Management of the third Stage; 5 to 10 units.

Prevention of PPH, by IM injection: 10 IU when the anterior shoulder is delivered or immediately after birth.

Prevention of PPH: by slow IV injection: 5 IU when the anterior shoulder is delivered or immediately after birth *Treatment of PPH:* by slow IV injection5–10 IU, or by IM injection 10 IU, followed in severe cases by a total of 40 IU by IV infusion, at a rate of 0.02–0.04 IU/min, which should be started after the placenta is delivered.

Side effects: Hyperstimulation leading to uterine rupture and foetal asphyxia, maternal hypertension and subarachnoid haemorrhage, water intoxication and pulmonary oedema.

Contraindications: Obstruction, foetal distress, placenta praevia.

Caution: High parity, previous caesarean section, concomitant use with prostaglandins.

ERGOMETRINE + OXYTOCIN

Presentation: Injection containing Ergometrine maleate 500mcg + Oxytocin 5 units/ml ampoule

Indications: Management of the third stage of labour, incomplete abortion, to prevent haemorrhage.

Administration: 1ml, intramuscular for incomplete abortion and management of the third stage of labour

Side effects: Vomiting, nausea and hypertension

Contraindications: Severe heart disease, severe hypertension.

ERGOMETRINE MALEATE

Presentation: Injection containing 500mcg Ergometrine maleate; tablets containing 250mcg, 500mcg Ergometrine maleate.

Indications: Incomplete abortion; management of the third stage of labour, postpartum haemorrhage.

Administration: Oral; 500mcg–1mg, intramuscular injection; 200 – 500mcg, intravenous injection; 100– 500mcg.

Side effects: Nausea, vomiting and transient increase in blood pressure

Contraindications: Severe hypertension, cardiac disease, eclampsia.

Caution: Hepatic and renal impairment, multiple pregnancies.

MISOPROSTOL

Presentation: Tablets containing 200mcg/100mcg Misoprostol.

Indications: Medical termination of pregnancy or induction of abortion, Induction of labour in intrauterine foetal death (IUFD), treatment of postpartum haemorrhage, incomplete/ missed abortion and miscarriage. Also used for prevention and treatment of NSAID-induced duodenal ulcers.

Administration: *Induction of labour with IUFD from 13 to 17 weeks:* 200mcg vaginally every 6 – 12 hours for a total of 4 doses.

IUFD from 18 – 26 weeks: 100mcg vaginally every 6 – 12 weeks for a total of 4 doses.

IUFD beyond 26 weeks: if cervix unripe (Bishop score <6), vaginally Misoprostol 25 – 50mcg is given every 4 hours (up to 6 doses). If the cervix is already ripe (Bishop score ≥6), use 25 – 50mcg initially, can double to 50 – 100mc (Max. daily dose should not exceed 600mcg). If expulsion has not occurred after 24 hours, repeat the same treatment course for the second time.

Termination of pregnancy following Mifepristone (gestation up to 49 days); 400mcg for 1 dose given 36 – 48 hours after Mifepristone.

Termination of pregnancy (gestation up to 49 days); Initially by vaginal, sublingual or buccal administration 800mcg for 1 dose given 24 – 48 hours after Mifepristone, if abortion has not occurred 4 hours after the first dose a further dose may be given (by mouth or vagina) 400mcg for 1 dose. *Termination of pregnancy (gestation >9weeks):* 800mcg for 1 dose given 36 – 48 hours after Mifepristone followed by 400mcg by mouth or vaginally every 3 hours if required for a maximum of 4 doses.

Treatment of incomplete abortion or miscarriage: 600mcg single dose orally in addition to antibiotics, IV fluids and analgesics needed on the condition of the patient.

Treatment of missed abortion in 1st trimester: 800mcg vaginally or sublingually every 24 hours for 2 days (subsequent evacuation of the uterus may be necessary).

Prevention of postpartum haemorrhage (PPH): 600mcg orally immediately after delivery of the baby and after confirmation that all foetuses have been delivered.

Treatment of PPH: 1000mcg rectally or 800mcg sublingually.

Side effects: Diarrhoea, abdominal pain, flushing, nausea, vomiting, abnormal vaginal bleeding, dizziness, dyspepsia, flatulence, menorrhagia, intermenstrual and postmenopausal bleeding, rash, uterine rupture.

Contraindications: Hypersensitivity to prostaglandins.

Caution: Hypotension, inflammatory bowel disease. If pregnancy occurred with an IUD in place, this must be removed prior to administering this medicine.

MIFEPROSTONE + MISOPROSTOL

Presentation: Tablets containing 200mg Mifeprostone + 200mcg Misoprostol.

Indications: Medical termination of intrauterine pregnancy.

Administration: *Adult*:

Up to 49 days gestation: Mifepristone 200mg for 1st dose followed 36 – 48 hours later by Misoprostol 400mcg orally, sublingually or vaginally.

From 50 – 63 days gestation: Mifepristone 200mg for 1st dose followed 36 – 48 hours later (unless abortion already complete) by Misoprostol 400mcg orally, sublingually or vaginally. Observe for at least 3 hours (or until bleeding or pain at an acceptable level); follow-up visit within 2 weeks to verify complete expulsion and assess vaginal bleeding.

13 – 24 weeks gestation: Mifepristone 200mg for 1st dose followed 36 – 48 hours later by Misoprostol 400mcg orally, sublingually or vaginally. If abortion does not occur 24 hours after the start of treatment, repeat course of Misoprostol by vaginal administration. Follow-up visit after appropriate intervals to assess vaginal bleeding recommended.

Side effects: Diarrhoea, abdominal pain, flushing, nausea, vomiting, abnormal vaginal bleeding, dizziness, dyspepsia, flatulence, menorrhagia, intermenstrual and postmenopausal bleeding, rash, uterine rupture.

Contraindications: Porphyria, adrenal disease, ectopic pregnancy, asthma, hypersensitivity to prostaglandins.

Caution: Hypotension, inflammatory bowel disease, adrenal suppression, anticoagulant therapy, asthma, cardiovascular disease, haemorrhagic disorders, endocarditis. If pregnancy occurred with an IUD in place, this must be removed prior to administering this medicine.

GEMEPROST

Presentation: Pessaries containing 1mg Gemeprost

Indications: Induction of abortion**,** cervical ripening for induction of labour in Intrauterine foetal death.

Administration: 1mg vaginal pessary inserted in posterior fornix 3 hours before surgery or every 3 hours to maximum of 5mg.

Side effects: Nausea, vomiting, diarrhoea, flushing, muscle weakness, dyspnoea, chest pain, mild pyrexia, uterine rupture.

Caution: Obstructive airway disease, cardiovascular insufficiency, raised intraocular pressure.

DINOPROSTONE

Presentation: Pessaries containing 3mg Dinoprostone, Tablets containing 500mcg Dinoprostone.

Indications: Induction and augmentation of labour

Administration: *By vaginal* induction of labour insert pessary high into posterior fornix 3mg followed after 6 hours by 3mg, maximum 6mg. *Oral;* 500mcg followed by 0.5 – 1 mg (1.5mg maximum) at hourly intervals.

Side effects: Nausea, vomiting, diarrhoea, flushing, muscle weakness, dyspnoea, chest pain, mild pyrexia, uterine rupture, hypertonus amniotic fluid embolism, abruption placenta, fever, stillbirth.

Contraindications: Active cardiac, pulmonary, renal or hepatic disease, placenta praevia cephalopelvic disproportion, fetal distress, major uterine surgery.

Caution: Glaucoma, cardiac, hepatic, renal impairment, hypertension and epilepsy.

6.2 Myometrial relaxants

Beta2 adrenoceptor stimulants relax the uterine muscle and are used in selected cases of premature labour.

No statistically significant effects on perinatal mortality have been observed. Their use permits a delay for transfers or the use of corticosteroids for fetal lung maturity.

SALBUTAMOL

Presentation: Tablets containing 2mg, 4mg salbutamol sulphate. Intravenous infusion containing 1mg/ml salbutamol as sulphate

Indications: Arrest uncomplicated premature labour.

Administration: 10 mcg/min, gradually increased to maximum of 45 mcg/min until contractions have ceased, then gradually reduced; or by IV or IM injection, 100–250 mcg repeated according to patient's response;

Oral: 4mg every 6 – 8 hours

Side effects: Nausea, vomiting, flushing, sweating, tremor, hypokalaemia, tachycardia and hypotension, rarely pulmonary oedema.

Caution: Hypertension, hypokalemia, diabetes mellitus moderate pre-eclampsia, pulmonary oedema, concomitant use of beta-blockers, sympathomimetics.

Contra-indications: Cardiac disease, eclampsia, intrauterine infection, antepartum haemorrhage, not for use in 1st and 2nd trimesters (not effective).

MAGNESIUM SULPHATE

Presentation: Injection containing 50% (5g) ampoule.

Indications: Premature labour, fulminant pre-eclampsia, Eclampsia.

Administration: Intravenous administration; 4g over up to 20 minutes followed by an intravenous rate of 1g every hour. intramuscular regimen; 4g intravenous. slowly over 5 minutes then 5g in each buttock. Total loading dose 14g. Maintenance dose; 5g magnesium sulphate in alternate buttock every 4 hours. A total of six maintenance doses are recommended.

Side effects: Hypermagnesaemia, nausea, vomiting, thirst, flushing, hypotension, arrhythmias, coma, respiratory depression, loss of tendon reflexes, muscle weakness, drowsiness, confusion.

Caution: Vital signs and magnesium sulphate blood levels must be closely monitored.

Antidote: 10cc of 10% calcium gluconate intravenous slowly.

6.3 Progestogens and Anti-progestogens

These modify some effects of and act mainly on tissues sensitised by oestrogens. There are two main groups of progestogens, the naturally occurring hormone progesterone and its analogues (dydrogesterone, hydroxyprogesterone, medroxyprogesterone) and testosterone analogues (norethisterone and norgestrel). Progestogens are used in abnormal uterine bleeding, dysmenorrhoea, menorrhagia, endometriosis, premenstrual syndrome, in contraceptive pills, in hormone replacement therapy together with oestrogens.

MIFEPROSTONE

Presentation: Tablets containing 200mg/50mg/10mg Mifepristone.

Indications: Cervical ripening for induction of abortion (up to 84 days gestation), Induction of labour in intrauterine foetal death (IUFD) where prostaglandins or oxytocin are inappropriate, Medical termination of intrauterine pregnancy.

Administration: *Adult*:

Cervical ripening for induction of abortion (up to 84 days gestation); 200mg single dose administered 24 – 48 hours before Misoprostol.

Induction of labour in intrauterine foetal death (IUFD) where prostaglandins or oxytocin are inappropriate; *Adult:* 600mg once daily for 2

days, if labour not started with 72 hours of the first dose, another method should be used.

Medical termination of intrauterine pregnancy;

Up to 49 days gestation, 200mg for 1st dose followed 36 – 48 hours later (unless abortion already complete) by Misoprostol 600mcg orally, sublingually or vaginally.

From 50 – 63 days gestation, 200mg for 1st dose followed 36 – 48 hours later (unless abortion already complete) by Misoprostol 600mcg orally, sublingually or vaginally. Observe for at least 3 hours (or until bleeding or pain at an acceptable level); follow-up visit within 2 weeks to verify complete expulsion and assess vaginal bleeding.

From 13 – 24 weeks gestation, 200mg for 1st dose followed 36 – 48 hours later by Misoprostol 600mcg orally, sublingually or vaginally or Gemeprost 1mg vaginally up to max. 5mg. A follow-up visit after appropriate interval to assess vaginal bleeding recommended.

Side effects: Abdominal cramps, uterine contractions, vaginal bleeding (can be severe), hypersensitivity, fever, chills, flushing, hypotension.

Contraindications: Porphyria, adrenal disease, ectopic pregnancy, asthma.

Caution: Adrenal suppression, anticoagulant therapy, asthma, cardiovascular disease, haemorrhagic disorders, endocarditis. If pregnancy occurred with an IUD in place, this must be removed prior to administering this medicine.

MEDROXYPROGESTERONE ACETATE

Presentations: Tablets containing 2.5mg, 5mg medroxyprogesterone acetate

Indications: As above.

Administration: Oral; 2.5 mg – 10 mg daily for 10 days beginning on 16 – 21st day of the cycle.

Endometriosis; 10mg 3 times daily for 3 months or i.m. 50mg weekly

Side effects: Acne, weight gain, changes in libido, premenstrual symptoms, irregular menstrual cycles.

Contraindications: Undiagnosed vaginal bleeding, mammary carcinoma, porphyria.

Caution: Diabetes, hypertension, hepatic, cardiac, renal disease.

NORETHISTERONE

Presentation: Tablets containing 5mg Norethisterone

Indications: See notes above; primary and secondary amenorrhoea.

Administration: *Endometriosis* 10mg daily starting on 5th day of the cycle (increase to 25mg daily if spotting occurs and reduce once bleeding has stopped).

Menorrhagia: 5mg 3 times daily for 10 days.

Dysmenorrhoea: 5mg 3 times daily from 5th to 24th day for 4 cycles.

Postponement of menstruation: 5mg 3 times daily starting 3 days before the anticipated onset.

Side effects: As above, but a more virilising exacerbation of epilepsy and migraine, liver disturbances and jaundice, gastrointestinal disturbances.

Contraindications: Thrombophlebitis, thromboembolic disorders, undiagnosed vaginal bleeding, carcinoma of the breast.

Caution: Conditions associated with fluid retention.

6.4 Oestrogens and Anti-oestrogens

CONJUGATED OESTROGENS

Presentation: Tablet containing 0.016mg and 0.3 mg; Vaginal cream containing 0.625mg/g base (30 g).

Indications: Atrophic vaginitis, Primary ovarian failure, Female hypogonadism, hormone replacement therapy in menopausal symptoms.

Administration: *Atrophic vaginitis,* vaginal cream, per vaginal or topically: 1–2 g daily, on a cyclical basis; maximum 4g/day.

0.625mg–1.25mg daily (with progesterone for 12-14 days per cycle if the uterus is intact).

Primary ovarian failure, oral: 1.25 mg daily

Female hypogonadism, oral: 0.3 or 0.625 mg daily given cyclically (e.g., 3 weeks on, 1 week off); adjust dose depending on the severity of symptoms and responsiveness of endometrium.

Side effects: Nausea and vomiting, weight changes, premenstrual-like syndrome, cholestatic jaundice, depression, headache.

Contraindications: Pregnancy, oestrogen dependent cancer.

Caution: In women with intact uterus, increased risk of myometrial cancer

Anti-oestrogens

The anti-oestrogens clomiphene citrate, cyclofenil, and tamoxifen are used in the treatment of female infertility due to anovulation. They induce gonadotrophin release by occupying oestrogen receptors in the hypothalamus thereby interfering with feedback mechanisms.

CLOMIPHENE CITRATE

Presentation: Tablets containing 50mg clomiphene citrate.

Indications: Anovulatory infertility

Administration: 50mg daily for 5 days starting from 2nd day of the cycle. A second course of 100mg daily for 5 days if ovulation is absent for 3 cycles only.

Side effects: Visual disturbances, ovarian hyperstimulation (withdraw), hot flushes, abdominal discomfort, vomiting, breast tenderness, weight gain.

Contraindications: Hepatic disease, ovarian cysts, endometrial carcinoma, pregnancy, abnormal uterine bleeding.

6.5 Endocrine Medicines

BROMOCRIPTINE

Dopamine receptor stimulant in the brain and inhibits the release of prolactin and lactation inhibits growth hormone release.

Presentation: Tablet containing 1mg, 2.5mg bromocriptine as mesylate

Indications: Suppression of lactation, galactorrhoea, cyclical benign breast disease, prolactinoma, rarely acromegaly.

Administration: *Suppression of lactation:* 2.5mg on 1st day, then 2.5mg twice daily for 14 days

Galactorrhoea/infertility: 1.25mg at bedtime, increase gradually to 7.5mg daily in divided doses – maximum 30 mg daily dose should be taken with food.

Side effects: Nausea, vomiting, headache, postural hypotension, drowsiness, high doses cause confusion, psychomotor excitation, pleural effusions, muscle cramps.

DANAZOL

Inhibits pituitary gonadotropins. It combines androgenic with anti-estrogenic and progestogenic activity. It is used in endometriosis, menorrhagia, menstrual disorders, mammary dysplasia, gynecomastia, hereditary angioedema, or preoperative preparations for fibroids, endometrial resection.

Presentation: Capsule containing 100mg, 200mg Danazol

Indications: as above

Administration: 200–800mg daily in divided doses, starting during menstruation, usually for 3–6 months (maximum 9 months).

Side effects: Nausea, dizziness, weight gain, backache, headache, menstrual disturbance,

muscle spasm androgenic effects, insulin resistance, alopecia, leukopenia, emotional liability.

Caution: Cardiac, hepatic, renal impairment, polycythaemia, epilepsy, breastfeeding, thromboembolic disease, uninvestigated vaginal bleeding, androgen dependant tumours.

BUSERELIN

Being a gonadotrophin analogue, after an initial stimulation phase, buserelin down-regulates pituitary gonadotrophin secretion leading to inhibition of ovarian steroid secretion.

Presentation: Nasal spray containing 150mcg buserelin as acetate, injection 1mg/ml

Indications: Endometriosis, pituitary desensitization before ovulation induction with gonadotrophins, pre-operative thinning of endometrium.

Administration: 150mcg spray in each nostril 3 times daily starting on 2nd day of menstruation for 6 months.

Side effects: Breakthrough bleeding, menopause-like symptoms, decreased bone density, ovarian cysts, leucorrhoea.

Contraindications: Pregnancy, undiagnosed vaginal bleeding, breastfeeding.

6.6 Contraceptives

The criteria by which contraceptive methods should be judged are effectiveness, acceptability and freedom from side effects. There are hormonal contraceptives, intrauterine devices, barrier methods and spermicides.

6.6.1 Combined oral contraceptives

These contain oestrogens and a progestogen. The oestrogen content ranges from 20 to 50 mcg and preparations with lowest oestrogen and progestogen and which give a good cycle and minimal side effects are chosen. The effectiveness of oral hormonal contraceptives may be reduced by Medicines that induce hepatic enzyme activity e.g. carbamazepine, phenytoin, phenobarbitone, primidone, rifampicin or antibiotics. They are available in monophasic and triphasic preparations.

Presentation: Tablets containing Ethinylestradiol + Levonorgestrel 30 mcg + 150 mcg.

Indications: Contraception, menstrual symptoms.

Administration: 1 tablet daily for 21 days starting on 1st day of cycle repeated after 7 days interval (during which withdrawal bleeding occurs).

Side effects: Nausea, vomiting, headache, weight gain, thrombosis, breast tenderness, depression, reduced menstrual loss, hypertension, changes in libido.

Contraindications: pregnancy, breast and genital carcinoma, breastfeeding, severe multiple risk factors for arterial disease, valvular heart disease with pulmonary hypertension, thromboembolism, focal migraine, liver disease, hypertension, diabetes mellitus, lipoprotein disorder.

Caution: Diabetes mellitus with vascular complication, sickle cell disease.

6.6.2 Emergency contraception

Presentation: Tablet containing 750 mcg (pack of 2) or 1.5 mg (pack of 1) Levonorgestrel

Indications: Postcoital contraception as an occasional emergency measure

Administration: 1.5mg Stat as soon as possible after coitus up to 72 hours OR 750mcg Stat (taken within 72 hours of unprotected intercourse) then repeat 12 hours later.

Side effects: see above.

Contraindications: See above

Caution: see above. Should not be administered if menstrual bleeding is overdue or if unprotected intercourse occurred more than 72 hours previously.

6.6.3 Oral progestogen-only contraceptives

Oral progestogen-only contraception may offer a suitable alternative when oestrogens are contraindicated, e.g. heavy smokers, valvular heart disease, diabetes mellitus, migraine and before major surgery.

The tablet is taken continuously from 1st day of the cycle and taken at the same time of the day. If one misses a tablet, it must be taken immediately one remembers and abstain or use a sheath for the next 7 days while continuing normal pill taking.

Presentation: Tablet containing either of the following:

Etnynodiol diacetate 500mcg

Norethisterone 350mcg

Levonogestrel 30 mcg

Norgestrel 75 mcg

Indications: Contraception (particularly when estrogens are contraindicated).

Administration: 1 tablet daily at the same time starting on 1st day of the cycle and then continuously.

Side effects: Menstrual irregularities, nausea, vomiting, headache, breast discomfort, weight gain, depression.

Contraindications: Pregnancy, undiagnosed vaginal bleeding, liver adenoma, severe arterial disease, porphyria, breast and genital carcinoma.

Caution: Heart disease, past ectopic pregnancy, functional ovarian cysts, jaundice in active liver disease.

6.6.4 Injectable progestogen-only contraceptives

Medroxyprogesterone acetate and norethisterone enanthate are acting progestogen is given intramuscularly and which provide effective contraception.

MEDROXYPROGESTERONE

Presentation: Inj containing Medroxyprogesterone 150mg/ml (IM) and 104mg/0.65 ml (SC) prefilled syringe.

Indications: Long term contraception

Administration: By deep IM injection 150 mg or by SC 104mg within the first 5 days of the menstrual cycle, repeat every 3 months.

Side effects: As above; delayed return of fertility, irregular cycles, heavy menstrual bleeding, headache, uterine bleeding.

Contraindications: As for progestogen-only pill

NORETHISTERONE

Presentation: Injection containing Norethisterone enanthate 200mg/ml

Indications: Short term contraception

Administration: By deep IM injection 200mg within the first 5 days of menstrual cycle immediately after parturition, repeat every 2 months.

Side effects: See above; more virilising effects, a greater possibility of liver disturbances and jaundice, gastro-intestinal disturbances, oedema, weight gain, breast discomfort, and irregular menstrual cycles.

Contraindications: As for progestogen-only pill, severe obesity, pre-menopause.

6.6.5 Progesterone implants

LEVONORGESTREL

Presentation: Implant containing 150 mg (2 × 75 mg rods), Two-rod levonorgestrel-releasing implant, each rod

containing 75 mg of levonorgestrel (150mg total); Subcutaneous implant containing 38mg Levonorgestrel.

Indications: Contraception.

Administration: *By subdermal implantation*

Insert set of 6 x 38mg implant capsules inserted within the first 5 days of the menstrual cycle (preferably on 1st day after which additional preCaution will be necessary for the following 7 days) or on 21st day after parturition (after this day additional precaution will be necessary for the following 7 days). Remove within 5 years of insertion.

Insert 2 implants of 75 mg each; insert in non-dominant upper arm 6–8 cm above the elbow within the first 7 days of the menstrual cycle.

Caution, contraindications: As for progestogen-only contraception.

6.6.6 Spermicidal Contraceptives

Spermicidal contraceptives e.g. Nonoxynol-9 are useful additional safeguards but do not give adequate protection if used alone. Use with barrier methods.

6.6.7 Contraceptive devices

INTRA-UTERINE DEVICES

Presentation: Copper-Containing Device and Levonorgestrel-releasing Intrauterine system Reservoir with 52 mg.

Indications: Contraception

Administration: Inserted at any time between day 4 and day 12 after the start of menstrual bleeding; do not fit during heavy menstrual bleeding.

Side effects: Uterine perforation, displacement, pelvic infection, menorrhagia, dysmenorrhea.

Caution: Menorrhagia, previous or present pelvic infection, diabetes, valvular heart disease, remove if pregnancy occurs.

Contraindications: Anaemia, menorrhagia, history of ectopic pregnancy, pelvic infection, immunosuppressive therapy

OTHER CONTRACEPTIVE DEVICES

These include the Cap, diaphragm, female and male condoms.

introduction of a corticosteroid by inhalation, cromoglycate or oral theophylline may stabilize asthma. For more severe attacks a short course of an oral corticosteroid may be necessary to bring asthma under control. In severe acute asthma or airways obstruction, it is safer to treat patients in hospitals where oxygen and resuscitation facilities are available.

The beta2-adrenoceptor stimulants such as salbutamol are the safest and most effective. They even partially give relief of irreversible airway obstruction in chronic bronchitis and emphysema. Hence beta2 adrenoceptor stimulants remain the Medicines of choice.

7 Medicines used in the treatment of diseases of the respiratory system

7.1 Bronchodilators

7.1.1 Adrenoceptor Stimulants

Most mild to moderate attacks of asthma respond rapidly to aerosol administration of selective $beta_2$-adrenoceptor stimulants such as salbutamol. Infrequently occurring moderate asthma, the introduction of a corticosteroid by inhalation, cromoglycate or oral theophylline may stabilize asthma. For more severe attacks a short course of an oral corticosteroid may be necessary to bring asthma under control. In severe acute asthma or airways obstruction, it is safer to treat patients in hospitals where oxygen and resuscitation facilities are available.

The $beta_2$-adrenoceptor stimulants such as salbutamol are the safest and most effective. They even partially give relief of irreversible airway obstruction in chronic bronchitis and emphysema. Hence $beta_2$ adrenoceptor stimulants remain the Medicines of choice.

The aerosol inhaler is an effective and convenient method of administration for mild to moderate airway obstruction. Sort acting $beta_2$ agonists are not useful regularly in patients with mild or moderate asthma as there is no clinical benefit. Longer-acting $beta_2$ agonists salbutamol and formoterol are of benefit for these patients.

7.1.1.1 Selective beta2 adrenoceptor stimulants

SALBUTAMOL

Presentation: Tablet containing 2mg, 4mg salbutamol sulphate. Syrup containing 2mg/5ml salbutamol sulphate. Injection containing 50mcg, 500mcg salbutamol sulphate. Aerosol inhalation containing 100mcg salbutamol metered. Nebules containing 0.1% (1mg/ml) salbutamol.

Indications: Asthma, reversible airway obstruction.

Administration: 2mg to be taken 3-4 times a day; maximum single dose 8mg.

Aerosol inhalation: 100-200mcg (or 1-2 puffs) up to 3-4 times a day for persistent symptoms

Prophylaxis: in exercise-induced bronchospasms 200mcg (2 puffs).

Injection; subcutaneously or intramuscularly: 500mcg repeated every 4 hours if necessary, slow intravenous injection 250mcg, repeated if necessary.

Children;

under 2 years: 100mcg/kg 4 times a day.

2-6 years: 1-2mg 3-4 times a day.

6-12 years 2mg 4 times a day.

Aerosol inhalation:

100mcg (1 puff) increase to 200mcg (2 puffs) if necessary.

Prophylaxis: Child; 100mcg (1 puff).

Side effects: fine tremor, nervous tension, headache, peripheral vasodilatation, tachycardia, hypokalaemia after high doses, hypersensitivity reaction.

Contraindications: Hypersensitivity to salbutamol. **Caution:** Hyperthyroidism, myocardial insufficiency, arrhythmias, hypertension, pregnancy and breastfeeding, intravenous administration in diabetes.

TERBUTALINE

Presentation: Tablet containing 5mg terbutaline sulphate, syrup containing 1.5mg/5ml terbutaline sulphate, an injection containing 500mcg/ml terbutaline sulphate, aerosol inhalation containing 250mcg/metered puff terbutaline sulphate, powder for inhalation containing 500mcg/inhalation of terbutaline sulphate, nebulised solution for inhalation containing 2.5mg/ml of terbutaline sulphate.

Indications*:* Asthma and other conditions

associated with reversible airway obstruction
Administration: *Adult:*

Inhalation of the nebulised solution; 5 - 10mg 2 - 4 times daily, additional doses may be necessary for severe acute asthma.

Orally; initially 2.5mg 3 times daily for 1 - 2 weeks, then up to 5mg 3 times daily.

Aerosol inhalation

250 - 500mcg (1 - 2 puffs), for persistent symptoms, 250 - 500mcg up to 3 - 4 times daily.

Continuous intravenous infusion

Solution containing 3 - 5mcg/ml given at a rate of 1.5 - 5mcg/minute for 8 - 10 hours.

Inhalation powder

500mcg (1 inhalation); for persistent symptoms, 500mcg up to 4 times daily.

Subcutaneous, intramuscular or slow intravenous injection 250 - 500mcg up to 4 times daily

Children:

Inhalation of the nebulised solution

Up to 3 years: 2mg 3 times daily;

3-6 years: 3mg 3 times daily;

6-8 years: 4mg 3 times daily

Over 8 years: 5mg 2 - 4 times daily.

***Orally*;**

Up to 6 years: 75mcg/kg 3 times daily

7-15 years: 2.5mg 3 times daily.

Aerosol inhalation

250 - 500mcg (1 - 2 puffs), for persistent symptoms, 250 - 500mcg up to 3 - 4 times daily.

Continuous intravenous infusion

Dose should be reduced from the adult dose.

Inhalation powder

500mcg (1 inhalation); for persistent symptoms, 500mcg up to 4 times daily.

Subcutaneous, intramuscular or slow intravenous injection

2-15 years, 10mcg/kg up to a maximum of 300mcg.

Side effects: Nervous tension, fine tremors (especially in hands), peripheral dilatation, headache, palpitations, tachycardia, arrhythmias, muscle cramps, sleep and behaviour disturbances in children, hypersensitivity reactions including paradoxical bronchospasm, urticaria and angioedema, pain associated with intramuscular injection.

Contraindications: Cardiac disease, eclampsia and severe pre-eclampsia, intrauterine infection, intrauterine foetal death, antepartum haemorrhage, placenta praevia, cord compression, threatened abortion.

Caution: Hyperthyroidism, cardiovascular disease, arrhythmias, hypertension, pregnancy and breastfeeding, diabetes, serious hypokalaemia may result from the use of this drug.

SALMETEROL

Presentation: Dry powder for inhalation containing 50mcg per blister, aerosol inhalation containing 25mcg per metered inhalation.

Indications: Reversible airway obstruction in patients requiring long term regular therapy.

Administration: *Adult:* 50mcg (1 blister or 2 puffs) twice daily up to 100mcg (2 blisters or 4 puffs) twice daily in more severe disease.

Children:
Under 1 year: not recommended
Over 4 years: 50mcg (I blister or 2 puffs) twice daily

Side effects: See under salbutamol

Contraindications: See under salbutamol, hypersensitivity, and severe liver cirrhosis.

Counselling: Salmeterol should not be used for relief of acute attacks.

Caution: See under salbutamol, pregnancy.

FORMOTEROL FUMERATE

Presentation: Inhalation powder containing 12mcg/dose of 120 doses, and inhalation aerosol containing 12mcg/dose of metered 100 doses.

Indications: Chronic asthma in patients who regularly use an inhaled corticosteroid, chronic obstructive pulmonary disease.

Administration: ***Adult:***

by inhalation of powder: 12 mcg twice daily, dose may be increased in more severe airway obstruction; increased to 24 mcg twice daily.

By inhalation of aerosol: 12 mcg twice daily, dose may be increased in more severe airway obstruction; increased to 24 mcg twice daily.

Children:

By inhalation of powder

6–*11 years*: 12 mcg twice daily, a daily dose of 24mcg of formoterol should be sufficient for the majority of children, particularly for younger age groups; higher doses should be used rarely, and only when control is not maintained on the lower dose.

12–17 years: 12 mcg twice daily, dose may be increased in more severe airway obstruction; increased to 24 mcg twice daily, a daily dose of 24 mcg of formoterol should be sufficient for the majority of children, particularly for younger age groups; higher doses should be used rarely, and only when control is not maintained on the lower dose.

By inhalation of aerosol

12–17 years: 12 mcg twice daily, dose may be increased in more severe airway obstruction; increased to 24 mcg twice daily, a daily dose of 24 mcg of formoterol should be sufficient for the majority of children, particularly for younger age groups; higher doses should be used rarely, and only when control is not maintained on the lower dose.

Side effects: Dizziness, muscle cramps, viral infections, angina pectoris, altered taste, sleep disorders, arrhythmias, broncospasms, hyperglycaemia, hypo/hyper-tension, QT-interval prolongation.

Contraindication: Hypersensitivity and asthma treatment without inhaled corticosteroids.

Cautions: Co-existing conditions including cardiovascular disorders especially coronary insufficiency, cardiac arrhythmias, pheochromocytoma. Life threatening paradoxical bronchospasms can occur. Discontinue immediately.

IPRATROPIUM BROMIDE

Presentation: Aerosol inhaler 20mcg/ metered-dose and 250mcg/ml nebuliser liquid containing Ipratropium bromide

Indication: Reversible airway obstruction

Administration: ***Adult:***

By inhalation of aerosol: 20-40mcg 3-4 times daily.

By inhalation of nebulized solution 250mcg-500mcg 3-4 times daily

Children:

By inhalation of aerosol

20-40mcg 3-4 times daily

By inhalation of nebulized solution

1-5years: 125-250mcg as required, maximum 1mg/day

6-11 years: 250mcg as required, maximum 1mg/day

12-17 years: 500mcg as required, maximum 2mg/day under medical supervision

Side effects: Gastrointestinal disorders, laryngospasm, pruritus, stomatitis, dizziness, nausea, vomiting

Caution: Avoid spraying near the eyes, cystic fibrosis

BUDESONIDE WITH FORMETEROL

Presentation: Powder for inhalation containing Formoterol fumarate dehydrate 6mcg per dose and Budesonide 200mcg per dose.

Indication: Asthma maintenance therapy

Administration: *Adult:* 1-2 inhalations twice daily increased if necessary up to 4 inhalations twice daily

Children:

12-17 years: 1-2 puffs twice daily –reduced to 1 puff daily, dose reduced only if control is maintained.

7.1.1.2 Other adrenoceptor stimulants

These stimulants are now regarded as less suitable and less safe for use as bronchodilators than the selective beta$_2$-adrenoceptors, as they are likely to cause arrhythmias and other side effects. They should be avoided whenever possible. Adrenaline injection (1 in 1000) is used in the emergency treatment of acute allergic and anaphylactic reaction

ADRENALINE

Presentation: Injection containing adrenaline 1 in 1000, 1ml ampoule.

Indications: Emergency treatment of acute allergic and anaphylactic reactions.

Administration: *Adult;* 0.2 – 0.5ml as a single dose by slow subcutaneous injection.

In anaphylactic shock; 1ml.

Children:

0.01ml/kg body weight, maximum 0.5ml, repeated 4 hourly, if necessary.

Side effects: Hypertension, anxiety and tachycardia. **Caution:** Avoid in asthma if the pulse is 120 per minute and above.

EPHEDRINE HYDROCHLORIDE

Presentation: Tablet containing 15mg ephedrine hydrochloride. Syrup containing 15mg/5ml ephedrine hydrochloride.

Indication: Reversible airway obstruction

Administration: *Adult:* 15 – 60 mg 3 times daily.

Children

Up to 1 year; 7.5 mg 3 times daily.

1–5 years; 15mg 3 times daily,

6–12 years; 30 mg 3 times daily.

Side effects: Tachycardia, anxiety, restlessness, insomnia, tremor, arrhythmias, dry mouth and cold extremities.

Caution: Hyperthyroidism, diabetes mellitus, ischaemic heart disease, hypertension, renal impairment, elderly, prostatic hypertrophy, interaction with MAOIs.

7.1.2 Xanthine Derivatives

Xanthine derivatives are used for the relief of bronchospasm. Theophylline is the principal compound with additive effect when used with small doses of beta2-adrenoceptor stimulants; however, the combination may increase the risk of side effects, including hypokalaemia.

Theophylline has a narrow therapeutic index. It is therefore important to be cautious in patients with liver diseases, heart failure, and those on medicines that affect liver metabolism such as cimetidine, ciprofloxacin, erythromycin and oral contraceptives. Its half-life is increased as the theophylline is metabolised by the liver. However, the half-life is decreased in smokers, heavy drinkers and medicines such as phenytoin, carbamazepine, rifampicin and barbiturates. Aminophylline is a stable combination of theophylline and ethylenediamine. The ethylenediamine improves the solubility of the aminophylline in water. Aminophylline must be given by **very slow** intravenous injection (over at least 20 minutes)

Caffeine citrate is a xanthine typically used in the management of very pre-term neonates, and continued until a corrected gestational age of 34 to 35 weeks is reached or longer if necessary. When given, it reduces the frequency of neonatal apnoea, and the need for mechanical ventilation during the first 7 days of treatment.

Pulmonary surfactants (though they are not xanthine derivatives) are used to prevent and treat respiratory distress syndrome in neonates and preterm neonates. Prophylactic use may reduce the need for mechanical ventilation and is more effective than 'rescue treatment' in preterm neonates of 29 weeks or less corrected gestational age. Pulmonary immaturity with surfactant deficit is the commonest reason for respiratory failure in the neonate, especially in those of less than 30 weeks corrected gestational age.

CAFFEINE CITRATE

Presentation: Sterile solution for IV or oral use containing 20 mg/mL (equivalent to 10 mg caffeine base/ml)

Indications: Neonatal apnoea in preterm infants

Administration:

Children

Neonate: 20 mg/kg as a loading dose, then 5 mg/kg once daily, starting 24 hours after loading dose; maintenance dose may be increased by 5 mg/kg every 24 hours to a maximum of 20 mg/kg/day, unless adverse effects develop; continue 4–5 days after cessation of apnoea.

Side effects: Gastric irritation (oral administration) including nausea and vomiting, feeding intolerance, irritability, agitation, hyperglycaemia or hypoglycaemia, tachycardia, diuresis, excessive CNS stimulation, necrotizing enterocolitis.

Contraindication: Hypersensitivity to Caffeine or Citrate.

Cautions: Cardiovascular disorders, gastrooesophageal reflux, seizure disorders, renal impairment and hepatic impairment.

THEOPHYLLINE

Presentation: Tablet containing 125mg, 300mg theophylline, a liquid containing 60mg/5ml theophylline, a capsule containing 60mg theophylline

Indications: Reversible airway obstruction, Severe-acute asthma

Administration: ***Adult***

Tablet 125mg 3-4 times daily after food, increased to 250mg if required.

Liquid; 120 - 240mg 3 - 4 times daily after food.

Capsule; 250 - 500mg every 12 hours.

Children

Tablet; *7 - 12 years:* 62.5 - 125mg 3 - 4 times daily.

Liquid;

2-6 years: 60 - 90mg 3 – 4 times daily

7-12 years: 90 - 120mg 3 - 4 times daily.

Capsule

2-6 years: 60 - 120mg every 12 hours

7-12 years: 125 - 250mg every 12 hours.

As for aminophylline below.

Caution: Theophylline has a narrow therapeutic window, the plasma concentration for optimum response is 10 –20 mg/litre (55-110 micromol/litre). Also caution in liver and cardiac diseases, epilepsy, disease, pregnancy in breastfeeding.

Counselling: Swallow the capsule whole with fluids or swallow granules enclosed in soft food such as yoghurt.

AMINOPHYLLINE

Presentation: Injection containing 250mg/10ml and tablet containing 100mg of Aminophylline.

Indications: Severe acute asthma and Severe acute exacerbation of chronic obstructive pulmonary disease, chronic asthma

Administration: ***Adult:***

Severe acute asthma in patients not previously treated with theophylline:

By slow intravenous injection: 250–500 mg (max. per dose 5 mg/kg), to be followed by intravenous infusion *Severe acute asthma*

by intravenous infusion: 500–700 mcg/kg/hour, adjusted according to plasma-theophylline concentration. Elderly: 300 mcg/kg/hour, adjusted according to plasma-theophylline concentration.

Chronic asthma:

by mouth using modified-release medicines: Initially 225 mg twice daily for 1 week, then increased if necessary to 450 mg twice daily, adjusted according to plasma theophylline concentration.

Children:

Severe acute asthma in patients not previously treated with theophylline

5 mg/kg (max. per dose 500 mg), to be followed by intravenous infusion.

Severe acute asthma

1 month–11 years: 1 mg/kg/hour, adjusted according to plasma-theophylline concentration.

12–17 years: 500–700 mcg/kg/hour, adjusted according to plasma-theophylline concentration.

Chronic asthma: by mouth using modified-release medicines

Body-weight 40 kg and above: Initially 225 mg twice daily for 1 week, then increased if necessary to 450 mg twice daily, adjusted according to plasma theophylline concentration.

Side effects: Headache, palpitations, seizures, nausea, abdominal pain, anxiety, arrythmia, confusion, delirium, diarrhea, gurd, hypotension, insomnia, electrolyte imbalance.

Contraindications: Hypersensitivity.

Cautions: Arrhythmias following rapid intravenous Injection, cardiac arrhythmias or other cardiac disease, elderly (increased plasma-theophylline concentration), epilepsy, fever, hypertension, peptic ulcer, risk of hypokalaemia, thyroid disorder.

SURFACTANT

Presentation: Suspension for intratracheal instillation containing 25 mg/ml or 80 mg/ml of pulmonary surfactant.

Indications: Treatment and prophylaxis of respiratory

distress syndrome (hyaline membrane disease) in preterm neonates.

Administration: ***By endotracheal tube***

Children:

Treatment of respiratory distress syndrome in preterm

Neonates (>700g weight)

Preterm neonate: 100 mg/kg, preferably administer within 8 hours of birth; dose may be repeated within 48 hours at intervals of at least 6 hours for up to 4 doses.

Prophylaxis of respiratory distress syndrome in preterm neonates (specialist use only)

Neonate up to 32 weeks corrected gestational age: 100 mg/kg, preferably administer within 15 minutes of birth; dose may be repeated within 48 hours at intervals of at least 6 hours for up to 4 doses.

Side effects: Pulmonary haemorrhage has been rarely associated with pulmonary surfactants, especially in more preterm neonates. Obstruction of the endotracheal tube by mucus secretions has been reported.

Cautions: Hyperoxaemia may occur due to rapid improvement in arterial oxygen concentration, monitor continuously.

MANAGEMENT OF ACUTE SEVERE ASTHMA IN GENERAL PRACTICE

Mild asthma in adults

- Speech normal
- Pulse <100 beats/minute
- Respiration >25 breaths/minute
- Peak flow < 80% of predicated or best, treat at home but the response to treatment must be assessed before doctor leaves.

Treatment:

Nebulised salbutamol 5mg or nebulised terbutaline 10mg.

Monitor response 15–30 minutes after nebulisation. If peak flow 50 –75% of predicted or best give*: Oral* prednisolone 30 –60 mg and step up usual treatment. Alternatively, if peak flow > 75% of predicted or best: Step up usual treatment modality.

Follow up

Monitor symptoms and peak flow, set up a self-management plan. Review in hospital/clinic setting within 48 hours. Modify treatment at review according to guidelines for chronic asthma.

IMPORTANT:

Regard each emergency consultation as being for acute asthma until shown otherwise.

Acute Severe Asthma in Adults

one of the above features is present.

Treatment:

Oxygen 40 – 50% if available.

Nebulised salbutamol 5mg or nebulised terbutaline

10mg

Oral prednisolone 30 – 60 mg or i.v hydrocortisone 200mg. Monitor response 15 – 30 minutes after nebulisation if any signs of acute asthma persist:

Arrange hospital admission while awaiting ambulance repeat nebulised beta$_2$ stimulant and give with nebulised ipratropium 500 mcg or give subcutaneous terbutaline or give slow intravenous aminophylline 250mg. Alternatively, if symptoms have improved, respiration and pulse settling, and peak flow > 50% of predicted or best: step up usual treatment and continue prednisolone.

Follow up

Monitor symptoms and peak flow. Set up self-management, plan review in hospital/ clinic setting within 24 hours. Modify at a review.

Life-threatening asthma in adults

- Silent chest
- Cyanosis
- Tachycardia or exhaustion
- Peak flow <33% of predicted or best arrange IMMEDIATE hospital admission.

Treatment:

Oxygen driven- nebuliser in an ambulance. hydrocortisone 200 mg (immediately).

Nebulised beta$_2$ stimulant with nebulised ipratropium or subcutaneous terbutaline or slow intravenous aminophylline 250mg. Oral prednisolone 30 –60 mg or intravenously

STAY WITH PATIENT UNTIL AMBULANCE ARRIVES

1. If no nebuliser available give 2 puffs of beta$_2$ stimulant using large –volume spacer and repeat 10 –20 times

IMPORTANT:
Do not give bolus aminophylline to a patient already taking oral theophylline.

IMPORTANT:
Patients with severe or life-threatening attacks may not be distressed and may not have all these abnormalities, the presence of just one of the signs should alert the doctor.

Signs of Acute-Severe Asthma in children

- Too breathless to talk
- Too breathless to feed
- Respiration ≥50 breaths/minute
- Peak flow ≤ 50% of predicted or best

IMPORTANT:
Failure to respond at any time requires immediate referral to hospital doctor.

Life-threatening features

- Peak flow <33% of predicted or best
- Cyanosis, silent chest, or poor respiratory effort
- Fatigue or exhaustion
- Agitation or reduced alertness

IMPORTANT:
Failure to respond adequately at any time requires immediate referral to hospital.

Treatment of acute asthma in children

- Short-acting beta2 stimulant from metered-dose inhaler using a large-volume spacer device may be as effective as the use of nebuliser; the dose is one puff every few seconds until improvement occurs (max. 20 puffs), using a face mask in a very young child.
- Terbutaline may be given subcutaneously in severe episodes.
- Oxygen is of benefit.
- A child requiring high-dose inhaled bronchodilators should also receive soluble tablets prednisolone 1-2 mg/kg body weight (maximum 40mg) once daily for up to 5 days if necessary; a child needs an immediate referral to the hospital if fails to respond.
- Aminophylline should no longer be used in children at home.

7.2 Corticosteroids

Corticosteroids are recommended for prophylactic treatment in patients using beta2-stimulants more than once daily. The aerosol preparation must be used regularly to obtain maximum benefit which is normally obtained after 3 – 7 days after initiation. Beclomethasone dipropionate is the drug of choice. High doses of corticosteroids are associated with some adrenal suppression and affect body metabolism. Oral preparations should be used for a short duration starting with high doses and lasting for about 5 - 7 days. For example, oral prednisolone should be given in adequate doses i.e.1 - 2mg/kg/ day given in divided doses, gradually reduced once the attack has been controlled.

Corticosteroids can be used in chronic continuing asthma when the response to other antiasthmatic Medicines has been relatively small. Inhaled doses should be increased to reduce on oral preparation dose. Oral doses could be taken as a single dose in the mornings.

BECLOMETHASONE DIPROPIONATE

Presentation: Aerosol containing, 50mcg, 100mcg and 200mcg metered doses Beclomethasone diproprionate

Indication: Prophylaxis of asthma not controlled by a bronchodilator.

Administration: 200mcg (2 puffs) 2 times a day or 100mcg (1 puff) 3 – 4 times a day. In more severe cases the initial dose of 600 – 800mcg (6 – 8 puffs) daily may be required.

Children:
50 - 100mcg (1 - 2 puffs of 50mcg metered inhaler) 2 –4 times a day.

Side effects: See notes above, and hoarseness and candidiasis of mouth and throat (usually with high doses), rarely hypersensitivity reaction including rash and angioedema.

Caution*:* See notes above, and also active or quiescent tuberculosis and may need systemic treatment when airway is obstructed with mucus, and in stress, paradoxical bronchospasm, (calls for discontinuation and alternative therapy). If mild, prevention is by inhalation of beta$_2$ adrenoreceptor stimulants or transfer to a dry powder inhalation.

FLUTICASONE

Presentation: Aerosol for inhalation containing 44mcg, 110mcg and 220mcg/ actuation, and powder for inhalation containing 50mcg, 100mcg and 250mcg/actuation.

Indications: For prophylaxis in asthma, for allergic rhinitis, chronic rhinosinusitis.

Administration: ***Adult:***

By inhalation of powder

Initially 100–500 mcg twice daily (max. per dose 1 mg twice daily), dose may be increased according to severity of asthma. Doses above 500 mcg twice daily initiated by a specialist.

By inhalation of aerosol

Initially 100–500 mcg twice daily (max. per dose 1 mg twice daily), dose may be increased according to severity of asthma. Doses above 500 mcg twice daily initiated by a specialist

Children:

By inhalation of powder

5–15 years: Initially 50–100 mcg twice daily (max. per dose 200 mcg twice daily), dose to be adjusted as necessary.

16–17 years: Initially 100–500 mcg twice daily (max. per dose 1 mg twice daily), dose may be increased according to severity of asthma. Doses above 500 mcg twice daily initiated by a specialist.

By inhalation of aerosol

4–15 years: Initially 50–100 mcg twice daily (max. per dose 200 mcg twice daily), dose to be adjusted as necessary

16–17 years: Initially 100–500 mcg twice daily (max. per dose 1 mg twice daily), dose may be increased according to severity of asthma. Doses above 500 mcg twice daily initiated by a specialist.

Side effects: Headache, epistaxis, pharyngitis, fever, dysphonia, cough, dyspepsia.

Contraindications: Hypersensitivity.

Caution: May mask an acute infection including fungal and exacerbate viral infections not for use in untreated localized infection involving the nasal mucosa.

7.3 Sodium cromoglycate and related substances

Sodium cromoglycate has no value in the treatment of an acute attack of asthma. However regular inhalation of the drug can reduce the frequency of attacks of asthma. This would necessitate a reduction in the use of beta$_2$-bronchodilators and corticosteroids.

Cromoglycate is also of value in the prevention of exercise-induced asthma, a single dose inhalation 30 minutes beforehand. The nebuliser solution is useful for young children who cannot manage the powdered aerosol.

SODIUM CROMOGLYCATE

Presentation: Aerosol for inhalation containing sodium cromoglycate 5mg/metered inhalation; nebulised solution containing 10mg/ml sodium cromoglycate.

Indication: Prophylaxis of asthma, food allergy, allergic conjunctivitis, allergic rhinitis.

Administration: ***Adult & child***

Aerosol inhalation; 10mg (2 puffs) 4 times a day initially, increased in severe cases or during periods of risk to 6 – 8 times a day. Additional doses may also be taken before exercise.

Powder inhalation; 20mg 4-times daily, increased in severe cases to 8 times daily.

Nebulised solution; 20mg 4-times daily, increased in severe cases to 6 times daily, regular use is necessary. Maintainance; 5mg (1 puff) 4 times daily).

Side effects: coughing, transient bronchospasm, throat irritation due to inhalation of powder.

Counselling: Regular use is necessary.

KETOTIFEN

Ketotifen is an antihistamine with action similar to cromoglycate but has no value in the treatment of acute asthma.

Presentation: Tablet containing 1mg Ketotifen, Capsule containing 1mg Ketotifen. Elixir containing 1mg/5ml ketotifen.

Indications: Allergic asthma poorly controlled with bronchodilators. Also, manifestations advise to avoid oral antidiabetics (fall in Thrombocyte count reported.

Administration: 1 mg daily with food, increase if necessary to 2mg twice daily with food. Initial treatment in readily sedated patients 0.5 - 1mg at night.

Children:
Over 2 years; 1mg 2 times daily with food.

Side effects: Dry mouth and sedation, slight dizziness, drowsiness, CNS stimulation, weight gain also reported.

Caution: previous anti-asthmatic treatment should be continued for a minimum of two weeks after initiation of ketotifen treatment.

Drowsiness may affect the performance of skilled tasks, enhances alcohol effects.

7.4 Antihistamines

All antihistamines are of potential value in the treatment of nasal allergies, particularly in seasonal (hay fevers), and maybe of some value in vasomotor rhinitis. Oral antihistamines are also of value in preventing urticaria and used for the treatment of urticaria rashes, pruritus and insect bites and stings; they are also used in drug allergies. Injection of promethazine and chlorpheniramine may be used as an adjunct to adrenaline in the emergency treatment of anaphylaxis and angioedema. Antihistamines are also useful in nausea and vomiting.

There is no evidence of the superiority of any of the older antihistamines over another. They only differ in the extent of sedativeness and duration of action.

Most of the antihistamines cause drowsiness and sedation. Patients must be warned that their ability to drive or perform any activity that requires high alertness may be affected. Antihistamines also may potentiate alcohol effect. Other side effects include headache, psychomotor impairment, antimuscarinic effects such as urinary retention, dry mouth, blurred vision and gastrointestinal disturbances, photosensitivity, occasional rashes. Antihistamines should be used with caution in epilepsy, prostatic hypertrophy, glaucoma and hepatic disease.

Most antihistamines should be avoided in porphyria although chlorpheniramine has been used. For further information on contra-indications and special problems, refer to specific sections, e.g., breastfeeding, pregnancy.

CHLORPHENAMINE MALEATE

Presentation: Tablets containing 2mg, 4mg Chlorphenamine maleate; Syrup containing 2mg/5ml Chlorphenamine maleate; injection10mg/ ml.

Indication: Symptomatic relief of allergy such as hay fever, urticaria, emergency treatment of anaphylactic reactions.

Administration: 4mg every 4 – 6 hours, maximum 24mg a day.

Children:
1 –2 years; 1 mg 2 times a day, maximum 6 mg a day.
6 – 12 years; 2 mg every 4 –6 hours a day, maximum 12 mg a day.
Not recommended for children under 1 year.

Side effects and Caution: see above. Besides, exfoliating dermatitis and tinnitus have been reported. An injection may cause transient hypertension or CNS stimulation and may be irritant.

CETRIZINE

Presentation: Tablet containing 10mg; oral solution containing 5mg/5ml of Cetrizine.

Indications: Symptomatic relief of allergy such as hay fever, chronic idiopathic urticaria, atopic dermatitis

Administration: *Adult*: 10 mg once daily

Children:
2–5 years: 2.5 mg twice daily
6–11 years: 5 mg twice daily
12–17 years: 10 mg once daily

Side effects: Headache, somnolence, fatigue, dry mouth, vomiting, epistaxis, dizziness, malaise, hallucinations, confusion, increased appetite.

Contraindications: Hypersensitivity

Caution: Avoid alcohol, sedatives and tranquilizers due to increased risk of drowsiness; epilepsy and hepatorenal impairment.

FEXOFENADINE

Presentation: Tablet containing 120mg and 180mg of Fexofenadine.

Indication: Symptomatic relief of seasonal allergic rhinitis; Symptomatic relief of chronic idiopathic urticaria.

Administration: *Adult:* 120-180 mg once daily.

Children:
6–11 years: 30 mg twice daily;
12–17 years: 120 mg once daily.

Side effects: Vomiting, diarrhea, nausea, headache, dizziness, backpain, dysmenorrhea, somnolence.

Containdications: Hypersensitivity

Caution: Hypersensitivity, pregnancy and breastfeeding.

PROMETHAZINE HYDROCHLORIDE

Presentation: Tablets containing 10mg, 25mg Promethazine hydrochloride. An injection containing 25mg/ml Promethazine hydrochloride. Elixir containing 5mg/5ml Promethazine hydrochloride.

Indication: Symptomatic relief of allergies such as hay fever, urticaria, emergency treatment of anaphylactic reactions, preoperative medication, sedation and motion sickness.

Administration: *By mouth*; 25mg at night increased to 50mg twice daily if necessary or 10 – 20mg taken 2 – 3 times a day.

Injection; IM 25 – 50 mg; maximum 100 mg.

In emergencies IV

25–50 mg maximum 100mg as a solution containing 2.5mg/ml in water for injection.

Children:

By mouth

1–5 years; 5–15mg per day.

5–10 years: 10 – 25 mg per day

Injection; IM

Under 2 years of age: Not recommended

2-5 years; 5-15mg daily in 1-2 divided doses

5–10 years; 10-25mg daily in 1-2 divided doses. ***Premedication***

Under 2 years not Recommended

2-5 years: 15- 20mg

5-10years: 20-25mg.

Side effects: see notes above.

Contraindications: See notes above.

Caution: IM injection may be painful. See notes above; also, pregnancy and breastfeeding.

LORATADINE

Presentation: Tablet containing 10mg and oral solution containing 1mg/ml

Indications: Symptomatic relief of allergy such as hay fever, chronic idiopathic urticarial.

Administration: *Adult* 10mg once daily.

Children:

2-11years (body weight up to 31kg) 5mg once daily

*12-17 years:*10mg once daily

Side effects: Drowsiness, nervousness in children.

Caution: Porphyria, epilepsy

DIPHENHYDRAMINE HYDROCHLORIDE

Presentation: Tablets containing 25mg Diphenhydramine hydrochloride. Liquid 10mg/5mls

Indications: Symptomatic relief of allergy such as hay fever, urticaria

Administration: *Adult;* 25 - 50mg 3 to 4 times a day (max. 300mg/day).

Children:

2 – 6 years; 6.25mg 4 times a day (max. 37.5mg/day).

6–12 years: 12.5 – 25mg 3 to 4 times a day (max. 150mg/day).

Side effects: See notes above.

Caution: Use with caution in hypertrophy, urinary retention, dry mouth, blurred vision, GIT disturbances, palpitations and Arrhythmias.

7.5 Allergic Emergencies

Adrenaline has the potential to reverse the immediate physiological symptoms associated with hypersensitivity reaction such as anaphylaxis, and angioedema.

Laryngeal oedema, bronchospasms and hypotension in anaphylactic shock require urgent treatment. The major causes of anaphylactic shock are as follows:

- Insect bites and stings such as bees and wasps
- Foods and food additives including eggs, milk protein, nuts, Arachis oil (peanuts),
- Medicinal products such as blood products, vaccines, antibiotics (particularly penicillins), aspirin, chloroquine, iron injections, heparin.

First-aid treatment may be offered on-site by securing the airway, restoration of blood pressure by laying down the patient flat and raising the feet. Adrenaline injection may be administered by i.m in a dose of 0.5-1mg. A dose of 300mg may be appropriate for immediate self-administration. The dose may be repeated until improvement occurs. Oxygen and an antihistamine (chlorpheniramine) may be given as essential adjuncts. If the patient continues to deteriorate, i.v fluids, intravenous aminophylline or nebulised beta-2 agonists should be given.

Furthermore, oxygen and respiratory with an emergency tracheostomy may be required in some situations. Intravenous hydrocortisone 100 -300mg may be necessary to prevent

further deterioration in severe conditions. If there is doubt about the adequacy of the circulations, the initial injection of adrenaline may be given intravenously as a dilute solution. **(See Adrenaline above under 7.1.1.2)**

7.6 Immuno-modulators

7.6.1 Montelukast
7.6.2 Tocilizumab
7.6.3 Baricitinib

MONTELUKAST

Presentation: Tablet containing 10mg of Montelukast

Indications: Prophylaxis in asthma, symptomatic relief of seasonal allergic rhinitis in patients with asthma.

Administration: *Adult and Children 15–17 years*: 10 mg once daily, dose to be taken in the evening

Children:
6 months–5 years: 4 mg once daily, dose to be taken in the evening;
6–14 years: 5 mg once daily, dose to be taken in the evening.

Side effects: Diarrhoea, fever, gastrointestinal discomfort, headache, nausea, skin reactions, upper respiratory tract infection, vomiting.

Caution: Pregnancy, breastfeeding, acute asthma attacks, aspirin sensitivity.

TOCILIZUMAB

Presentation: Injection containing 180mg/ml of Tocilizumab

Indications: Severe Covid-19 infection

Administration: *Adult:* 8 mg/kg, max. per dose 800mg;

Children:
2 years and above (<30kg): 12mg/kg Stat, can be repeated after 8 hours. Maximum of 2 doses.
>30kg: 8 mg/kg, max. per dose 800mg;

Side effects: Abdominal pain, conjunctivitis, cough, gastrointestinal disorders, dizziness, dyslipidemia, dyspnea, hypersensitivity, hypertension, leucopenia, infusion related reactions, peripheral oedema.

Contraindications: Hypersensitivity

Cautions: Neutropenia, hepatic impairment, increased risk of GI perforation, thrombocytopenia.

BARICITINIB

Presentation: Tablet containing 4mg of Baricitinib

Indications: Severe Covid pneumonia

Administration: *Adult:* 4mg once daily for 14 days or until discharge whichever comes first.

Children:
>9years: 4mg once daily for 14 days or until discharge.
2-9years: 2mg once daily for 14 days or until discharge whichever comes first.

Side effects: Increased ALT and AST, thrombocytosis, DVT, pulmonary embolism, UTIs, rhabdomyolysis.

Contraindication: Severe neutropenia and anaemia <8g/dL.

Cautions: Increased risk of developing serious infection, avoid use of live vaccines during treatment, coadministration with other JAK inhibitors; and rifampicin, probenecid, rilpivirine, simvastatin.

7.7 Oxygen

Oxygen is prescribed for hypoxaemic patients to increase alveolar oxygen tension and reduce effort breathing to maintain the necessary arterial oxygen tension. The concentration depends on the condition being treated.

High concentrations of up 60% are necessary for short periods in pneumonia, pulmonary thromboembolism, and fibrosing alveoli. In acute asthmatic attacks, high concentrations of oxygen are necessary. But where blood gas measuring facilities are not available 35% to

50% oxygen concentrations are adequate. In asthmatic patients with a long history of chronic bronchitis and probable respiratory failure, about 24 – 28% may be needed to limit oxygen-induced reduction of respiratory drive.

Oxygen treatment is to provide the patient with just enough oxygen to improve the hypoxaemia without worsening pre-existing carbon-dioxide retention and respiratory acidosis. Only 24 – 28% is reserved for patients with ventilatory failure due to chronic obstructive airway diseases and other causes. Repeated gas administrations should be measured to determine the required correct concentrations.

7.7.1 Intermittent Oxygen Therapy

Oxygen can be given intermittently for hypoxaemia of short duration. For example, asthma, advanced irreversible respiratory disorders (e.g. Chronic obstructive airways disease). It may be supplied as oxygen cylinders. The cylinders can have medium (2 litres/min) or high (4 litres/min) setting. There are special masks, which are preset to deliver a specific percentage of oxygen irrespective of the flocculate and breathing pattern.

7.7.2 Long-term Oxygen therapy

Long- term administration of oxygen for at least 15 hours daily prolongs survival for some patients with chronic obstructive airway disease.

7.8 Cough preparations

7.8.1 Antitussives (Cough suppressants)
7.8.2 Expectorants
7.8.3 Demulcents preparations

A cough is generally a useful reflex which serves to get rid of inhaled foreign bodies or clear the air passages of sputum. Such a cough is described as productive. A cough which is dry and irritating serves no purpose and is called unproductive. In most cases of acute cough, no medicine is needed, unless there is evidence of more serious lower respiratory illness.

Most of the compound preparations on the market contain three or more active ingredients that may sometimes have opposing pharmacological action. They may contain antitussives as well as compounds with expectorant action and anti-muscarinic effects. Such compounds have no place in the treatment of cough.

7.8.1 Cough suppressants

Opioid cough suppressants such as codeine, dextromethorphan and pholcodine are effective in severe cough although they can cause constipation and rarely dependence in some patients. These Medicines are not recommended in children and should be avoided altogether in those under one year.

Sedative antihistamines are used as cough suppressants ingredients and they all tend to cause drowsiness, which may reflect their main mode of action. The use of cough suppressants containing codeine or similar opioid analgesics are not generally recommended in children and should be avoided altogether in those under 1 year of age.

CODEINE PHOSPHATE

Presentation: Linctus containing 15mg/5ml Codeine phosphate. Paediatric preparation containing 3mg/5ml Codeine phosphate.

Indication: Dry painful cough.

Administration: *Adult:* 5 – 10ml 3 to 4 times a day

Children*: but not generally recommended*
1–5 years 5 ml 3 – 4 times a day
5–12 years 2.5 to 5 ml

Side effects: Constipation, respiratory depression sensitive patients or if given in large doses respiratory depression.

Contraindications: Liver disease, ventilatory Failure.

Caution: Asthma, Hepatic and renal impairment, history of drug abuse. See interaction: Appendix 2 (opioid analgesics).

PHOLCODINE

Presentation: Linctus containing Pholcodine 5mg/5ml; paediatric linctus (sugar-free) containing Pholcodine 2mg/5ml.

Indication: Dry irritating and painful cough.

Administration: *Adult:* Linctus 5mg/5ml 5 to 10ml 3 times daily

Children: ***but not generally recommended***
5–12 years: 2.5 to 5ml 3 times daily. Linctus 5mg/5mls, 3 times daily.
Paediatrics Linctus;
1-5 years: 5ml 3 times daily
6-12 years: 5 to 10mls 3 times daily.

Side effects, Caution and contraindication: See under Codeine phosphate

MORPHINE HYDROCHLORIDE

Presentation: Solution containing 10mg/5ml Morphine hydrochloride.

Indication: Distressful cough in terminal disease.

Administration: *Adult:* Initially 5mg every 4 hours.

Side effects: Constipation, sedation, drowsiness, nausea, vomiting, euphoria, tachycardia, bradycardia, palpitations, mental detachment, micturition difficulty, sweating, dry mouth and respiration depression. **Caution:** Drowsiness may affect the performance of skilled tasks, may enhance the effect of alcohol, hypotension, hypothyroidism, asthma (avoid during an attack) elderly and debilitated (reduced dose). **Interactions:** See Appendix (opioid analgesics)

Contraindications: Avoid in acute respiratory depression, acute alcoholism, paralytic ileum, head injury, raised intracranial pressure, avoid injection in pheochromocytoma.

7.8.2 Expectorants

Expectorants supposedly help to expel the bronchial secretions more easily, but there is no evidence to support this myth. They may serve as a simple placebo function for there is no rationale for their use.

AMMONIA AND IPECACUANHA

Presentation: Ammonia and ipecacuanha mixture BP, containing; ammonia bicarbonate 200mg, liquorice liquid extract 0.5ml, ipecacuanha tincture 0.3ml, conc. Camphor water 0.1ml conc. Anise water 0.05ml, double-strength chloroform water 5ml, water to 10ml. (Reserve for hospital use as it should be freshly prepared extemporaneously)

Indication: Productive cough.

Administration: 10-20ml 3-4 times a day.

Caution and side effects: May cause nausea, vomiting.

GUAIPHENESIN, PSEUDOEPHEDRINE, TRIPROLIDINE

7.8.3 Demulcent preparations

These preparations have soothing preparations believed to have the relieving effect of dry irritating cough. They contain substances such as syrup and glycerol that are harmless and inexpensive.

SIMPLE LINCTUS

Presentation: Simple linctus BP containing Citric acid monohydrate 2.5% in a suitable vehicle (with anise flavour). Simple linctus paediatric BP containing; contain citric acid monohydrate

0.625% in a suitable vehicle with anise flavour
Indication: Productive cough.

Administration: *Adult;* 5 ml 3 – 4 times a day

Children: 5 – 10ml 3 – 4 times a day.

7.9 Nasal decongestants

There is little evidence whether these preparations have value. However, they do not cause rebound nasal congestion. They contain sympathomimetic and produce constriction of other blood vessels in the body and cause a rise in blood pressure. They are best avoided in patients with hypertension, hyperthyroidism, coronary heart disease and patients taking monoamine-oxidase inhibitors; many preparations also contain antihistamines, which may cause drowsiness and affect the ability to drive and maintain alertness.

PSEUDOEPHEDRINE

Presentation: Tablets containing 60mg Pseudoephedrine hydrochloride. Linctus/ elixir containing 30mg/5ml Pseudoephedrine hydrochloride

Indication: Nasal congestion

Administration: 1 tablet 4 times a day; 10ml 3 times a day.

Children:
2-6 years; 2.5ml 3-4 times daily
6-12years 5ml 4 times daily.

Caution: Use with caution in diabetics, hypertension, hyperthyroidism, ischaemic heart disease *and patients taking monoamine oxidase inhibitor.*

Side effects: See under ephedrine, may cause rare incidences of visual hallucination in children. **Interactions:** See Appendix (sympathomimetics)

7.10 Mucolytics

Mucolytics reduce sputum viscosity and may be of some benefit in patients with chronic obstructive pulmonary disease.

ACETYLCYSTEINE

Presentation: Effervescent tablet containing 200-600mg of Acetylcysteine.

Indications: Reduction of sputum viscosity in pulmonary disease**.**

Administration: *Adult:* 600mg once daily.

Children:
6-12years: 200mg once daily

Side effects: Diarrhea, fever, vomiting, stomatitis, hypotension, tinnitus, nausea.

Contraindications: Acute asthma, hypersensitivity.

Cautions: History of peptic ulceration.

7.11 Aromatic inhalations

Inhalations containing volatile substances like eucalyptus oil encourage deliberate inspiration of warm moist air, which is often comforting in bronchitis.

In children, the use of strong aromatic decongestants is not advised under the use of 3 months. The mother should, however, be advised on alternative methods of socking mucus from the nostrils.

MENTHOL AND EUCALYPTUS INHALATION

Inhalation capsules, Levomenthol 35.55mg with chlorobutanol, pine oils, terpineol and thymol. Inhalation, racementhol or levomenthol 2g, eucalyptus oil 10ml, light magnesium carbonate 7g, water to 100ml.

Administration: Check instructions on the manufactures advise.

8 Medicines used in the treatment of diseases of the cardiovascular system

8.1 Anti-hypertensives

Antihypertensives belong to one of four types; Diuretics, vasodilators, beta-blockers and centrally acting Medicines. Use the drug from one group to the maximum dosage before adding another one unless side effects are intolerable. The added drug must be from another group, preferably in a fixed dose combination to reduce on pill burden.

8.1.1 Diuretics

Diuretics are used in fluid retention resulting from cardiac, renal or hepatic failure. They cause electrolyte loss, especially potassium and sodium in addition to water. They should not be used in conditions like kwashiorkor. Different types are available and their potency varies according to the site of action.

8.1.1.1 Thiazide diuretics

Thiazides act at the beginning of the distal convoluted tubule and are moderately potent diuretics. Small doses of thiazides in combination with other antihypertensives are used in hypertension.

HYDROCHLOROTHIAZIDE

Presentation: Tablet containing 25mg, 50mg Hydrochlorothiazide.

Indications: Oedema, hypertension, heart failure, Nephrogenic diabetes insipidus.

Administration: *Adult, oedema*; initially 12.5 – 100mg daily, maintenance 25 – 50mg on alternate days. *Hypertension*; 25mg daily which can be increased to 100mg daily if necessary.

Children

Oedema,

Infant under 6 months: 2–3.3 mg/kg daily in two divided doses; maximum dose 37.5 mg daily

over 6 months: 2 mg/kg daily in two divided doses; maximum dose 200 mg daily.

Hypertension, oral,

Child all ages: Initially 1 mg/kg once daily; may increase to a maximum 3 mg/kg daily (maximum 50 mg daily).

Side effects: Hypokalaemia, hypercalcaemia and other electrolyte imbalance, hyperglycemia, hyperuricemia, photosensitisation, hypotension.

Contraindications: Severe renal and hepatic impairment, hypercalcaemia.

Caution: Avoid in diabetes and gout, hypercalcaemia

METALOZONE

Presentation: Tablet containing 5mg Metolazone

Indications: Oedema, Hypertension

Administration: *Oedema*, 5 – 10mg in the morning daily.

Resistant oedema 20mg daily, max 80mg daily. *Hypertension*: 5mg daily, maintenance 5mg on alternate days.

Side effects: See hydrochlorothiazide above.

Contraindications: See hydrochlorothiazide above. **Caution:** See hydrochlorothiazide above.

8.1.1.2 Loop Diuretics

These inhibit reabsorption from the ascending loop of Henle in the renal tubule and are powerful diuretics. Hypokalaemia frequently develops and care should be taken to avoid hypotension.

FRUSEMIDE

Presentation*:* Tablet containing 20mg, 40mg Frusemide. Injection containing 10mg/ml Frusemide.

Indications: Oedema, oliguria due to renal failure.

Administration: *Adult,*

Oedema; *orally* initially 40mg in the morning; maintenance 20mg daily or 40mg on alternate days, increased in resistant oedema to 80mg daily.

Oliguria, *orally* 250mg daily initially, increasing by steps of 250mg to a maximum of a single daily dose of 2g. *By intravenous infusion*; initially 250mg over 1 hour (rate not exceeding 4mg/minute). If satisfactory urine output is not obtained in the subsequent 1 hour, a further 500mg over 2 hours, if no satisfactory response within the subsequent 1 hour, a further 1g over 4 hours can be given, if no satisfactory response is obtained, dialysis is probably required.

Children:
Oedema: 1–3mg/kg body weight daily.
***Oliguria*:** orally; 0.5–1.5mg/kg body weight to a maximum daily dose of 20mg. *By intramuscular or slow intravenous injection*, initially 20–50mg.

Side effects: Hypokalaemia, fluid depletion, electrolyte imbalance, metabolic alkalosis, hyperuricemia, hyperglycemia, hypotension.

Caution: Pregnancy, liver failure, aggravates diabetes and gout.

TORASEMIDE

Presentation: Tablet containing 5mg and 10mg of Torasemide

Indications: Oedema and hypertension

Administration: ***Oedema*** *Adult:* 5 mg once daily, to be taken preferably in the morning, then increased if necessary to 20 mg once daily; maximum 40 mg per day

Hypertension Adult: 2.5 mg daily, then increased if necessary to 5 mg once daily

Side effects: Excessive urination, headache, electrolyte imbalance, dizziness, constipation, nausea, dyspepsia, asthenia.

Contraindications: Anuria, hepatic coma, hypersensitivity.

Cautions: In diabetes mellitus, electrolyte imbalance, gout, hyperlipidemia, cirrhosis.

8.1.1.3 Potassium Sparing Diuretics

SPIRONOLACTONE

Presentation: Tablet containing 25mg, 50mg and 100mg of Spironolactone; Oral suspension containing 5mg/ml.

Indications: Refractory oedema in congestive heart failure, adjunct to ACEI and a loop or thiazide diuretic in severe congestive heart failure, nephrotic syndrome, hepatic cirrhosis with ascites and oedema, ascites associated with malignancy, primary hyperaldosteronism.

Administration: ***Adult*** oral;

Oedema, oral: 100–200 mg daily, increase if necessary to 400 mg daily in resistant oedema; usual maintenance dose, 25–200 mg daily.

Primary hyperaldosteronism: 100-400 mg daily for 3–4 weeks

Preoperative management: 100–400 mg daily, if not suitable for surgery, give the lowest effective dose for long-term maintenance

Adjunct in severe heart failure: usually 25 mg daily.

Children:
Oedema: Initially 1–3 mg/kg daily in 1–2 divided doses

Side effects: Hyperkalaemia, hyponatraemia, hyperchloraemic acidosis, dehydration (for symptoms of fluid and electrolyte imbalance, transient increase in blood urea nitrogen, diarrhoea, gynaecomastia, menstrual irregularities, impotence, hirsutism, deepening of voice, rash, ataxia, fever, hepatotoxicity.

Contraindications: Hyperkalaemia, hyponatraemia, moderate renal impairment, Addison disease, coadministration with Eplerenone.

Cautions: Monitor blood urea nitrogen and plasma electrolytes (discontinue if hyperkalaemia), the elderly (reduce dose), diabetes mellitus, porphyria, monitor high doses.

EPLERENONE

Presentation: Tablet containing 25mg and 50mg of Eplerenone

Indications: Adjunct patients with left ventricular ejection fraction <40% evidence of heart failure, following myocardial infarction within 3-14days of event, Adjunct in chronic mild heart failure with left ventricular ejection fraction <30%

Administration: *Post-MI:* Start with 25 mg daily, then increased to 50 mg daily, increased within 4 weeks of initial treatment.

In chronic mild heart failure with left ventricular ejection fraction <30%: Start with 25 mg daily, then increased to 50 mg daily, increased within 4 weeks of initial treatment.

Contraindications: Serum potassium of >5.5mEq/L at initiation, creatinine clearance of ≤30ml/min, concormitant use with strong CYP3A inhibitors. Hypersensitivity to spironolactone

Cautions: Hyperkalemia, liver dysfunction, renal impairment, metabolic or respiratory acidosis.

AMILORIDE WITH HYDROCHLOROTHIAZIDE

Presentation: Tablet containing 5mg Amiloride hydrochloride and 50mg Hydrochlorothiazide
Indications: Oedema and mild hypertension

Administration: 1 – 4 tablets daily in two divided doses.

Side effects: See under Hydrochlorothiazide. Also, dry mouth, hypotension.

Contraindications: Diabetes mellitus, hyperuricemia.

Caution: May precipitate diabetes mellitus and gout, do not give potassium supplements.

8.1.1.4 Osmotic Diuretics

MANNITOL

Presentation: Intravenous infusion containing 10%, 20% solution, 500ml.

Indications: Fluid retention, cerebral oedema and induction of forced diuresis.

Administration: 50-200g over 24 hours, preceded by a test 200mg/kg body weight by slow intravenous injection.

Side effects: Chills, fever, fluid depletion, hypotension.

Caution: IV solution should be kept at room temperature.

Contraindication: Dehydration, congestive heart failure.

8.1.2 Angiotensin Converting Enzyme Inhibitors (ACEIs)

ENALAPRIL

Presentation: Tablet (scored), containing 5 mg, 10 mg, 20 mg of Enalapril as hydrogen maleate.

Indications: Hypertension, Heart failure and prevention of symptomatic heart failure in patients with asymptomatic left ventricular dysfunction

Administration: ***Adults***

Hypertension: Initially 5 mg once daily, lower if used in addition to a diuretic or in renal impairment; give first dose at bedtime; increase if necessary; usual maintenance dose 20 mg once daily; maximum 40 mg once daily.

Heart failure and prevention of symptomatic heart failure in patients with asymptomatic left ventricular dysfunction: Initially 2.5 mg daily under close medical supervision, increased over 2–4 weeks to usual maintenance dose of 20 mg daily, either as a single dose or in 2 divided doses; maximum 40 mg daily.

Children:

Hypertension and heart failure, oral

Neonate: Initially 10 mcg/kg once daily, increased as necessary up to 500 mcg/kg daily in 1–3 divided doses; monitor blood pressure and urine output carefully for at least 2 hours following first dose and during dose escalation until blood pressure is stable.

1 month–11 years (under expert supervision): Initially 100 mcg/kg once daily, monitor blood pressure carefully for 1–2 hours, then increase if necessary up to 1 mg/kg daily in 1–2 divided doses

12–17 years (under expert supervision) (body weight up to 50 kg): Initially 2.5 mg once daily, monitor blood pressure carefully for 1–2 hours, maintenance 10–20 mg daily in 1–2 divided doses.

12–17 years (under expert supervision) (body weight 50 kg and above): Initially 2.5 mg once daily, monitor blood pressure carefully for 1–2 hours, maintenance 10–20 mg daily in 1–2 divided doses, maximum 40 mg.

Side effects: Dizziness, headache, less commonly, nausea, hypotension (severe in rare cases), dry cough, fatigue, asthenia, muscle cramps, rash, and renal impairment, GI disturbance, peptic ulcer, glossitis, stomatitis, ileus, pancreatitis, liver damage, chest pain, palpitations, arrhythmias, Raynaud syndrome, angioedema, bronchospasm, rhinorrhoea, dry mouth, sore throat, pulmonary infiltrates, paraesthesia, vertigo, nervousness, depression, confusion, drowsiness, insomnia, dream abnormalities, pruritus, urticaria, alopecia, flushing, impotence, gynaecomastia, SJS, toxic epidermal necrolysis, exfoliative dermatitis, pemphigus, tinnitus, and blurred vision, electrolyte disturbances and hypersensitivity-like reactions (including fever, myalgia, arthralgia, eosinophilia, and photosensitivity), hypoglycaemia

Contraindications: hypersensitivity to ACEIs (including angioedema), renovascular disease, pregnancy.

Cautions: concomitant use of diuretics (initiate at low dose and monitor closely), hypotension with first doses, especially in patients on diuretics, on a low-sodium diet, on dialysis, if dehydrated, or with heart failure, peripheral vascular disease or generalized atherosclerosis (risk of clinically silent renovascular disease), severe or symptomatic aortic stenosis (use with great care), possibly increased risk of agranulocytosis in collagen vascular disease, history of idiopathic or hereditary angioedema (use with care or avoid).

CAPTOPRIL

Presentation: Tablet containing 12.5mg, 25mg, 50mg captopril

Indications: Alone or in combination with thiazides in essential hypertension, adjunct in heart failure.

Administration: *Hypertension;* Used alone, initially 12.5mg twice daily, if used in addition to diuretic, in the elderly and renal impairment, initially 6.25mg twice daily. Usual maintenance dose is 25mg twice daily to a maximum of 50mg twice daily (rarely up to 3 times daily in severe hypertension).

Side effects: Hypotension, dizziness, dry cough, voice changes, throat discomfort, fatigue, headache, gastrointestinal disturbances, renal impairment, hypersensitivity reactions, blood disorders.

Caution: May cause profound hypotension at induction, monitor renal function before and during treatment, reduce dose in renal impairment, breastfeeding. Monitor for possible hyperkalemia.

Contraindications: Hypersensitivity to ACE inhibitors, aortic stenosis, or left ventricle outflow tract obstruction, pregnancy, porphyria.

LISINOPRIL

Presentation: Tablet 2.5mg, 10mg, 20mg containing lisinopril.

Indications: Hypertension, heart failure, diabetic nephropathy, prophylaxis after myocardial infarction.

Administration: *Hypertension,* initially 2.5mg daily, usual maintenance dose 10-20mg daily; max 40mg daily, heart failure (adjunct), initially 2,5mg daily, usual maintenance dose 5-20mg daily.

Prophylaxis after myocardial infarction: 2.5 – 10mg daily.

Diabetic nephropathy 2.5 – 10mg daily

Side effects: See Captopril

Contraindications: See Captopril.

Caution: See Captopril

8.1.3 Angiotensin-Receptor Blockers

LOSARTAN

Presentation: Tablet (scored) containing 25mg, 50 mg, and 100mg of Losartan

Indications: Hypertension, chronic heart failure, diabetic nephropathy in type 2 diabetes.

Administration: *Adult*

Hypertension, oral: Initially 25mg once daily for several weeks, then increase if necessary to a maximum of 100mg once daily.

Chronic heart failure when ACEIs are unsuitable or contraindicated, oral: Initially 12.5 mg once daily, increase if tolerated up to 150 mg once daily; doses to be increased at weekly intervals

Diabetic nephropathy in type 2 diabetes mellitus, oral 18–75 years: Initially 50 mg once daily for several weeks, then increase if necessary to 100mg once daily; 76 years and over: Initially 25 mg once daily for several weeks, then increase if necessary to 100mg once daily

Children

Hypertension

6–17 years (under expert supervision) *(body weight 20–49 kg)*: Initially 700 mcg/kg once daily (max. per dose 25 mg), adjusted according to response to 50 mg daily, lower initial dose may be used in intravascular volume depletion, maximum 50 mg per day

6–17 years (under expert supervision) *(body weight 50 kg and above):* Initially 50 mg once daily, adjusted according to response to 1.4 mg/kg once daily, maximum 100 mg per day.

Side effects: Hypoglycaemia, dizziness, vertigo, hyperkalaemia, hypotension, dyspnoea, cough, liver disorder, hypersensitivity, depression, malaise, urinary tract infection, renal impairment.

Contraindications: Hypersensitivity to the active substance or to any of the excipients, in pregnancy, Severe hepatic impairment, electrolyte imbalance.

Cautions: Severe heart failure, aortic or mitral stenosis, or obstructive hypertrophic cardiomyopathy.

TELMISARTAN

Presentation: Tablet containing 40 mg, 80 mg of Telmisartan.

Indications: Hypertension, Prevention of cardiovascular events in patients with established atherosclerotic cardiovascular disease or type 2 diabetes mellitus with target-organ damage.

Administration: *Adult*

Hypertension, oral: Initially 20–40 mg once daily for at least 4 weeks, increased if necessary up to 80 mg once daily

Prevention of cardiovascular events in patients with established atherosclerotic cardiovascular disease or type 2 diabetes mellitus with target-organ damage- oral: 80 mg once daily.

Children:
No or insufficient experience in children and adolescents, therefore its use is not recommended.

Side effects: See Losartan above.

Contraindications: Hypersensitivity to the active substance or to any of the excipients, in pregnancy, Biliary obstructive disorders, cholestasis, Severe hepatic impairment.

Cautions: Electrolyte imbalance, Aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy.

8.1.4 Centrally Acting

METHYLDOPA

Presentation: Tablet containing 250mg and 500mg of Methyldopa.

Indications: Hypertensive disorders in pregnancy.

Administration: *Adult:* oral: Initially 250 mg 2–3 times daily, gradually increased at intervals of 2 or more days, if necessary; maximum 3 g daily.

Children:
No or insufficient experience in children and adolescents, therefore its use is not recommended.

Side effects: sedation, dizziness, lightheadedness, postural hypotension, weakness, fatigue, headache, fluid retention and oedema, sexual dysfunction, impaired concentration and memory, depression, mild psychosis, disturbed sleep and nightmares, drug fever, influenza-like syndrome, nausea, vomiting, constipation, diarrhoea, dry mouth, stomatitis, sialadenitis, liver function impairment, hepatitis, jaundice, rarely fatal hepatic necrosis, bone marrow depression, haemolytic anaemia, leukopenia, thrombocytopenia, eosinophilia, parkinsonism, rash including toxic epidermal necrolysis, nasal congestion, black or sore tongue, bradycardia, exacerbation of angina, myalgia, arthralgia, paraesthesia, Bell palsy, pancreatitis, hypersensitivity reactions including lupus erythematosus-like syndrome, myocarditis, pericarditis, gynaecomastia, hyperprolactinaemia.

Contraindications: depression, active liver disease,

phaeochromocytoma, porphyria.

Cautions: blood counts and liver-function tests advised, history of depression, positive direct Coomb test in up to 20% of patients (affects blood crossmatching), interference with laboratory tests. May impair ability to perform skilled tasks, for example, operating machinery or driving.

8.1.5 Vasodilators

HYDRALAZINE

Presentation: Tablet containing 25mg, 50mg Hydralazine hydrochloride. An injection containing 20mg/2ml Hydralazine hydrochloride.

Indications: Adjunct (orally) to other antihypertensives like beta-blockers, thiazides, in the treatment of moderate to severe hypertension. Hypertension emergency (intravenous injection), severe hypertension in Pregnancy (with a diastolic BP of ≥110mmHg).

Administration: *Oral*; 25mg twice daily, increased to a maximum of 50mg twice daily

By slow intravenous injection; 5 – 10mg over 5 minutes, maybe repeated after 20 – 30 minutes.

By intravenous infusion; initially 200 – 300 mcg/minute, maintainance usually 50 – 150mcg per minute.

Children:

Resistant hypertension (adjunct), oral

Neonate: 250 to 500 mcgs/kg every 8 to 12 hours, increase if necessary to a maximum of 2 to 3mg/kg every 8 hours

1 month–11 years: 7.5 mg/kg (maximum 200 mg) daily

12 years and over: Use adult dose

Resistant hypertension (adjunct), slow IV injection

Neonate to child 11 years: 100 to 500 mcg/kg, repeated every 4 to 6 hours as necessary (maximum 3 mg/kg or 60 mg daily).

12 years and over: 5 to 10 mg, repeated every 4 - 6 hours as necessary

Resistant hypertension (adjunct), continuous IV infusion (preferred route in cardiac patients)

Neonate: 12.5 to 50 mcg/kg per hour, to a maximum of 2 mg/kg daily

1 month to 11 years: 3 mg/kg daily

12 years and over: 3 to 9 mg/hour (maximum 3 mg/kg daily)

Side effects: Tachycardia, nausea and vomiting, fluid retention, headache, systemic lupus erythematosus like syndrome after prolonged treatment with over 100mg daily.

Caution: Reduce initial dose in renal impairment, coronary heart disease, over rapid blood pressure reduction is occasionally encountered even with low parenteral doses, pregnancy and breastfeeding.

Contraindications: Severe tachycardia, myocardial insufficiency due to a mechanical obstruction, porphyria, idiopathic systemic lupus erythematosus.

BOSENTAN

Presentation: Tablet containing 62.5mg and 125mg of Bosentan

Indications: Pulmonary arterial hypertension

Administration: Adult- ***Pulmonary arterial hypertension*** (initiated under specialist supervision):

> *40kg*: Start 62.5mg twice daily for 4 weeks, then increased to 125 mg twice daily (max. per dose 250 mg); maximum 500 mg per day.

<*40 kg:* Maintain dose at 62.5 mg twice daily. Discontinuation of treatment: Consider a reduction in dosage to 62.5 mg twice daily for 3-7 days.

Children:

12 years of age and weighs less than 40Kg: 62.5 mg two times a day.

Below 12 years of age: Dose is based on body weight and must be determined by a specialist.

Contraindications: Pregnancy, hypersensitivity, concomitant cyclosporine or glyburide use, acute liver failure or decompesated cirrhosis.

Cautions: Dose-related decrease in hemoglobin and hematocrit may occur with treatment; it is recommended that hemoglobin concentrations be checked regularly.

SILDENAFIL

Presentation: Tablet containing 50mg and 100mg of Sildenafil

Indications: Pulmonary arterial hypertension, erectile dysfunction

Administration: Adult

Pulmonary arterial hypertension, oral: 25mg 3 times a day

Children:

Pulmonary artery hypertension*, oral*

Neonate: Initially 250–500 mcg/kg every 4–8 hours, adjusted according to response; start with the lower dose and frequency, especially if used with other vasodilators; maximum 30 mg per day

1–11 months: Initially 250–500 mcg/kg every 4–8 hours, adjusted according to response; start with the lower dose and frequency, especially if used with other vasodilators; maximum 30 mg per day.

1–17 years (body weight up to 20 kg): 10 mg 3 times a day

1–17 years (body weight 20 kg and above): 20 mg 3 times a day

Contraindications: Hereditary degenerative retinal disorder. History of non-arteritic anterior ischaemic optic neuropathy, recent history of MI, recent history of stroke, sickle-cell anaemia.

Cautions: Active peptic ulceration, anatomical deformation of the penis (e.g., angulation, cavernosal fibrosis, Peyronie's disease). Autonomic dysfunction, bleeding disorders, cardiovascular disease, hypotension (avoid if severe). Intravascular volume depletion. Left ventricular outflow obstruction, predisposition to priapism (e.g., in sickle-cell disease, multiple myeloma, or leukaemia). Pulmonary veno-occlusive disease. Avoid abrupt withdrawal.

PRAZOSIN

Presentation: Capsule containing 500mcg, 1 mg, 2mg and 5mg of Prazosin.

Indications: Hypertension secondary to pheochromocytoma, Congestive heart failure (rarely used), Benign prostatic hyperplasia.

Administration: **Adult-** ***Hypertension****, oral:* Initially 500 mcg 2–3 times a day for 3–7 days; initial dose should be taken on retiring to bed at night to avoid collapse, increased to 1 mg 2–3 times a day for a further 3–7 days, then increased if necessary up to 20 mg daily in divided doses

Congestive heart failure (rarely used), *oral:* 500 mcg 2–4 times a day, initial dose to be taken at bedtime, then increased to 4 mg daily in divided doses; maintenance 4–20 mg daily in divided doses

Benign prostatic hyperplasia*, oral:* Initially 500 mcg twice daily for 3–7 days; subsequent doses should be adjusted according to response; maintenance 2 mg twice daily

Elderly: Initiate with lowest possible dose

Children:

Hypertension, *oral*

1 month–11 years: Initially 10–15 mcg/kg 2–4 times a day, initial dose to be taken at bedtime, then increased to 500 mcg/kg daily in divided doses, dose to be increased gradually, maximum 20 mg per day

12–17 years: Initially 500 mcg 2–3 times a day for 3–7 days, initial dose to be taken at bedtime, then increased to 1 mg 2–3 times a day for a further 3–7 days, then increased if necessary up to 20 mg daily in divided doses, dose should be increased gradually.

Congestive heart failure (rarely used), *oral*

1 month–11 years: 5 mcg/kg twice daily, initial dose to be taken at bedtime, then increased to 100 mcg/kg daily in divided doses, doses should be increased gradually.

Side effects: Asthenia, constipation, depression, diarrhoea, dizziness, drowsiness, dry mouth, dyspnoea, headache, nasal congestion, nausea, nervousness, oedema, palpitations, postural hypotension, sexual dysfunction, skin reactions, syncope, urinary disorders, vertigo, vision blurred, vomiting, hepatic dysfunction, pancreatitis.

Contraindications: History of micturition syncope (in patients with benign prostatic hyperplasia), history of postural hypotension, not recommended for congestive heart failure due to mechanical obstruction (e.g., aortic stenosis).

Cautions: Cataract surgery (risk of intra-operative floppy iris syndrome), elderly, first dose hypotension.

MAGNESIUM SULPHATE

Indications: Pre-eclampsia and Eclampsia.

For Administration, Side Effects, Contraindications and Cautions - See myometrial relaxants

SACUBITRIL + VALSARTAN

Presentation: Tablet containing 24 mg + 26 mg, 49 mg + 51 mg of Sacubitril+Valsartan.

Indications: Symptomatic chronic heart failure with reduced ejection fraction

Administration: ***Adult***

Symptomatic chronic heart failure with reduced ejection fraction (in patients not currently taking an ACEI or angiotensin II receptor antagonist or stabilised on low doses of either of these agents), *oral:* Initially 24/26 mg twice daily for 3–4 weeks, increased if tolerated to 49/51 mg twice daily for 3–4 weeks, then increased if tolerated to 97/103 mg twice daily

Symptomatic chronic heart failure with reduced ejection fraction (in patients currently stabilised on an ACEI or angiotensin II receptor antagonist), *oral:* Initially 49/51mg twice daily for 2–4 weeks, increased if tolerated to 97/103 mg twice daily; consider a starting dose of 24/26mg if systolic blood pressure less than 110 mmHg.

Children:
Safety and efficacy of sacubitril + valsartan in children and adolescents below 18 years have not been established. No data are available.

Side effects: Anaemia, asthenia, cough, diarrhoea, dizziness, electrolyte imbalance, gastritis, headache, hypoglycaemia, hypotension, nausea, renal impairment, syncope, vertigo.

Contraindication: Concomitant use with an ACEI (do not initiate until at least 36 hours after discontinuing ACEI—risk of angioedema), concomitant use with an angiotensin II receptor blocker (ARB), systolic blood pressure less than 100 mmHg, serum potassium level >5.4 mmol/L, hypersensitivity to the active ingredients of any of the excipients, history of angioedema related to ACEI of ARB therapy, hereditary angioedema, severe hepatic impairment, biliary cirrhosis and cholestasis, 2nd and 3rd trimester of pregnancy.

Cautions: Renal artery stenosis (monitoring of renal function is recommended) and patients with New York Heart Association functional classification IV due to limited clinical experience in this population. Psychiatric events such as hallucinations, paranoia and sleep disorders, in context of psychotic events, have been associated with sacubitril/valsartan use. If a patient experiences such events, discontinuation of sacubitril/valsartan treatment should be considered.

8.2 Anti-arrhythmic Medicines

Beta-adrenoceptor blocking medicines (beta-blockers) block the beta-adrenoceptors in the heart, peripheral vasculature, bronchi, pancreas, and liver. Many beta-blockers are now available and in general, they are all equally effective. There are, however, differences between them which may affect choice in treating particular diseases or individual patients.

Intrinsic sympathomimetic activity (ISA, partial agonist activity) represents the capacity of beta-blockers to stimulate as well as to block adrenergic receptors.

Beta-blockers with a relatively short duration of action have to be given two or three times daily. Many of these are, however, available in modified-release formulations so that administration once daily is adequate for hypertension.

For angina twice-daily treatment may sometimes be needed even with a modified-release formulation. Some beta-blockers such as atenolol and carvedilol, have an intrinsically longer duration of action and need to be given only once daily.

Beta-blockers slow the heart and can depress the myocardium; they are contraindicated in

patients with second- or third-degree heart block. Beta-blockers should also be avoided in patients with worsening unstable heart failure; care is required when initiating beta-blocker in those with stable heart failure. (important: particular care is required to avoid hypokalaemia in patients taking sotalol). Carvedilol has, also, an arteriolar vasodilating action, by diverse mechanisms, and thus lower peripheral resistance.

Beta-blockers can precipitate asthma and this effect can be dangerous. Beta-blockers should be avoided in patients with a history of asthma or bronchospasm; if there is no alternative, a cardioselective beta-blocker can be used with extreme caution under specialist supervision. Atenolol and metoprolol, have less effect on the beta (bronchial) receptors and are, therefore, relatively cardioselective, but they are not cardio specific.

Beta-blockers are also associated with fatigue, the coldness of the extremities and sleep disturbances with nightmares (may be less common with the water-soluble beta-blockers, Beta-blockers are not contraindicated in diabetes; however, they can lead to a small deterioration of glucose tolerance and interfere with metabolic and autonomic responses to hypoglycaemia.

Cardioselective beta-blockers may be preferable and beta-blockers should be avoided altogether in those with frequent episodes of hypoglycaemia. Beta-blockers, especially when combined with a thiazide diuretic, should be avoided for the routine treatment of uncomplicated hypertension in patients with diabetes or in those at high risk of developing diabetes.

IVABRADIN

Presentation: Tablet (scored) containing 5 mg, 7.5 mg of Ivabradin.

Indications: Angina in patients in normal sinus rhythm; Mild to severe chronic heart failure.

Administration: ***Adult***

Angina in patients in normal sinus rhythm, oral: Initially 2.5–5 mg twice daily for 3–4 weeks, then increase if necessary up to 7.5 mg twice daily, dose to be increased gradually, reduced if not tolerated to 2.5–5 mg twice daily; heart rate at rest should not be allowed to fall below 50 beats per minute; discontinue treatment if no improvement in symptoms within 3 months.

Mild to severe chronic heart failure, oral: Initially 5 mg twice daily for 2 weeks, then increase if necessary to 7.5 mg twice daily, reduced if not tolerated to 2.5–5 mg twice daily; heart rate at rest should not be allowed to fall below 50 beats per minute.

Children:
No or insufficient experience in children and adolescents, therefore its use is not recommended.

Side effects: Arrhythmias, atrioventricular block, dizziness, headache, hypertension, vision disorders, pain, angioedema, constipation, diarrhoea, eosinophilia, hyperuricaemia, hypotension, muscle cramps, nausea, QT interval prolongation, skin reactions, syncope, vertigo.

Contraindications: Acute decompesated heart failure and MI, cardiogenic shock, congenital QT syndrome, do not initiate for angina if heart rate below 70 beats per minute, do not initiate for chronic heart failure if heart rate below 75b/min, immediately after cerebrovascular accident, patients dependent on pacemaker, second- and thirddegree heart block, severe hypotension, sick-sinus, syndrome, sino-atrial block, unstable angina, unstable or acute heart failure.

Cautions: Atrial fibrillation or other arrhythmias (treatment ineffective), elderly, in angina, consider stopping if there is no or limited symptom improvement after 3 months, intraventricular conduction defects, mild to moderate hypotension (avoid if severe), retinitis pigmentosa.

AMIODARONE HYDROCHLORIDE

Presentation: Tablet containing 100mg Amiodarone hydrochloride, injection containing 50mg/ml amiodorane hydrochloride

Indication: Paroxysmal supraventricular Tachycardia, nodal and ventricular tachycardias, atrial fibrillation/ flutter, ventricular fibrillation.

Administration: *Oral* 200mg 3 times daily for a week, reduced to 200mg twice daily for a further week; maintenance usually 100-200mg daily to control arrhythmia.

Intravenous infusion via the venal catheter, 5mg/kg over 20 – 120 minutes with ECG monitoring; maximum 1.2g in 24 hours.

Side effects: Reversible corneal microdeposits, peripheral neuropathy and myopathy, thyroid dysfunction, diffuse pulmonary alveolitis, pneumonitis, lung fibrosis, jaundice, hepatitis, cirrhosis, phototoxicity, nausea, vomiting, nightmares, tremors, fatigue, alopecia impotence, haematological disorders, ataxia hypersensitivity.

Caution: Should be initiated in hospital or under specialist supervision. Chest x-ray, Liver function and thyroid function tests required before treatment and then every 6 months. Heart failure, renal impairment, elderly, severe bradycardia and conduction disturbances, porphyria.

ADENOSINE

Presentation: Injection containing 6mg/2ml and 12mg/4ml of Adenosine.

Indications: Rapid reversal of paroxysmal supraventricular tachycardias

Administration: ***Adult***

Rapid reversal of paroxysmal supraventricular tachycardias to sinus rhythm, including those associated with accessory conducting pathways (e.g., Wolff-Parkinson-White syndrome); used to aid diagnosis of broad or narrow, complex supraventricular tachycardias, by rapid IV injection

Patients without heart transplant (cardiac monitoring required): Initially 6 mg, administer into central or large peripheral vein and give over 2 seconds followed by rapid saline flush, followed by 12 mg after 1–2 minutes if required, then 12 mg after 1–2 minutes if required; increments should not be given if high-level AV block develops at any particular dose

Patients with a heart transplant: Initially 3 mg, administer into a central or large peripheral vein and give over 2 seconds then give a rapid saline flush, followed by 6 mg after 1–2 minutes if required, then 12 mg after 1–2 minutes if required; patients with a heart transplant are very sensitive to the effects of adenosine.

Children:

Termination of supraventricular tachycardias, including those associated with accessory conducting pathways; diagnosis of supraventricular arrhythmias, by rapid IV injection

Neonate: Initially 150 mcg/kg, then increased in steps of 50–100 mcg/kg every 1–2 minutes (max. per dose 300 mcg/kg) if required; dose to be repeated until tachycardia terminated, or maximum single dose given.

1–11 months: Initially 150 mcg/kg, then increased in steps of 50–100 mcg/kg every 1–2 minutes (max. per dose 500 mcg/kg) if required; dose to be repeated until tachycardia terminated, or maximum single dose given

1–11 years: Initially 100 mcg/kg, then increased in steps of 50–100 mcg/kg every 1–2 minutes (max. per dose 12 mg) if required; dose to be repeated until tachycardia terminated, or maximum single dose given.

12–17 years: Initially 3 mg, followed by 6 mg after 1–2 minutes if required, followed by 12 mg after 1–2 minutes if required; in some children over 12 years, 3 mg dose ineffective (e.g., if a small peripheral vein is used for administration) and higher initial dose sometimes used, however, those with heart transplant are very sensitive to

the effects of adenosine and should not receive higher initial doses.

Side effects: Abdominal discomfort, arrhythmias, atrioventricular block, chest discomfort, chest pain (discontinue), dizziness, dry mouth, dyspnoea, flushing, headache, hypotension (discontinue if severe), pain, paraesthesia, throat discomfort.

Contraindications: Asthma, chronic obstructive lung disease, decompensated heart failure, long QT syndrome, second- or third-degree AV block and sick sinus syndrome (Unless pacemaker fitted), severe hypotension, known hypersensitivity to adenosine or to any of the excipients, concomitant administration of adenosine with dipyridamole (if this combination must be used then the dose of adenosine should be greatly reduced).

Cautions: used with caution in patients with left main coronary stenosis, uncorrected hypovolemia, stenotic valvular heart disease, left to right shunt, pericarditis or pericardial effusion, QT-interval prolongation, autonomic dysfunction or stenotic carotid artery disease with cerebrovascular insufficiency, recent MI, severe heart failure, or in patients with minor conduction defects (first degree A-V block, bundle branch block), atrial fibrillation or flutter and especially in those with an accessory by-pass tract. Dose should be reduced in patients with heart transplant.

ATROPINE

Presentation: Injection containing 1 mg (as sulphate) in 1-ml amp

Indications: Symptomatic bradycardia due to acute over dosage of beta-blockers, Intra-operative bradycardia, Excessive bradycardia associated with beta-blocker use, Bradycardia following myocardial infarction (particularly

if complicated by hypotension)

Administration: ***Adults***

Symptomatic bradycardia due to acute over dosage of beta-blockers, intravenous injection: 0.5–1.2 mg, repeat doses may be necessary.

Intra-operative bradycardia, intravenous injection: 300–600 mg mcg, larger doses may be used in emergencies.

Excessive bradycardia associated with beta-blocker use: intravenous injection: 0.6–2.4 mg in divided doses (max. per dose 600 mcg).

Bradycardia following myocardial infarction (particularly if complicated by hypotension), intravenous injection: 500 mcg every 3–5 minutes; maximum 3 mg per course.

Children:

Symptomatic bradycardia due to acute massive overdosage of beta-blockers, intravenous injection:

0.02 mg/kg (max. per dose 1.2 mg), repeat doses may be necessary.

Intra operative Bradycardia, intravenous injection;

Neonate: 10–20 mcg/kg

1 month – 11 years: 10–20 mcg/kg

12–17 years: 300–600 mcg, larger doses may be used in emergencies

Side effects: Dry mouth, blurred vision, photophobia, flushing and dryness of skin, rash, difficulty in micturition, constipation, arrhythmias, tachycardia, palpitations, fever, nausea, vomiting, confusion, closed-angle glaucoma, seizures.

Contraindications: Closed-angle glaucoma, myasthenia

gravis, prostatic enlargement, severe gastrointestinal (GI) inflammatory disease, GI obstruction.

Cautions: May result in paradoxical bradycardia, hepatic and renal impairment, autonomic neuropathy, myocardial ischaemia, heart failure, hyperthyroidism.

Beta-blockers

LABETALOL

Presentation: Injection containing 5 mg/ml (20-ml amp). Tablet containing 50mg, 100mg, 200mg of Labetalol.

Indications: Hypertension, Hypertension of pregnancy, Hypertensive emergencies, Hypertension following MI.

Administration: ***Adult***

Hypertensive emergencies, by IV injection: 20 mg, dose to be given over at least 2 minutes, then 40-80mg after 5-10 minutes if required, maximum 300 mg per course.

By IV infusion: Initially 2 mg/min until a satisfactory response is achieved, then discontinue; usual dose 50–200 mg.

Hypertension following MI, by IV infusion: 15 mg/hour, then increased to up to 120 mg/hour, dose to be increased gradually.

Hypertension of pregnancy, oral: Initially 100 mg twice daily, dose to be increased at intervals of 14 days; usual dose 200 mg twice daily, increased if necessary up to 800 mg daily in 2 divided doses, to be taken with food, higher doses to be given in 3–4 divided doses; maximum 2.4 g per day.

By IV infusion: Initially 20 mg/hour, then increased if necessary to 40 mg/hour after 30 minutes, then increased if necessary to 80 mg/hour after 30 minutes, then increased if necessary to 160 mg/hour after 30 minutes, adjusted according to response; usual maximum 160 mg/hour.

Children:
The safety and efficacy of labetalol in children has not been established. Unlicensed use for hypertensive emergencies must be prescribed under specialist advise.

Side effects: Dizziness, light headedness, nausea, Drug fever, hypersensitivity, urinary disorders, Hepatic disorders, SLE, toxic myopathy, tremor, Cyanosis, hyperkalaemia, interstitial lung, lichenoid keratosis, muscle cramps, nasal congestion, peripheral oedema, photosensitivity reaction, postural hypotension, psychosis.

Contraindication: Cardiogenic shock, Uncontrolled, incipient or digitalis refractory heart failure, Sick sinus syndrome (including sino-atrial block), Second or third degree heart block, Prinzmetal's angina, History of wheezing or asthma, Untreated phaeochromocytoma, Metabolic acidosis, Bradycardia (<45–50 bpm), Hypotension, Hypersensitivity to labetalol, Severe peripheral circulatory disturbances, Where peripheral vasoconstriction suggests low cardiac output, the use of Labetalol Injection to control hypertensive episodes following acute MI is contraindicated.

Cautions: Peripheral circulatory disorders (Raynaud's disease or syndrome, intermittent claudication), pulse rate of 50 – 55 bpm, first degree heart block, psoriasis.

BISOPROLOL

Presentation: Tablet containing 2.5 mg, 5 mg, and 10mg of Bisoprolol.

Indications: Hypertension, angina pectoris, supraventricular arrhythmias and acute/chronic coronary syndromes, Heart failure.

Administration: ***Adult***

Hypertension, angina pectoris, supraventricular arrhythmias and acute/chronic coronary syndromes:

5 to 10 mg orally as a single daily dose; maximum recommended dose is 20 mg daily; dose reduction may be necessary in patients with hepatic or renal impairment.

Heart failure: Initial oral dose of bisoprolol (as fumarate) is 1.25 mg once daily for 1 week, dose to be taken in the morning, then increased if tolerated to 2.5 mg once daily for 1 week, then increased if tolerated to 3.75 mg once daily for 1 week, then increased if tolerated to 5 mg once daily for 4 weeks, then increased if tolerated to 7.5 mg once daily for 4 weeks, then increased if tolerated to 10 mg once daily, maximum 10 mg per day.

Children:
No or insufficient experience in children and adolescents, therefore its use is not recommended.

Side effects: Nausea, vomiting, diarrhoea, constipation, dizziness, headache, bradycardia (in patients with chronic heart failure), worsening of pre-existing heart failure (in patients with chronic heart failure), feeling of coldness or numbness in the extremities, hypotension especially in patient with heart failure, asthenia (in patients with chronic

heart failure), fatigue, postural hypotension, hepatitis, hypersensitivity.

Contraindications: Chronic heart failure patients with: acute heart failure or during episodes of heart failure decompensation requiring i.v. inotropic therapy, cardiogenic shock, second- or third-degree AV block (without a pacemaker), sick sinus syndrome, sinoatrial block, Symptomatic bradycardia, Symptomatic hypotension, severe bronchial asthma or severe chronic obstructive pulmonary disease, late stages of peripheral

arterial occlusive disease and Raynaud's syndrome, untreated phaeochromocytoma, metabolic acidosis, hypersensitivity to the active substance or to any of the excipients.

Cautions: Hyperthyroidism or thyrotoxicosis. Pheochromocytoma**,** Asthma, ensure heart failure not worsening before increasing dose. Cessation of therapy must not be done abruptly unless clearly indicated, because this may lead to transition worsening of heart condition.

ATENOLOL

Presentation: Tablet containing 25mg, 50mg, 100mg Atenolol. Injection containing 500mcg/ml Atenolol.

Indications: Hypertension, angina, arrhythmias
Administration: *Oral, hypertension*; Initially 50mg daily. *Angina*; 100mg daily in 1 or 2 doses

A*rrhythmias*; 50 – 100mg daily.

By intravenous injection, arrhythmias; 2.5mg at a rate of 1mg/minute, repeated at 5-minute intervals to a maximum of 5mg.

By intravenous infusion, arrhythmias; 150mcg/kg body weight over 20 minutes, repeated every 12 hours if necessary.

Side effects: Bradycardia, heart failure, conduction disorders, bronchospasms, peripheral vasoconstriction, gastro-intestinal disturbances, sleep disorders, fatigue.

Contraindications: Asthma or history of obstructive airways disease, uncontrolled heart failure, marked bradycardia, 2nd or 3rd degree AV block, cardiogenic shock.

Caution: Reduce dose in renal impairment, late pregnancy and breastfeeding, avoid abrupt withdrawal in angina, diabetes, myasthenia gravis.

CARVEDILOL

Presentation: Tablets containing Carvedilol 3.125mg, 6.25mg, 12.5mg and 25mg.

Indications Hypertension; angina; adjunct to diuretics, digoxin, or ACE inhibitors in symptomatic chronic heart failure

Administration: *Hypertension,* initially 12.5 mg once daily, increased after 2 days to the usual dose of 25 mg once daily; if necessary may be further increased at intervals of at least 2 weeks to the max. 50 mg daily in single or divided doses;

Angina, initially 12.5 mg twice daily, increased after 2 days to 25 mg twice daily.

Adjunct in heart failure, initially 3.125 mg twice daily (with food), dose increased at intervals of at least 2 weeks to 6.25 mg twice daily, then to 12.5 mg twice daily, then to 25 mg twice daily; increase to highest dose tolerated, max. 25 mg twice daily in patients with severe heart failure or bodyweight less than 85 kg and 50 mg twice daily in patients over 85 kg.

Side effects: see above under Labetalol

Contraindications: see above under Labetalol; severe chronic heart failure; acute or decompensated heart failure requiring intravenous inotropes; hepatic impairment

Cautions: see above under Labetalol; monitor renal function during dose titration in patients with heart failure who also have renal impairment, low blood pressure, ischaemic heart disease, or diffuse vascular disease; severe heart failure

METOPROLOL TARTRATE

Presentation: Tablets containing Metoprolol tartrate 50 mg, Metoprolol tartrate 200 mg SR tablets, Metoprolol tartrate 1 mg/ml injection,

Indications: See see under Dose

Administration: *By mouth,*

Hypertension: initially 100 mg daily, increased if necessary to 200 mg daily in 1–2 divided doses; max. 400 mg daily (but high doses rarely necessary)

Angina, 50–100 mg 2–3 times daily Arrhythmias, usually 50 mg 2–3 times daily; up to 300 mg daily in divided doses if necessary

Migraine prophylaxis, 100–200 mg daily in divided doses

Hyperthyroidism (adjunct), 50 mg 4 times daily

By intravenous injection,

Arrhythmias, up to 5 mg at rate 1–2 mg/minute, repeated after 5 minutes if necessary, total dose 10–15 mg

In surgery, by slow intravenous injection 2–4 mg at induction or *to control arrhythmias developing during anaesthesia*; 2-mg doses may be repeated to a max. of 10 mg.

Early intervention within 12 hours of infarction, by intravenous injection 5 mg every 2 minutes to a max. of 15 mg, followed after 15 minutes by 50 mg by mouth every 6 hours for 48 hours; maintenance 200 mg daily in divided doses.

Side effects: see under Carvedilol and Labetalol above.

Cautions: see under Carvedilol and Labetalol above.

Contraindications: see under Carvedilol and Labetalol above

PROPRANOLOL

Presentation: Tablet containing 10mg, 40mg, 80mg Propranolol hydrochloride. Oral Solution containing 5mg/5ml, 10mg/5ml, 50mg/5ml propranolol hydrochloride. An injection containing 1mg/ml Propranolol hydrochloride.

Indications: Hypertension, angina, arrhythmias.

Administration: Oral, *hypertension,* initially 80mg twice daily increased as required to a maintenance dose of 160 – 320mg daily.

Arrhythmias; 10 – 40mg daily.

Side effects: See under Carvedilol and Labetalol above.

Caution: See under Carvedilol and Labetalol above.

Contra-indications: See under Carvedilol and Labetalol above.

DIGOXIN (See under 8.4. below)

LIGNOCAINE HYDROCHLORIDE

Presentation: Infusion solution, 0.1% containing 1mg/ml Lignocaine hydrochloride. 0.2% containing 2mg/ml Lignocaine hydrochloride and 5% containing 50mg/ml Lignocaine hydrochloride all in glucose intravenous infusion. Injection, containing 1% (10mg/ml) lignocaine hydrochloride, 2% (20mg/ml) lignocaine hydrochloride.

Indications: Arrhythmias, especially frequent ventricular extra-systoles.

Administration: 1mg/kg body weight by slow intravenous injection given in 1 - 2 minutes, maybe repeated after 10 – 20 minutes. Alternatively, a loading dose of 1 – 2mg/ kg body weight may be given followed by 0.1 – 0.2% infusion at 1 – 2mg per minute for 12 – 48 hours.

Side effects: Dizziness, paraesthesia, drowsiness (particularly when given too rapidly), confusion, respiratory depression and convulsions, hypotension and bradycardia (which may lead to cardiac arrest), hypersensitivity has been reported.

Caution: Lower doses in congestive heart failure, hepatic impairment, following cardiac surgery.

Contra-indications: Heart block, porphyria

QUINIDINE

Presentation: Tablet containing 250mg Quinidine bisulphate.

Indications: Ventricular arrhythmias, supraventricular tachycardia.

Administration: 250 – 500mg 3 – 4 times daily.

Side effects: Nausea, diarrhoea, ventricular arrhythmias, thrombocytopenia, haemolytic anaemia, rarely cinchonism, granulomatous hepatitis.

Contraindications: Heart block.

Caution: Test for hypersensitivity can be done by giving a 200mg test dose initially.

8.3 Anti-anginas

ATENOLOL (see under 8.2)

GLYCERYL TRINITRATE

Presentation: Sublingual tablet containing 300mcg, 500mcg Glyceryl trinitrate.

Indications: Prophylaxis and treatment of angina pectoris, left ventricular failure

Administration: Sublingually; 300mcg – 1.20mg repeated as required.

Side effects: Throbbing headache, dizziness, flushing, hypotension, tachycardia.

Caution: Severe hepatic or renal impairment, malnutrition, hypothermia, hypothyroidism.

Contra-indications: Hypersensitivity to nitrates, hypotensive conditions and hypovolaemia, shock, mitral stenosis, marked anaemia, head trauma, cerebral haemorrhage, closed-angle glaucoma.

ISOSORBIDE MONONITRATE

Presentation: Tablet containing 10mg, 20mg, 40mg isosorbide mononitrate

Indications: acute attacks of angina pectoris, prophylaxis of angina pectoris, adjunct in the treatment of congestive heart failure

Administration: Initially 20mg 2 –3 times daily or 40mg twice daily (10mg twice daily for those who have not previously received nitrates); up to 120mg daily in divided dose if required.

Side effects: See Glyceryl trinitrate above.

Contra-indications: See Glyceryl trinitrate above.

Caution: See Glyceryl trinitrate above.

ISOSORBIDE DINITRATE

Presentation: Tablet/Capsule containing 2.5mg, 5mg, 10mg, 20mg, 30mg and 40mg

Indications: Prophylaxis and treatment of angina, Left ventricular failure/congestive cardiac failure.

Administration: **Adult**

Prophylaxis and treatment of angina, oral: 20–120 mg daily in 2-3 divided doses (8-12 hourly).

By sublingual tablet (prophylaxis): 2.5-5 mg 15 minutes before performing activities likely to cause angina.

By sublingual tablet (treatment): 2.5-5 mg; may be repeated every 5-10 minutes; not to exceed 3 doses in 15-30 minutes.

Left ventricular failure/congestive cardiac failure, oral: 30–60 mg daily in divided doses, increased if necessary up to 240 mg daily in divided doses.

Children: No or insufficient experience in children and adolescents, therefore its use is not recommended.

Side Effects: Peripheral oedema, throbbing headache (nitrate headache), flushing, dizziness, postural hypotension, tachycardia, paradoxical bradycardia, angioedema, angle closure glaucoma, hypoventilation, hypoxia, pituitary haemorrhage, SJS.

Contraindications: See Glyceryl trinitrate contraindications.

Precautions: Hypothyroidism, malnutrition, hypothermia, recent history of MI, closed angle glaucoma, G6PD deficiency, patients with seriously damaged myocardia.

NITROGLYCERINE (NTG)

Presentation: Injection containing 2.5 mg/ml (10 ml amp) and Spray containing 0.4mg/spray

Indications: Unresponsive congestive heart failure, HF secondary to acute MI, acute left-sided heart failure, and acute MI, angina pectoris.

Administration: ***Adult***

Unresponsive congestive heart failure, HF secondary to acute MI, acute left-side, heart failure, and acute MI, by IV infusion: 20–25 mcg/min; this may be decreased to 10 mcg/min or increased

in steps of 20–25 mcg/min every 15–30 minutes until the desired effect is obtained.

Refractory unstable angina pectoris and coronary insufficiency, including Prinzmetal's angina, by IV infusion*:* 10 mcgs/min is recommended with increments of 10 mcg/min being made at approximately 30-minute intervals.

Hypertensive episodes and/or myocardial ischaemia during and after cardiac surgery, by IV infusion: 15–20 mcg/min, with subsequent increments of 10–15 mcg/min until the required effect is obtained.

Induction of controlled hypotension for surgery, by IV infusion: 25 mcg/min is recommended to control hypertension or produce hypotension during surgery; this may be increased by increments of 25 mcg/min at 5-minute intervals until blood pressure is stabilized; doses of 10–200 mcg/min are usually sufficient during surgery, although doses of up to 400 mcg/min have been required in some cases.

For Angina Pectoris: 1-2 sprays under the tongue, PRN, may repeat every 3-5 minutes, not to exceed 3 sprays in 15 minutes.

Children:

Hypertension during and after cardiac surgery, heart failure after cardiac surgery, coronary vasoconstriction in myocardial ischaemia, vasoconstriction in shock, by continuous IV infusion

Neonate: 0.2–0.5 mcg/kg/min, adjusted according to response, maintenance 1–3 mcg/kg/min (max. per dose 10 mcg/kg/min).

***Child*:** Initially 0.2–0.5 mcg/kg/min, adjusted according to response, maintenance 1–3 mcg/kg/min (max. per dose 10 mcg/kg/min), maximum 200 mcg/min.

Side effects: See under Glyceyl trinitrate

Contraindications: Acute circulatory failure (shock, collapse), Cardiogenic shock (unless a sufficient end-diastolic pressure is maintained by appropriate measures), severe anaemia, Toxic pulmonary oedema (See Glyceryl trinitrate contraindications for more).

Cautions: Hypothermia, hypothyroidism, Low filling pressures, Orthostatic dysfunction, hypoxaemia, Methaemoglobinaemia has been reported following nitroglycerine infusion, monitor.

NIFEDIPINE

Presentation: Capsule or tablet containing 5mg, 10mg, 20mg Nifedipine

Indications: Hypertensive disorders in pregnancy, Prophylaxis and treatment of angina, hypertension, Raynaud's phenomenon.

Administration: *Angina and Raynaud's phenomenon treatment*; 10mg 3 times daily with or after food. The usual maintenance dose is 5 – 20mg 3 times daily.

For immediate effect in angina bite on the capsule and swallow the liquid.

Prophylaxis of angina and treatment of hypertension; 20mg once daily increased if necessary to maximum 80mg once daily. Alternatively, 20mg twice daily after food up to maximum 40mg twice daily.

Children:

No or insufficient experience with slow-release tablets in children and adolescents, therefore its use is not recommended.

Side effects: Headache, dizziness, flushing, hypotension, tachycardia, lethargy, palpitations.
Caution: Withdraw if ischaemic pain occurs or existing pain worsens shortly after initiating treatment, poor cardiac reserve, impaired left ventricular function, severe hypotension, reduce doses in diabetes mellitus and hepatic impairment.

Contra-indications: Cardiogenic shock, advanced aortic stenosis, porphyria.

AMLODIPINE

Presentation: Tablet containing 5 mg, 10 mg of Amlodipine

Indications: Angina, Hypertension, hypertensive disorders in pregnancy.

Administration: ***Adult***

Angina, oral: Initially 5 mg once daily, increased if necessary; maximum 10 mg once daily

Hypertension, oral: Initially 5 mg once daily, increased if necessary; maximum 10 mg once daily

Children:
Hypertension, oral
1 month–11 years: Initially 100–200 mcg/kg once daily, increased if necessary up to 400mcg/kg once daily, adjusted at intervals of 1–2 weeks; maximum 10 mg per day.
12 years and over: Give adult dose

Side effects: Palpitation, flushing, oedema, headache, dizziness, sleep disturbances, fatigue, GI disturbances, constipation, dry mouth, hypotension, syncope, chest pain, dyspnoea, rhinitis, mood changes, tremor, paraesthesia, increased sweating, urinary disturbances, impotence, gynaecomastia, myalgia.

Contraindications: Severe hypotension, hypersensitivity

to amlodipine, cardiogenic shock, unstable angina, significant aortic stenosis, haemodynamically unstable heart failure after acute MI (during the first 28 days).

Cautions: Congestive heart failure, elderly, titrate downwards in severe hepatic impairment.

NIMODIPINE

Presentation: Tablet containing 30mg of Nimodipine

Indications: Prevention and Treatment of ischaemic neurological defects following subarachnoid haemorrhage.

Administration: *Adult:* 60 mg every 4 hours, to be started within 4 days of subarachnoid haemorrhage and continued for 21 days

Side effects: hypotension, diarrhea, headache, abdominal discomfort, arrythmias, thrombocytopenia.

Contraindication: unstable angina within 1 month of MI, hypersensitivity.

Cautions: cerebral oeadema, hypotension, hepatic impairment, severely raised ICP.

DILTIAZEM HYDROCHLORIDE

Presentation: Tablet/Capsule containing 30mg-420mg of Diltiazem.

Indications: Angina, hypertension, paroxysmal supraventricular tachycardia, artrial fibrillation/flutter

Administration: *Adult:* Initially 60 mg 3 times a day, adjusted according to response; maximum 360 mg per day

Elderly: Initially 60 mg twice daily, adjusted according to response; maximum 360 mg per day.

Mild to moderate hypertension; Adult: 120 mg twice daily, dose form not appropriate for initial dose titration.

Side effects: oedema, headache, dizziness, Cardiac conduction disorders, constipation, gastrointestinal discomfort, malaise, bradyarrhythmias, insomnia, nervousness, postural hypotension

Contraindications: wolff-parkinson-white syndrome, cardiogenic shock, heart failure (with reduced ejection fraction), left

ventricular failure with pulmonary congestion, second or third-degree AV block (unless pacemaker fitted), severe bradycardia, sick sinus syndrome, significant aortic stenosis, with systemic use Acute porphyrias

Cautions: Bradycardia (avoid if severe), first degree AV block, prolonged PR interval, significantly impaired left ventricular function.

VERAPAMIL

Presentation: Tablet/Capsule containing 40-360mg and injection containing 2.5mg/ml of Verapamil.

Indications: Treatment of supraventricular arrhythmias, Paroxysmal tachyarrhythmias, Angina, Hypertension, Prophylaxis of cluster headache (initiated under specialist supervision)

Administration: *Adult:*

Treatment of supraventricular arrhythmias- *by mouth using immediate-release medicines* 40–120 mg 3 times a day*; by slow intravenous injection:* 5–10 mg, to be given over 2 minutes, preferably with ECG monitoring. *Elderly*: 5–10 mg, to be given over 3 minutes, preferably with ECG monitoring.

Paroxysmal tachyarrhythmias**:** *by slow intravenous injection*: Initially 5–10 mg, followed by 5 mg after 5–10 minutes if required, to be given over 2 minutes, preferably with ECG monitoring; *Elderly*: Initially 5–10 mg, followed by 5 mg after 5–10 minutes if required, to be given over 3 minutes, preferably with ECG monitoring.

Angina *by mouth using immediate-release medicines:* Adult: 80–120 mg 3 times a day.

Hypertension *by mouth using immediate-release medicines***;** Adult: 240–480 mg daily in 2–3 divided doses

Prophylaxis of cluster headache (initiated under specialist supervision) *by mouth using immediate-release medicines* Adult: 240–960 mg daily in 3–4 divided doses

Hypertension (in patients new to verapamil) *by mouth using extended release* Adult: Initially 120 mg daily, increased if necessary up to 480 mg daily, doses above 240mg daily as 2 divided doses

Prophylaxis after myocardial infarction where betablockers are not appropriate

by mouth Adult: 360 mg daily in divided doses, started at least 1 week after infarction, given as either 240mg in the morning and 120mg in the evening or 120mg 3 times daily

Side effects: headache, hypotension, giginval hyperplasia, constipation, oeadema, dizziness.

Contraindications: cardiogenic shock, bradycardia, second- and third-degree heart block, congestive heart failure and heart failure with reduced ejection fraction, symptomatic hypotension, wolff-parkinson white syndrome and other atrial flutter or fibrillation associated with accessory conducting pathways.

Cautions: aortic stenosis, acute phase MI, first degree AV block, neuromuscular disorders, Hypertrophic cardiomyopathy.

8.4 Cardiac Glycosides

Cardiac glycosides are a small group of Medicines that improve contractility of diseased hearts. They also reduce the heart rate in such hearts. They occur widely in nature and they can also be prepared synthetically.

They are prepared from two plants called digitalis lanata and Digitalis purpurea. The term digitalis applies to the entire class of glycosides which consist of digoxin, digitoxin. They are useful in congestive heart failure, atrial fibrillation and paroxysmal atrial tachycardia. They are useful in sinus tachycardia caused by congestive heart failure but are ineffective in the treatment of sinus tachycardia such as that due to fever, anaemia or hyperthyroidism which are not associated with heart failure.

DIGOXIN

Presentation: Tablet containing digoxin 0.25mg, 0.125mg; Elixir containing digoxin 0.05mg/ml; Injection containing digoxin 0.25mg/ml.

Indications: Heart failure, cardiac arrhythmias (particularly atrial fibrillation)

Administration: Digoxin is normally administered orally as a single dose except in children under the age of 10years where it may be given in divided doses.

Intravenous digoxin can be given undiluted over 5 minutes or diluted in a four-fold volume of 5% dextrose, water for injection or normal saline over a period of 5 minutes. Digoxin intravenous should not be mixed with other Medicines.

Rapid Digitalisation: Digoxin has a low therapeutic index and therefore cautious dosage determination is of paramount importance. Rapid digitalisation should not be given in somebody who has taken digoxin in the past two weeks.

Digitalisation doses for Oral Digoxin; Premature neonates*:* 0.02mg to 0.03mg/kg body weight. Full term neonates; 0.025mg to 0.035mg/kg body weight. 1 to 24 months; 0.035mg to 0.060mg/kg body weight. 2 to 5 years; 0.03mg to 0.04mg/kg body weight. 5 to 10 years; 0.02mg to 0.035mg/ kg body weight. Older than 10 years; 0.01mg to 0.015mg/kg body weight.

Digitalisation doses for intravenous digoxin (with normal renal function); Premature neonates; 0.015mg to 0.025mg/kg body weight. Full term neonates; 0.02mg to 0.03mg/ kg body weight. 1 to 24 months; 0.03mg to 0.05mg/kg body weight. 2 to 5 years; 0.025mg to 0.035mg/kg weight. 5 to 10years; 0.015mg to 0.03mg/kg body weight. Older than 10 years; 0.008mg to 0.012mg/kg body weight.

Maintainance dose: 20 to 30 % of the digitalisation dose. In patients under 10 years give in divided doses.

Loading doses are administered in divided doses as follows;

Oral: 50% of the total dose given as the first dose; the remaining portion is given in fractions of 25% of the loading dose at 6 to 8-hour intervals.

Intravenous: 50% of the total dose given as the first dose; the remaining portion is given in fractions of 25% of the loading dose at 4 to 8-hour intervals.

Patient's clinical response should be carefully assessed before each additional dose is given. If the desired therapeutic response has been achieved or the patient has toxic effects then the remaining portion of the full digitalisation dose should not be administered. Patients with renal failure should be given a much lower dose. Patients with hypokalaemia should not be given digoxin until after the Hypokalaemia has been corrected. Digoxin should be avoided in patients with conduction abnormalities including severe bradycardia.

Children:

Supraventricular arrhythmias, chronic heart failure, oral

Neonate under 1.5 kg: Initially 25 mcg/kg in 3 divided doses for 24 hours then 4–6 mcg/kg/day in 1–2 divided doses.

Neonate 1.5–2.5 kg: Initially 30 mcgs/kg in 3 divided doses for 24 hours then 4–6 mcg/ kg/day in 1–2 divided doses.

Neonate over 2.5 kg or child under 2 years: initially 45 mcg/kg in 3 divided doses for 24 hours then, 10 mcg/kg/day in 1–2 divided doses.

2–5 years: Initially 35 mcg/kg in 3 divided doses for 24 hours then, 10 mcg/kg/day in 1–2 divided doses

5–10 years: Initially 25 mcg/kg (maximum 750 mcg) in 3 divided doses for 24 hours then, 6 mcg/kg/day (maximum 250 mcg daily) in 1–2 divided doses.

over 10 years: Initially 0.75–1.5 mg in 3 divided doses for 24 hours then 62.5–250 mcg/daily in 1–2 divided doses (higher doses may be necessary)

Side effects: Usually associated with excessive dosage, include nausea, vomiting, anorexia, diarrhoea, abdominal pain, visual disturbances, headache, fatigue, drowsiness, confusion, delirium, hallucinations, arrhythmias, heart block.

Contraindications: Supraventricular arrhythmias caused by Wolff-Parkinson-White syndrome.

Caution: Recent infarction, hypothyroidism, reduce dose in the elderly and renal impairment.

8.5 Inotropic sympathomimetics

DOPAMINE HYDROCHLORIDE

Presentation: Sterile concentrate Dopamine hydrochloride 40mg/ml. For dilution and use as an intravenous infusion.

Indication: Cardiogenic shock, renal failure.

Administration: 2 – 5mkg/kg/minute, slow intravenous infusion, BP monitoring

Side effects: Nausea and vomiting, peripheral vasoconstriction, hypertension, hypotension, tachycardia.

Contraindication: Tachyarrhythmia, phaeochromocytoma.

Caution: Correct hypovolaemia.

DOBUTAMINE HYDROCHLORIDE

Presentation: Sterile solution 12.5mg/ml dobutamine hydrochloride. For dilution and use as an intravenous infusion.

Indication: Inotropic support in infarction, cardiac surgery, cardiomyopathies, septic and, cardiogenic shock.

Administration: ***Adult***

By IV infusion: Usual dose 2.5–10 mcg/kg/min, adjusted according to response, alternatively 0.5–40 mcg/kg/min

Children:

Neonate: Initially 5 mcg/kg/min, then adjusted according to response to 2–20mg/kg/min; doses as low as 0.5–1 mcg/kg/min have been used.

Child: Initially 5 mcg/kg/min, then adjusted according to response to 2–20 mcg/kg/min; doses as low as 0.5–1 mcg/kg/min have been used.

Side effects: Tachycardia and a marked increase in systolic blood pressure indicate an overdose.

Caution: Severe hypotension.

ADRENALINE/EPINEPHRINE

Presentation: Injection containing 100mcg/ml Adrenaline (epinephrine) hydrogen tartrate.

Indication: Cardiac arrest, severe anaphylactic reaction, severe angioedema.

Administration: *In cardiac arrest* 1mg by intravenous injection through a central line (if one is in place) otherwise through a peripheral vein then flushed with some sodium chloride 0.9%. Repeat every 3 minutes according to the response or subcutaneous.

In anaphylaxis: By intramuscular injection, *adult* and *adolescent*, 500 mcg

Children:

Infant under 6 months: 50 mcg,

6 months – 6 years 120 mcg

6-12 years 250 mcg.

The above doses may be repeated several times if necessary at 5 minutes intervals, according to blood pressure, pulse and respiratory function.

Side effects: Anxiety, tremor, tachycardia, arrhythmias, hypertension (risk of cerebral hemorrhage) and pulmonary oedema, nausea, vomiting, sweating, dizziness, weakness.

Caution: Hypertension, hyperthyroidism, diabetes mellitus, ischaemic heart disease, elderly.

Note: See also Local anaesthesia/Eye preparation.

8.6 Anti-Cholesterol Medicines

ARTOVASTATIN

Presentation: Tablet containing 10mg, 20 mg, 40 mg and 80mg of Artovastatin

Indications: Primary cholesterolaemia or combined hyperlipidemia in patients who have not responded adequately to diet and other measures, Primary and secondary prevention of cardiovascular events in patients at high risk of a first cardiovascular event.

Administration: *Adult*

Primary cholesterolaemia or combined (mixed) hyperlipidemia in patients who have not responded adequately to diet and other measures: Usual dose is 10 mg once daily, increased if necessary up to 80mg once daily; dose to be increased at intervals of at least 4 weeks.

Primary prevention of cardiovascular events in patients at high risk of a first cardiovascular event: 20 mg once daily, dose can be increased if necessary.

Secondary prevention of cardiovascular events: 80 mg once daily.

Children:

Hyperlipidaemia including familial/ Hypercholesterolaemia

10–17 years: Initially 10 mg once daily, then increase if necessary up to 20 mg once daily; dose to be adjusted at intervals of at least 4 weeks.

Side effects: GI disturbance, rhabdomylosis, muscle rupture, Myalgia associated with muscle stiffness or weakness, elevations of creatine kinase and serum transaminase, hepatitis, headache, skin rash, peripheral neuropathy, hypersensitivity, urinary tract infections, myopathy, sinusitis, epistaxis, hyperglycaemia, joint disorders, pharyngolaryngeal pain, nasopharyngitis, pain, decreased appetite, chest pain, hypoglycaemia, vision disorders, hearing loss, SCARs.

Contraindications: Hemmorhagic stroke, known hypersensitivity to the drug or any of its excipients, Active liver disease or unexplained persistently raised serum-aminotransferase concentrations > 3 times upper limit of normal (ULN), Creatinine Kinase level >5 times ULN.

Cautions: patients with pre-disposing factors for Rhabdomyolysis, renal impairment, hypothyroidism, personal or familial history of muscular toxicity, past history of liver disease or alcoholism, elderly, haemorrhagic stroke.

9 Medicines Used in the Treatment of Malignant Diseases

The interdisciplinary approach in the treatment of cancer patients of specific surgery, sophisticated multi-cytostatic treatment and radiation are only possible in specialised clinics where different types of treatments are available.

The therapy for malignant tumour demands qualified and experienced personnel including doctors, pharmacists and nurses. A laboratory should offer valid and reproducible tests. Only if these conditions are guaranteed should oncology treatment be performed.

For most neoplasms, combination therapy is considered superior to single-drug treatment. But the timing of doses and selection of cytotoxic Medicines (often in combination with prednisolone) is very important and depends not only on the type of tumour but also on the general condition of the patient being treated.

Chemotherapy may cure some malignant diseases in their early stages. Often it is said that chemotherapy improves the quality of life of the patient (especially in the reduction of pain caused by the tumour) but this is an evaluation which only the patient can make. In the later stages of the tumour, the chemotherapy has to be balanced carefully between the palliative effect of the Medicines and the toxic side effects.

General contraindications for cytotoxic Medicines include signs of infection (bacterial or viral), especially where there is fever and anaemia.

Note: In cancer therapy, treatment doses are usually calculated according to skin surface area rather than per kg body weight.

Prescriptions should not be repeated except on the instructions of the specialist.

9.1 Alkylating Medicines

BUSULPHAN

Presentation: Tablet containing 2mg and 4mg Busulphan; Solution for infusion containing 60mg/10ml

Indication: Chronic myeloid leukemia, induction of remission; Conditioning treatment before hematopoietic progenitor cell transplantation

Administration: Adult: 60 mcg/kg daily (max. per dose 4 mg), maintenance dose 0.5–2 mg daily.

Side effects: Alopecia, diarrhoea, hepatic disorders, nausea, respiratory disorders, sinusoidal obstruction syndrome, skin reactions, thrombocytopenia, bone marrow suppression, pulmonary fibrosis, thrombocytopenia, amenorrhoea, gout, diarrhoea.

Contraindication: Pregnancy, lactation, Lung toxicity, acute porphyrias. Not to be used in patients with disease resistant to Busulfan. Avoid in patients with previous hypersensitivity reactions to the drug or any of its components.

Caution: Use of effective contraception is advised for both men and women during and until six months after treatment ceasation; hepatic impairment, monitor cardiac and liver function, use central IV line, monitor full blood cell count at regular intervals, avoid in porphyria.

CHLORAMBUCIL

Presentation: Tablet containing 2mg, 5mg Chlorambucil

Indications: Chronic lymphocytic leukaemia

Administration: 4mg – 10mg per day

Side effects: Neutropenia, thrombocytopenia, nausea, vomiting, liver damage

Caution: Should not be used within one month of radiation therapy, Pregnancy.

CYCLOPHOSPHAMIDE

Presentation: Tablet containing 50mg Cyclophosphamide. An injection containing 200mg, 500mg, 1g cyclophosphamide in sodium chloride for dilution with water for injection.

Indications: Hodgkin's disease, lymphomas, multiple myeloma, acute leukaemia Chronic myeloid leukaemia, carcinoma of the breast, neuroblastoma sarcoma.

Administration: Adult: IV 600mg/m2 intravenously or 20 – 50mg/m2 daily depending on the condition being treated and tolerance. Oral: usual dose is 1-5mg/kg/day..

Children: Consult local specialist protocols.
3 months–17 years: 500 mg/m2 once a month for 6 months

Side effects: Alopecia, anorexia, fever, nausea, vomiting, aspermia, permanent sterility, haemorrhagic cystitis, myelosuppression.

Contraindications: Pregnancy.

Caution: High serum uric acid and potassium levels may need treatment during therapy. Ensure high fluid intake.

MELPHALAN

Presentation: Tablet containing 2mg, 5mg Melphalan

Indications: Multiple myeloma, chronic lymphocytic leukemia, lymphoma.

Administration: 1mg/kg body weight every 4 weeks.

Caution: Myelosuppression, renal impairment, pregnancy and alopecia. Frequent blood counts advisable.

MUSTINE (MECHLORETHAMINE)

Presentation: Vials containing 10mg powder for preparation for intravenous injection.

Indications: Lymphoma, Hodgkin disease, mycoses fungicides, solid tumour, brain tumour.

Administration: Single dosed 400mg/kg or 100mg/kg intravenously daily for 4 – 5 days.

Side effects: Nausea, vomiting alopecia, myelosuppression, bone marrow depression.

9.2 Cytotoxic antibiotics

ACTINOMYCIN D

Presentation: Injection containing 500mcg actinomycin powder for the preparation of injection.

Indications: Neuroblastoma, Wilms tumour, Kaposi's sarcoma and Ewing's sarcoma.

Administration: Adults; 500mcg intravenously daily for 5 days.

Children:
15mcg/kg body weight daily for 5 days. The single total dose may be considered in certain circumstances.

Side effects: Abdominal pain, anorexia, nausea, vomiting, diarrhoea, stomatitis.

Caution: May cause phlebitis if given subcutaneously or intramuscularly, may cause bone marrow depression.

BLEOMYCIN

Presentation: Injection containing 15- or 30-units bleomycin sulphate powder

Indications: Hodgkin's disease, lymphomas, squamous-cell carcinoma, carcinoma of the testis and lung.

Administration: 6 – 15 units/m^2 subcutaneously or intravenously

Side effects: Allergic reactions, fever, dermatitis, pulmonary fibrosis, alopecia, Dysuria, proteinuria.

Caution: Anaphylaxis, chills, fever, pulmonary fibrosis.

CALCIUM FOLINATE (CALCIUM LEUCOVORIN)

Presentation: Injection containing 10mg/ml of folinic acid in a 5ml vial; Tablet containing 15 mg of Calcium Folinate.

Indications: High dose methotrexate rescue. Fluorouracil potentiation.

Administration: IV: 10 mg/m² IV every 6 hours for 10 doses; start 24 to 36 hours after beginning of methotrexate infusion 3 – 6mg intravenously daily depending upon the clinical situation.

Side effects: Fever, allergic reactions such as itchy rash, swelling of the hands, feet, ankles, face, lips, mouth or throat.

Contraindications: do not give by intrathecal injection.

Precautions: Not for use in patients with pernicious anemia.

DAUNORUBICIN

Presentation: Lyophilized or Liposomal Powder or solution for IV infusion containing 20mg, 50mg Daunorubicin.

Indication: Acute myelogenous leukaemia (AML), Acute lymphocytic leukaemia (ALL), Advanced AIDS-related Kaposi's sarcoma (liposomal formulation only).

Administration: *For <60 years old*: 45 mg/m² IVP days 1, 2, 3 first course, days 1, 2 subsequent courses,

> 60 years old: 30 mg/m² IVP days 1, 2, 3 first course, days 1, 2 subsequent courses.

Children:

<2 years old or <0.5 m² BSA: 1 mg/kg IV push every week (Limit lifetime dose 10 mg/kg).

>2 years old or >0.5 m² BSA: 25 mg/m² IV push every week (Limit lifetime dose 300 mg/m²)

Side effects: Abdominal pain, alopecia, amenorrhoea, anaemia, arrhythmias, ascites, atrioventricular block, azoospermia, bone marrow disorders, cardiac inflammation, cardiomyopathy, cyanosis, death, dehydration, dyspnea, gastrointestinal disorders, haemorrhage, hepatomegaly, hyperpyrexia, hyperuricaemia, hypoxia, infection, ischaemic heart disease, leucopenia, mucositis, nausea, nephropathy, neutropenia, oedema, pain, paraesthesia, pleural effusion, radiation injuries, shock, thrombocytopenia, Urine red, venous sclerosis

Contraindication: Myocardial insufficiency, recent myocardial infarction, severe arrhythmia

Caution: Dose adjustment and drug formulation should be considered in Hepatic and Renal impairment.

DOXORUBICIN

Presentation: Injection containing 50mg doxorubicin powder with water for injection.

Indications: Acute leukaemia, Hodgkin's disease, lymphomas, Wilms tumour, neuroblastoma, kaposis sarcoma, carcinoma of breast and lung, ewings sarcoma.

Administration: 40 – 75mg/m² intravenously

Side effects: Rash, buccal mucosa and skin folds, cardiomyopathy (ventricular dysfunction, heart failure, conduction disturbances), coloured urine, conjuctivitis, lacrimation and facila flushing, nausea and vomiting, stomatitis, GI ulceration, hyperpigmentation of nails, itch, fever, chills, myelosuppression, erythrodysaesthesia.

Caution: Must be given intravenously, extravasation causes necrosis of tissues. ECG must be performed as it causes cardiotoxicity.

LIPOSOMAL DOXORUBICIN

Presentation: Injectable solution containing 50mg/25ml

Indication: Kaposi Sarcoma, Multiple Myeloma, Ovarian Cancer; Paediatric Indications: Ewing's sarcoma, Wilm's

tumour, Neuroblastoma, Retinoblastoma, Acute lymphoblastic leukaemia, Hodgkin's lymphoma, Non-Hodgkin's lymphoma

Administration: *Kaposi Sarcoma:* 20 mg/m² IV every 3 weeks

Ovarian Cancer: 50 mg/m² IV every 4 weeks for 4 courses;

Multiple Myeloma: 30 mg/m² IV on day 4 followed by treatment with bortezomib.

Children:
Hodgkin's lymphoma: 25mg/m² on D1 and D15;
Wilm's tumour: 50mg/m² on D1 and D15

Side effects: Anemia, Thrombocytopenia, Neutropenia, Nausea, Hand-foot syndrome, Nausea, Stomatitis, Asthenia, Vomiting, Rash, Constipation, Abdominal pain, Fever, Anorexia, Diarrhea, Peripheral edema, Dyspepsia, Pharyngitis, Dyspnea, Alopecia, Increased alkaline phosphatase, Tachycardia, Dyspnea, Hemolysis ovarian cancer, Abscess, Acute myeloid leukemia Cardiomegaly, Cardiomyopathy, Erythema nodosum, Hyperkalemia, Hyperuricemia, Ketosis

Contraindication: Hypersensitivity, anaphylaxis.

Caution: Myocardial toxicity, infusion-related reactions.

AZATHIOPRINE

Presentation: Tablet containing 50mg, 75mg, 100mg; Powder for injection containing 100mg/vial; Solution for infusion containing 500mg, 450mg.

Indication: Suppression of transplant rejection, systemic lupus erythematosus, autoimmune conditions, severe ulcerative colitis and severe Crohns disease.

Administration: 1–3 mg/kg daily

Side effects: Nausea, diarrhea, stomach pain, hair loss, skin rash, allergic reaction**,** serious brain infection, problems with speech, thought, vision, or muscle movement.

Contraindication: Hypersensitivity to azathioprine or mercaptopurine.

Caution: Azathioprine may cause a rare type of lymphoma (cancer) of the liver, spleen, and bone marrow that can be fatal, mainly in teenagers and young men with Crohn's disease or ulcerative colitis.

9.3 Antimetabolites

CYTARABINE

Presentation: Injection containing 100mg cytarabine (5ml vials with water for injection).

Indications: Non-lymphocytic acute leukaemia, lymphoma.

Administration: 100mg/M² iv or Subcutaneously.

Side effects: Myelosuppression, liver damage, nausea, vomiting, diarrhoea, Skin rash, hair loss, mouth ulcers.

FLUOROURACIL

Presentation: Injection containing 25mg/ml fluorouracil sodium for intravenous administration. Capsules containing 250mg Fluorouracil, Fluorouracil 5% Cream.

Indications: Carcinoma of the stomach, breast and colon

Administration: 300mg – 1000mg/m²/ intravenously or continuous infusion. May be given orally.

Side effects: Alopecia, inflammation of mucosal membrane, bone marrow suppression, diarrhoea, hyperpigmentation.

MERCAPTOPURINE

Presentation: Tablet containing 50mg mercaptopurine.

Indications*:* Acute lymphocytic leukaemia

Administration: 100 – 200mg daily.

Children:
2.5mg/kg body weight per day.

Side effects: Liver toxicity, crystalluria, fever, mouth ulcers

Caution: Bone marrow depression.

METHOTREXATE

Presentation: Tablet containing 2.5mg methotrexate. A vial containing 5mg, 50mg powder methotrexate for preparing solution for intravenous injection

Indications: All osteogenic sarcoma, squamous carcinoma, choriocarcinoma, lymphatic carcinoma of the head and neck.

Administration: Oral; 5mg/kg bodyweight weekly in combination with other Medicines

Side effects: Gastrointestinal ulceration, megaloblastic anaemia, hepatic impairment

Caution: Renal disease.

THIOGUANINE

Presentation: Tablet containing 40mg thioguanine

Indications: Acute leukaemia especially acute myeloid leukaemia in combination with other cytotoxics.

Administration: 2mg/kg body weight daily – dosage titrated according to clinical factors.

Caution: It is an anti-metabolic.

9.4 Vinca alkaloids

VINCRISTINE

Presentation: Vial containing 1mg, 5mg powder for intravenous injection

Indications: Acute leukaemia. Hodgkin's disease, lymphomas, Wilms tumour, neuroblastoma Sarcoma, brain tumour, carcinoma of the breast, carcinoma of the testis.

Administration: 2mg/m^2 intravenously every one to two weeks.

Side effects: Neuropathies, marrow suppression, alopecia, nausea, vomiting, anorexia.

Caution: Extravasation causes severe necrosis of tissue, must be given in big vein with IBV running.

9.5 Other Neoplastic Medicines

ASPARAGINASE

Presentation: Injection containing 10,000 i.u. asparaginase powder for reconstitution per vial
Indications: Acute lymphoblastic leukaemia

Administration: 100,000 i.u. /m^2 /day weekly intramuscularly or intravenously

Side effects: Anaphylactic shock, nausea and vomiting, hepatotoxicity

Caution: Do not give if allergic to E. coli substances.

CARBOPLATIN

Presentation: Solution for infusion containing 50mg, 150mg, 450mg Carboplatin.

Indication: Advanced ovarian cancer, Cervical cancer, small cell lung cancer, High risk seminoma; Testicular germ cell tumours [adjuvant treatment]

Children: Stage 4 neuroblastoma, Germ cell tumours, Brain tumours, Rhabdomyosarcoma, Soft-tissue sarcomas, Retinoblastoma, High risk Wilms' tumour

Administration: *Ovarian Cancer and cervical cancer*-use the specified Calvert method AUC formula to calculate the total carboplatin dose needed to achieve a given AUC.

Children:
Solid tumor: 300-600 mg/m^2 IV q4Weeks;
Sarcoma (bone/soft tissue): 400 mg/m^2/day for 2 days every 21 days;
Brain tumor: 175 mg/m^2 week x 4 weeks with a 2 weeks recovery period between courses;
Retinoblastoma 1-2 ml subconjunctival injection of 10 mg/ml solution per dose

Side effects: Alopecia, anemia, asthenia, cardiovascular disorder, constipation, diarrhea, gastrointestinal discomfort, haemorrhage, hypersensitivity. increased risk of infection, leucopenia, mucosal abnormalities, musculoskeletal disorder, nausea, neutropenia, ototoxicity, peripheral neuropathy, respiratory disorders, skin reactions, altered taste, thrombocytopenia, urogenital disorder, vision disorders, vomiting, cardiac discomfort, dyspnea.

Contraindication: Avoid if creatinine clearance less than 20 ml/minute. Severe hypersensitivity to carboplatin, other platinum compounds, mannitol. Severe myelosuppression, significant bleeding, pregnancy and lactation.

Caution: Monitor and adjust dose for hematological parameters and in renal impairment and reduced renal function

CISPLATIN

Presentation: Injection containing 1mg/ml Cisplatin.

Indications: Carcinoma of lungs (small cell), testis, breast, ovary, stomach.

Administration: 60 – 100mg/m^2 intravenously daily.

Side effects: Nephrotoxicity, bone marrow suppression, ototoxicity, tetarym alopecia, neurotoxicity, severe vomiting, anaphylaxis.

Caution: Maintain a high fluid intake.

CHLORAMBUCIL

Presentation: Tablet containing 2mg Chlorambucil.

Indication: Some lymphomas and chronic leukemias (used either alone or in combination therapy), Hodgkin's Lymphoma, Chronic Lymphatic (Lymphocytic) Leukemia

Administration: 0.1-0.2 mg/kg PO daily for 3 -6 weeks. In adults, increase by 0.1 mg/kg/dose until response/toxicity observed on a biweekly or monthly basis.

Side effects: Anemia, bone marrow disorders, diarrhea, gastrointestinal disorder, leucopenia, Nausea, neoplasms, neutropenia, oral ulceration, seizures, thrombocytopenia, vomiting, Cystitis, fever, hepatic disorders, movement disorders, muscle twitching, peripheral neuropathy, respiratory disorders, severe cutaneous adverse reactions (SCARs), Tremor, Amenorrhea, azoospermia, secondary malignancy, rash resulting in Stevens-Johnson syndrome and toxic epidermal necrolysis.

Contraindication: WBC <3000/mm^3 or platelets <150,000, Pregnancy, lactation.

Caution: Dose reduction in severe hepatic impairment, liver toxicity.

ETOPOSIDE

Presentation: Injection containing 20mg/ml etoposide, Capsules containing 50mg etoposide.

Indication:

Adults: small cell lung cancer, Hodgkin's disease, acute non-lymphocytic leukaemia, testicular tumours, lymphomas of head and neck.

Children: Stage 4 neuroblastoma, Germ-cell tumours, Intracranial germ-cell tumours, Rhabdomyosarcoma, Soft-tissue sarcomas, Neuroectodermal tumours, Relapsed Hodgkin's disease, Non-Hodgkin's lymphoma, Ewing tumour, Acute lymphoblastic leukaemia, Acute myeloid leukaemia

Administration: 100-200mg/m^2 days 1, 3 and 5 every 3 to 4 weeks in combination with other drugs.

Children: 100mg/m^2 days 1, 3 and 5 every 3 to 4 weeks in combination with other drugs.

Side effects: Myelosuppression, Nausea and vomiting, transient hypotension, anaphylactic-like reactions, alopecia.

Caution: Myelosuppression.

FLUDARABINE

Presentation: tablet 10mg, solution for injection 50mg/2ml, Powder for solution 50mg

Indication: Initial treatment of advanced B-cell chronic lymphocytic leukaemia (CLL) or after first line treatment in patientswith sufficient bone-marrow reserves.

Administration: *By mouth Adult*: 40 mg/m2 for 5 days every 28 days, usually given for 6 cycles

25 mg/m^2 IV infusion over 30 minutes daily for 5 days (up to 30 mg/m^2).

Side effects: Anemia, appetite loss, asthenia, bone marrow depression, chills, cough, diarrhea, fever, increased risk of infection, malaise, mucositis, nausea, neoplasms, nerve disorders, neutropenia, oedema, stomatitis, Thrombocytopenia, vision disorders, Vomiting, Autoimmune disorder, confusion, haemorrhage, tumor lysis syndrome, Agitation, arrhythmia, coma, Heart failure, seizure, severe cutaneous adverse reactions(SCARs),With oral use Progressive multifocal leukoencephalopathy(PML), skin reactions, viral infection reactivation, rash ,with oral use Acquired Haemophila, crystalluria, Dyspnoea, electrolyte imbalance, haemolytic anaemia, hyperuricaemia, metabolic acidosis, renal failure, respiratory disorders, With parenteral use Pulmonary toxicity Encephalopathy, intracranial haemorrhage

Contraindication: Pregnancy, lactation, creatinine clearance less than30 ml/minute

Caution: Adjust dose in renal impairment. Reduce dose by up to 50% if creatinine clearance 30–70 ml/minute. Use of effective contraception is advised for both men and women during and until six months after treatment ceasation.

FILGRASTIM

(Recombinant human Granulocyte-colony stimulating factors, G-SCF)

Presentation: Injectable solution, prefilled syringe for SC 300mcg/ml ,480mcg/0,8ml.

Indications: Reduction in duration of neutropenia and incidence of febrile neutropenia in cytotoxic chemotherapy for malignancy (except chronic myeloid leukemia and myelodysplastic syndromes)

Administration: *Induction or Consolidation Chemotherapy*, 5 mcg/kg SC/IV daily initially, may increase by 5 mcg/kg for each chemotherapy cycle according to duration and severity of ANC

Myelosuppressive Chemotherapy Treatment: 5 mcg/kg/day SC or IV infusion (short 15-30 min or continuous), may increase by 5 mcg/kg increments according to duration and severity of ANC usually for up to 14 days (up to 38 days in acute myeloid leukaemia).

Severe Chronic Neutropenia: ***Congenital:*** Initial 6 mcg/kg SC ever 12hrs, ***Idiopathic/ cyclic***: initial 5 mcg/kg/day SC

*Acute Radiation Syndrome:*10 mcg/kg SC as a single daily injection for patients exposed to myelosuppressive doses of radiation

Side effects: Anaemia, diarrhoea, dysuria, haemorrhage, hepatomegaly, hyperuricaemia, hypotension, osteoporosis, Rash, fluid imbalance, graft versus host disease, peripheral vascular disease, pseudogout, rheumatoid arthritis aggravated, urine abnormalities

Contraindications: Severe congenital neutropenia (Kostmann's syndrome) with abnormal cytogenetics. **Caution**: Osteoporotic bone disease (monitor bone density if given for more than 6 months), secondary acute myeloid leukemia

IFOSFAMIDE

Presentation: Powder for solution for injection 1 gram, 2gram

Indications: Malignant disease, Rhabdomyosarcoma, soft tissue sarcomas, Ewing tumor, germ cell tumor, osteogenic sarcoma

Administration: 1.2 g/m^2/day IV infusion over 30 minutes on days 1-5 every 3-4or weeks. Or after recovering from hematologic toxicity (>100,000 cells/mm^3 platelets or

≥4,000 cells/mm³ WBC. Ifosfamide should be used concomitantly with mesna (240 mg/m² IV at 0, 4, 8 hr) to prevent hemorrhagic cystitis

Side effects: Common or very common Alopecia. appetite decreased. Bone marrow disorders. haemorrhage. hepatic disorders. infection. leucopenia. nausea. reactivation of infection. renal impairment. thrombocytopenia. Vomiting, Cardiotoxicity. diarrhea. Hypotension, Skin reactions. Use concomitant with mesna (240 mg/m² IV at 0, 4, 8 hr) to prevent hemorrhagic cystitis.

Contraindications: Acute infection, urinary-tract infection. urinary-tract obstruction. urothelial damage, pregnancy, lactation, Not recommended if CrCl <10 ml/min.

Caution: Avoid in Acute Porphyria, diabetes Mellitus, cardiac disease

IMATINIB

Presentation: Tablet containing 100mg, 400mg Imatinib.

Indications: Hypereosinophilic Syndrome and/or Chronic Eosinophilic Leukemia, Myelodysplastic/Myeloproliferative Diseases, Acute Lymphoblastic Leukemia, Dermatofibrosarcoma Protuberans, Mastocytosis, Gastrointestinal Stromal tumors. Treatment of newly diagnosed Philadelphia-chromosome-positive chronic myeloid leukaemia when bone marrow transplantation is not considered first line treatment. Treatment of Philadelphia-chromosome-positive chronic myeloid leukaemia in chronic phase after failure of interferon alfa, or in accelerated phase, or in blast crisis. Treatment of newly diagnosed Philadelphia-chromosome-positive acute lymphoblastic leukaemia in combination with chemotherapy

Administration: *Adult*: 400-600mg once daily, increased, if necessary, up to 800 mg daily in 2 divided doses.

Children:
<1 year: Safety and efficacy not established
≥1 year: 340 mg/m²/day PO, not to exceed 800 mg/day

Side effects: Stomach upset, nausea, vomiting, diarrhea, headache, muscle/joint pain, muscle cramps, dizziness, blurred vision, drowsiness, fluid retention, alopecia, anaemia, asthenia, bone marrow disorders, chills, Constipation, cough, diarrhoea, dizziness, dry eye, dry mouth, dyspnea, excessive tearing, eye inflammation, fever, fluid imbalance, flushing, gastrointestinal discomfort.

Contraindications: Hypersensitivity to the active substance or to any of the excipients.

Caution: Cardiac disease, hepatitis B infection, history of renal failure, risk factors for heart failure, Hepatitis B carriers, pregnancy, lactation, renal and hepatic impairment.

INTERFERON

Presentation: Solution for injection, subcutaneous injection, 100mcg, 50mcg80mcg, 120mcg 150mcg 25iu, 18iu

Indications: Chronic myelogenous leukaemia (as monotherapy or incombination with cytarabine), Hairy cell leukemia, Follicular lymphoma, Lymph or liver metastases of carcinoid tumour, Chronic hepatitis B, Chronic hepatitis C, Adjunct to surgery in malignant melanoma, Maintenance of remission in multiple myeloma

Administration: ***Adult:***

Hairy Cell Leukemia: 2 million Units/m² IM/SC 3 times/week for up to 6 months.

Malignant Melanoma: Induction 20 million Units/m² IV over 20 min, 5 days/week for 4 weeks; Maintenance dose: 10 million Units/m² SC 3 times/week for 48 weeks.

Follicular Lymphoma: 5 million units 3 times/week for up to 18 months in conjunction with anthracycline-containing combination chemotherapy in patients >18 years old.

Condylomata Acuminata: 1 million units injected into each lesion 3 times/week every other day for 3week. May repeat course if unsatisfactory results 12-16 week after initial treatment.

AIDS-related Kaposi's Sarcoma: 30 million Units/m² IM/SC 3 times/week for 16 weeks.

Chronic Hepatitis C: 3 million units IM/SC 3 times/week for 16 weeks.

Children:

Chronic Hepatitis B: 3 million Units/m² IM/SC 3 times/week for 1 week, increase to 6 million U/m² 3 times/week SC for 16-24 week, not to exceed 10 million Units/ dose, 3 times/week.

Side effects: Dizziness, pain, redness, or swelling at the point of injection, hair loss , appetite and weight loss, breathlessness and pale skin, predisposition to bruising and bleeding, prone to infection, fatigue, flu-like symptoms, diarrhea, nausea, depression and anxiety, insomnia, sore throat, headache, cough, joint and muscle pain, skin rash

Contraindications: Hypersensitivity, autoimmune hepatitis, decompensated liver disease, combination therapy with ribavirin, pregnant women and men whose female partners are pregnant, hemoglobinopathies, Creatinine clearance less than 50 ml/min.

Caution: Renal impairment, hepatic impairment, effective contraception required during treatment.

IRINOTECAN

Presentation: Injection containing 100mg/5ml Irinotecan.

Indications: Indicated as a component of first line therapy in combination with 5FU and leucovorin for patients with metastatic carcinoma of the colon or rectum. It is also indicated for patients with metastatic carcinoma of the colon or rectum whose disease has recurrent t or progressed following initial 5FU based regimen.

Administration: *Premedicate with antiemetic agents and atropine for cholinergic symptoms*: Use ***Regimen 1*** (6-week cycle with infusional 5-fluorouracil/ leucovorin): 180 mg/m² IV infusion over 30-90 minutes once on days 1, 15, and 29 IV (infuse over 30-90 min), followed by infusion with leucovorin and 5-fluorouracil, next cycle begins on day 43. In ***regimen 2*** (6-week cycle with bolus 5-fluorouracil/ leucovorin): 125 mg/m² on days 1, 8, 15, and 22 (infuse over 90 min), followed by bolus doses of leucovorin and 5-fluorouracil.

Side effects: Alopecia, anaemia (dose limiting), nausea, vomiting, weight loss, reduced appetite, asthenia, cholinergic syndrome, constipation, decreased leucocytes, diarrhoea (delayed diarrhoea requires prompt treatment), dizziness, dysphonia, dyspnea, electrolyte imbalance, embolism and thrombosis, febrile neutropenia (dose- limiting), fever, fluid imbalance, GI disorders, hypoalbuminemia, hypoglycaemia, hypotension, increased risk of infection, infusion related reaction, insomnia, mucositis, neutropenia (doselimiting), oedema, renal impairment, sepsis, stomatitis, altered taste, thrombocytopenia (dose limiting). **Contraindications:** Bowel obstruction. Chronic, inflammatory bowel disease, Pregnancy, lactation.

Cautions: Diarrhoea and cholinergic reactions, myelosuppression, patients with reduced UGTIAI activity, hypersensitivity, renal impairment/renal failure, pulmonary toxicity, embryo-fetal toxicity, hepatic impairment.

LETROZOLE

Presentation: Tablet containing 2.5mg Letrozole.

Indications: First-line treatment in postmenopausal women with hormone-dependent advanced breast cancer; Adjuvant treatment of oestrogen-receptor-positive invasive early breast cancer in postmenopausal women; advanced breast cancer in postmenopausal women in whom other antioestrogen therapy has failed

Administration: 2.5 mg daily

Side effects: Alopecia; abnormal appetite; arthralgia; asthenia; bone fracture; bone pain; constipation; depression; diarrhea; dizziness; headache; hot flush; hypercholesterolemia; hyperhidrosis; hypertension; malaise; myalgia; nausea; oedema; osteoporosis; skin reactions; vaginal haemorrhage; vomiting; weight changes.

Contraindications: Not indicated for pre-menopausal women.

Caution: Susceptibility to osteoporosis

LOMUSATINE

Presentation: Capsule containing 5mg, 10mg, 40mg, 100mg of Lomusatine.

Indications: Brain Tumors, Hodgkin Lymphoma

Administration: ***Adult and Child:***

Brain Tumors, Hodgkin Lymphoma: 120-130 mg/m² PO once every 6weeks. Round dose to nearest 5 mg.

For Compromised bone marrow: 100 mg/m² PO once every 6 weeks.

Side effects: Leucopenia, alopecia, anaemia, apath, appetite, decreased, Azotemia, bone marrow failure, confusion, coordination abnormal, diarrhoea, hepatic disorders, Lethargy, Nausea, Neoplasms, Neurological effects, renal impairment, respiratory disorders. speech impairment, stomatitis, vision loss (irreversible), vomiting**.**

Contraindications: Coeliac disease, hypersensitivity.

Caution: Pregnancy, lactation, renal impairment, hepatic impairment, delayed pulmonary toxicity may occur, acute leukemia and myelodysplasia can occur with long-term use, hepatoxicity may occur, mylosuppression.

MELHALAN

Presentation: Tablet containing 2mg Melhalan; Injection, lyophilized powder for reconstitution containing 50mg.

Indications: Multiple myeloma, Polycythaemia vera, localised malignant melanoma of the extremities, Localised soft-tissue sarcoma of the extremities, ovarian cancer

Administration: *Multiple myeloma:* 150 mcg/kg daily for 4 days, dose to be repeated every 6 weeks OR 6 mg PO daily for 2-3 weeks, OR 10 mg PO daily for 7-10 days, OR 150 mcg/kg daily for 7 days, followed by 1-3 mg OR 0.05 mg/kg PO every day after adequate recovery from hematologic toxicity. For intravenous use: 16 mg/m2 IV q2 weeks for 4 doses, followed by 16 mg/m2 IV q 4 weeks until unacceptable toxicity.

Ovarian cancer: 0.2 mg/kg/day PO for 5 days, repeat every 4-5 weeks depending on hematologic tolerance.

Polycythaemia vera: Initially 6–10 mg daily for 5-7 days, then reduced to 2–4 mg daily until satisfactory response, then reduced to 2–6 mg once weekly repeated every 4-5 weeks.

Side effects: Alopecia. anaemia. bone marrow depression (delayed), diarrhoea, nausea, vomiting, stomatitis. Thrombocytopenia, haemolytic anaemia, hepatic disorders, respiratory disorders, skin reactions, Leucopenia, feeling hot, myalgia, myopathy, paraesthesia use peripheral vascular disease.

Contraindications: Hypersensitivity to melphalan or chlorambucil, prior resistance to melphalan, hepatic periprocedural risks.

Caution: Avoid getting pregnant; could lead to secondary cancers.

MITOMYCIN

Presentation: Powder for Injection containing 5mg, 10mg, 20mg, 40mg Mitomycin.

Indications: Recurrent superficial bladder tumours (bladder instillation); Upper gastro-intestinal cancers; Pancreatic Cancer; Breast cancers; Non-small cell lung cancer

Administration: *Stomach Cancer, Pancreatic Cancer:* 20mg/m² IV q6-8weeks*;*

Bladder Cancer and Breast Cancer (Consult product literature or local protocols).

Side effects: Dyspnoea; extravasation necrosis; glomerulonephropathy; nephropathy; renal impairment, hypersensitivity; urinary disorders; urinary tract discomfort

Contraindications: Hypersensitivity.

Caution: Handle with care. Causes irritation to tissues

PACLITAXEL

Presentation: 300 mg/25ml, equivalent to 6 mg/ml of the IV concentrate.

Indications: Used in treatment of epithelial ovarian cancer, early stage and metastatic breast cancers, Kaposi's sarcoma, nasopharyngeal cancer, non-small cell lung cancer, and ovarian germ cell tumour.

Administration: ***Adults***

First-line treatment of ovarian cancer, by IV infusion: Paclitaxel 175 mg/m^2 BSA administered as an IV infusion over a period of three hours followed by 75 mg/m^2 of cisplatin and the therapy is repeated at 3-week intervals.

Second-line treatment of ovarian cancer, by IV infusion: 175 mg/m^2 administered over 3 hours, with a 3-week interval between courses.

Adjuvant chemotherapy in breast carcinoma, by IV infusion: 175 mg/m^2 administered over a period of 3 hours every 3 weeks for four courses, following AC therapy

First-line chemotherapy of breast carcinoma, by IV infusion:

- When used in combination with doxorubicin (50 mg/m^2), paclitaxel should be administered 24 hours after doxorubicin. A dose of paclitaxel is 220 mg/m^2 administered intravenously over a period of 3 hours, with a 3-week interval between courses.
- When used in combination with trastuzumab, a dose of paclitaxel 175 mg/m^2 is administered intravenously over a period of 3 hours, with a 3-week interval between courses.

Second-line chemotherapy of breast carcinoma, by IV infusion: 175 mg/m^2 is administered over a period of 3 hours, with a 3-week interval between courses

Advanced non-small cell lung cancer, by IV infusion: 175 mg/m^2 is administered over 3 hours followed by 80 mg/m^2 of cisplatin, with a 3-week interval between courses.

AIDS-related KS, by IV infusion: 100 mg/m^2 administered as 3-hour IV infusion every two weeks.

Children:
Not recommended for use in children below 18 years because of the lack of data on safety and efficacy.

Side effects: Bone marrow suppression, neurotoxicity, peripheral neuropathy, myalgia or arthralgia, CME, injection site reactions, Disseminated intravascular coagulation, alopecia.

Contraindications: Severe hypersensitivity reactions to paclitaxel, macrogolglycerol ricinoleate (polyoxyl castor oil) or to any of the excipients. Paclitaxel is contraindicated during breastfeeding. Paclitaxel should not be used in patients with baseline neutrophils <1.5 x 10^9/L (<1 x 10^9/L for KS patients) or platelets <100 x 10^9/L (<75 x 10^9/L for KS patients). In KS, paclitaxel is also contraindicated in patients with concurrent, serious, uncontrolled infections. Patients with severe hepatic impairment must not be treated with paclitaxel.

Caution: Subsequent doses of paclitaxel should be administered according to individual patient tolerance. Paclitaxel should not be re-administered until the neutrophil count is ≥1.5 × 10^9/L (≥1 × 10^9/L for KS.

Pregnancy: Paclitaxel may cause foetal harm when administered to pregnant women.

Breastfeeding: Breastfeeding should be discontinued for the duration of therapy with paclitaxel.

DIETHYLSTILBESTROL (STILBOESTROL)

Presentation: Tablet containing 1mg of Diethylstilbestrol.

Indications: Used in treatment of breast cancer in postmenopausal women and in prostate cancer.

Administration: 10-20 mg daily in breast cancer and 1-3 mg daily in prostate cancer.

Side effects: Bone pain in breast cancer, breast

abnormalities, cervical mucus increased, cholelithiasis, contact lens intolerance, depression, erectile dysfunction, erythema nodosum, feminization, fluid retention, gynaecomastia, headaches, hypercalcaemia (in breast cancer), hypertension, increased risk of thrombosis, jaundice cholestatic, mood altered, nausea, neoplasms, skin reactions, sodium retention, testicular atrophy, uterine disorders, vomiting, weight changes, and withdrawal bleed.

Caution: In first trimester; high doses associated with vaginal carcinoma, urogenital abnormalities, and reduced fertility in female offspring. Increased risk of hypospadias in male offspring. Thromboembolic phenomenon.

ALL-TRANS RETINOID ACID (ATRA) OR TRETINOIN

Presentation: Capsule containing 10 mg and 20mg of Tretinoin.

Indications: Acute promyelocytic leukemia.

Administration: ***Adult***

For all therapy phases: a total daily dose of 45 mg/m^2 BSA divided in two equal doses is recommended for adults and elderly APL patients. This is approximately 8 capsules per adult dose (one capsule contains 10 mg tretinoin).

Children:
The optimal dose of tretinoin has not yet been established. To reduce tretinoin-related toxicity, the daily dose administered to children can be reduced to 25 mg/m^2.

Side effects: Shortness of breath, headache, numbness, depression, skin dryness, itchiness, hair loss, vomiting, muscle pains, and vision changes, high WBC counts, blood clots.

Contraindications: Hypersensitivity to tretinoin, retinoids, soya, peanut or to any of the excipients. Tretinoin is teratogenic. It is contraindicated during breastfeeding.

Caution: Dose reduction should be particularly considered for children with toxicity symptoms, such as intractable headache.

HYDROXYUREA

Presentation: Capsule containing 500mg Hydroxyurea

Indications: Chronic myeloid leukaemia and malignant melanoma

Administration: 30 – 50mg/kg body weight in 2 divided doses

Children:
20 mg/kg orally once a day, increase by 5 mg/kg/day. Maximum dose is 35 mg/kg/day in one or two divided doses.

Side effects: Bone marrow depression, nausea and vomiting, dizziness, confusion, skin rashes and diarrhoea

Caution: Not to be used in pregnancy and patients with renal.

PROCARBAZINE

Presentation: Capsule containing 50 mg Procarbazine as HCl.

Indications: (Adult and Peadiatric) -treatment of Hodgkin lymphomas (In combination Chemotherapeutic regimens)

Administration: 100 mg/m^2 daily on the first 10–14 days in repeated four to six-weekly cycles.

As sole therapeutic agent: start with small doses, increase gradually up to a maximum daily dose of 250 or 300 mg divided throughout the day (1st day - 50 mg, 2nd day - 100 mg, 3rd day - 150 mg, 4th day - 200 mg, 5th day - 250 mg, 6th day and thereafter: 250–300 mg). Continue with 250 or 300 mg daily until the greatest possible remission has been achieved. Then give maintenance dose at 50–150 mg daily, total dose 6 g.

Side effects: Loss of appetite, nausea and vomiting, leucopenia, thrombocytopenia.

Contraindications: Pre-existing severe leucopenia or thrombocytopenia, severe hepatic or renal damage (CrCl less than 10 ml/min) trimester one of pregnancy and during breastfeeding), hypersensitivity to Procarbazine or to any of the excipients.

Caution: used with caution in the elderly, cardiovascular or cerebrovascular disease, phaeochromocytoma, or epilepsy. Suspend treatment temporarily the total white cell count falls to 3,000 per mm3 or the platelet count to 80,000 per mm^3 suspended until the leucocyte and/or platelet levels recover; also interrupted treatment on the appearance of allergic skin reactions.

TAMOXIFEN

Presentation: Tablet containing 10mg tamoxifen. **Indications:** Carcinoma of the breast and prevention in high-risk individuals.

Administration: 10mg twice daily orally.

Side effects: Hot flushes vaginal bleeding, suppression of menstrual bleeding in premenopausal, pruritus valvae, gastrointestinal disturbances, headache, light-headedness, tumour flare, decreased platelet counts, occasionally oedema, alopecia, rashes, uterine fibroids, visual disturbances, leucopenia.

Caution: Occasionally, cystic ovarian swellings in premenopausal women, hypercalcaemia if bony metastases; increased risk of thromboembolic events when used with cytotoxics; breastfeeding, porphyria.

10 Medicines acting on the Eye

Preparations for the eye should be sterile. Single-use containers should therefore never be reused. Combination preparations containing an antibiotic and a steroid should only be used under specialist supervision. They should not be used in undiagnosed "red-eye" which may be caused by a viral infection.

Prescribers are advised to bear in mind the possibility of Medicines which are administered as eye drops being absorbed into the general circulation via conjunctival vessels or from the nasal mucosa after the excess of the preparation has drained down through the tear ducts.

When two different preparations of eye drops are required at the same time of day an interval of a few minutes should be left between the two applications. This is to avoid dilution and overflow. Application of an ointment at night reduces the problem.

FLUORESCEIN SODIUM

Presentation: Single-use sterile eye drops containing 1% or 2% fluorescein sodium.

Indications: Diagnostic agent for detecting corneal abrasions and foreign bodies in the eye. Also used in the fitting of hard contact lenses.

Administration: Sufficient solution should be applied to stain the damaged areas. Excess should be washed away with sterile saline solution.

Side effects: The skin and urine may be transiently coloured.

Caution: Not to be used with soft contact lenses, may cause transient blurring of vision, patients should not drive or operate hazardous machinery until vision is clear.

ACICLOVIR EYE OINTMENT

Presentation: Eye ointment containing 3% aciclovir

Indications: Local treatment of herpes simplex
Administration: Apply five (5) times daily. Continue for at least 3 days after complete healing.

Side effects: Mild stinging immediately after application may occur; local irritation and inflammation have been reported.

Contra-indications: Not to be used with steroids

GANCICLOVIR EYE GEL

Presentation: Eye gel containing 0.15% of Ganciclovir.

Indication: Acute herpetic keratitis

Administration: Apply 5 times a day until healing is complete, then apply 3 times a day for a further 7 days, treatment does not usually exceed 21 days.

Side Effects: Eye stinging, punctate keratitis, visual acuity loss, retinal detachment, vitreous haemorrhage.

Caution: avoid contact lenses during treatment. Women of childbearing potential should use effective contraception during treatment; men with partners of childbearing potential should be advised to use barrier contraception during and for at least 90 days after treatment.

CHLORAMPHENICOL

Presentation: Eye drops containing 0.5% Chloramphenicol, eye ointment containing 1% Chloramphenicol.

Indications: Superficial bacterial infections of the eye.

Administration: *Eye drops;* Instill at least every 2 hours then reduce the frequency as the infection is controlled and continue for 48 hours after healing.

Eye ointment; apply either at night (if eye drops used during the day) or 3 – 4 times daily (if ointment alone used).

Side effects: Transient irritation, burning, stinging, itching and dermatitis. Adverse haematological events (bone marrow depression, aplastic anaemia and death) have been reported following ocular use of chloramphenicol.

Contraindications: Hypersensitivity to chloramphenicol.

Caution: Avoid prolonged use (sensitization and resistance), remove contact lenses during the period of treatment, use only when essential in pregnancy.

TETRACYCLINE

For mass control of communicable ophthalmia, WHO recommends the application of tetracycline eye ointment to both eyes twice daily for 5 days every 4 weeks for 6 months.

TETRACYCLINE HYDROCHLORIDE

Presentation: Eye ointment containing 1% tetracycline hydrochloride.

Indications: Superficial bacterial infections, particularly the treatment of chlamydial infections including trachoma, Prophylaxis of neonatal conjunctivitis.

Administration:

Superficial bacterial infection: 1 application of ointment directly to the eye 3–4 times daily.

Trachoma; 1 application of ointment directly to the eye three times daily for six weeks.

Children:

Prophylaxis of neonatal conjunctivitis

Neonate at birth: As soon as possible after delivery after cleansing eyes with sterile gauze, one application of ointment into each eye; close eyelids

and massage gently to aid spread of ointment.

Superficial bacterial infection and Trachoma

As in Adults.

Side effects: Allergic reactions, irritation, stinging, burning, itching, dermatitis may occur, transient loss of vision.

Contra-indications: Hypersensitivity to tetracycline.

BETAMETHASONE

Presentation: Eye drops, eye ointment containing 0.1% Betamethasone sodium phosphate.

Indications: Local treatment of inflammation (Short term)

Administration: Eye drops: apply every 1 – 2 hours until controlled then reduce frequency. Eye ointment; apply 2 – 4 times daily or at night when used with eye drops.

Side effects: Hypersensitivity reactions (usually of delayed-type) may occur (itching, stinging, irritation, burning and dermatitis) and may result in increased intraocular pressure. Intensive or prolonged use may lead to the formation of posterior subcapsular cataracts.

Contra-indications: Viral, fungal, tuberculosis or purulent conditions of the eye, glaucoma and herpetic keratitis.

DEXAMETHASONE EYE DROPS

Presentation: Eye drops containing 0.1% Dexamethasone

Indications: Local treatment of inflammation, macular oedema, corneal injury from chemical, radiation, thermal burns or foreign body penetration

Administration: Adult: Apply every 30–60 minutes until controlled, then reduced to 4–6 times a day. Child: Apply every 30–60 minutes (in severe cases) until controlled, then reduce frequency when control achieved. In non-severe, Apply 4–6 times a day.

Side Effects: cataracts (prolonged use), glaucoma, optic nerve damage, eye discomfort, photophobia, altered taste.

ContraIndication: Herpes Simplex, mycobacterial eye infection or any fungal disease of the ocular structures

HYDROCORTISONE EYE DROPS

Presentation: Eye drops containing 1%-2.5% of Hydrocortisone

Indications: Local treatment of conjunctival inflammation

Administration: 2 drops 2–4 times a day for up to 14 days, to avoid relapse, frequency may be gradually reduced to once every other day

Side Effects: Eye discomfort/stinging

PREDNISOLONE EYE DROPS

Presentation: Eye drops containg 0.1-1% of Prednisolone

Indication: Ophthalmic inflammatory conditions

Administration: Apply every 1–2 hours until controlled then reduce frequency.

Side Effects: Eye discomfort, taste altered, visual Impairment.

Contraindications: acute untreated purulent ocular infections, viral, fungal, mycobacterial diseases of the cornea and conjunctiva

SODIUM CROMOGLYCATE EYE DROPS

Presentation: Eye drop containing 2% of Sodium Cromoglycate

Indications: Allergic conjunctivitis and seasonal keratoconjuctivitis

Administration: Apply 4 times a day

Side Effects: Eye discomfort such as stinging, burning, dryness, itchness, watery eyes, rash, dyspnea (in anaphylactic reactions)

Caution: Do not wear contact lenses during treatment.

PILOCARPINE HYDROCHLORIDE

Presentation: Eye drops containing 0.5%, 1%, 2%, 3%, 4% Pilocarpine hydrochloride.

Indications: Glaucoma

Side effects: Small pupil, sweating, bradycardia, hypersalivation, bronchospasm and intestinal colic **Administration:** *Induction of miosis;* 1- 2 drops.

Emergency treatment of acute narrow-angle glaucoma; 1 drop every 5 minutes until miosis is achieved.

Caution: Use only when essential in pregnancy and lactation. Do not drive or machinery until the vision is clear.

TIMOLOL MALEATE

Presentation: Eye drops containing 0.25%, 0.5%

of Timolol maleate

Indications: Chronic simple glaucoma. **Administration:** Apply twice daily

Side effects: Transitory dry eyes, skin rashes.

Contraindications: In patients with bradycardia, heart failure, heart block, bronchial asthma, chronic obstructive pulmonary disease, hypersensitivity to timolol or other beta-blockers.

Caution: Concomitant use with Medicines like verapamil and other beta-blockers.

ATROPINE SULPHATE

Presentation: Eye drops, eye ointment containing 1% Atropine sulphate.

Indications: As a mydriatic and cycloplegic used in refraction procedures in young children.
Administration: 1 drop three times daily

Side effects: Contact dermatitis, toxic systemic reactions may occur in the very young and very old.

Caution: Patients advised not to drive for one or two hours after mydriasis

Contraindications: In narrow-angle glaucoma, soft contact lenses.

CYCLOPENTOLATE HYDROCHLORIDE

Presentation: Eye drops containing 0.5%, 1%, 2% of Cyclopentolate Hydrochloride

Indications: Cycloplegia, Uveitis

Administration: *Cycloplegia:* Apply 1 drop, 30–60 minutes before examination, using 1% eye drops.

Uveitis: Apply 1 drop 2–4 times a day, using 0.5% eye drops (1% for deeply pigmented eyes).

Side Effects: In children: Abdominal distension, Arrhythmias, behaviour abnormal, cardiorespiratordistress, psychotic disorder.

On prolonged administration: conjunctivitis, Constipation, dry mouth, eye oedema, flushing, gastrointestinal disorders, hyperaemia, mydriasis, palpitations, staggering, urinary disorders, vomiting.

Contraindication: Hypersensitivity

Caution: In elderly, may cause increased intraocular pressure

TROPICAMIDE

Presentation: Eye drop containing 0.5% or 1% of Tropicamide

Indication: Fundoscopy and Refraction

Administration: 1-2 drops of 0.5% (for fundoscopy) and 1% (for Refraction) in the eyes, repeat in 5 minutes and perform exam within 30minutes of second instillation.

Side Effects: Eye erythema, eye irritation (on prolonged administration), eye pain, headache, hypotension, nausea, syncope, vision blurred.

Contraindications: Angle closure glaucoma.

Caution: in hypertension, diabetes, hyperthyroidism and cardiac disorders

HOMATROPINE HYDROBROMIDE

Presentation: Eye drops containing 1%, 2% Homatropine hydrobromide.

Indications: Mydriatic and cycloplegic
Administration: 1 drop as required.

Side effects: As for atropine sulphate above.

Contraindications: As for atropine, not to be used in patients hypersensitive to atropine.

ACETAZOLAMIDE

Presentation: Tablet containing 250mg acetazolamide, injection (iv) containing 500mg acetazolamide as the sodium salt.

Indications: Tablets; glaucoma of all types; Injection; used in the pre-operative treatment of closed-angle glaucoma.

Administration: Orally or intravenous injection 0.25 – 1g daily in divided doses.

Side effects: Diuresis and hypokalaemia, appetite loss, drowsiness and depression.

BETAXOLOL HYDROCHLORIDE

Presentation: Eye drops containing 0.5% Betaxolol hydrochloride

Indications: Treatment of chronic simple glaucoma.

Administration: Apply twice daily

Side effects: May be absorbed systemically, so side effects of beta-blockers may be experienced, transitory dry eyes.

Contraindications: In bradycardia, heart block or heart failure. In asthma, history of obstructive airways disease, unless no alternative treatment is available.

Caution: In concomitant use with Medicines such as verapamil

GENTAMICIN EYE DROPS

Presentation: Eye/eardrops containing 0.3% Gentamicin sulphate.

Indications: Blepharitis; bacterial conjunctivitis.

Administration: *Mild to moderate infection,* by instillation into the eye, adult and child 1 drop every 2 hours, reducing frequency as the infection is controlled, then continue for 48 hours after healing is complete.

Severe infection, by instillation into the eye, Adult and Child 1 drop every hour, reducing frequency as the infection is controlled, then continue for 48 hours after healing is complete

Side effects: Burning, stinging, itching, dermatitis.

Contraindications: Hypersensitivity to aminoglycoside group of antibiotics.

Caution: Prolonged use may lead to skin sensitization and emergence of resistant organisms including fungi; discontinue if purulent discharge, inflammation or exacerbation of pain.

CIPROFLOXACIN EYE DROPS

Presentation: Eye drop containing 0.3% of Ciprofloxacin

Indications: Superficial bacterial eye infection and corneal ulcers

Administration: ***Adult and Children***

Superficial bacterial eye infection: Apply 4 times a day for maximum duration of treatment 21 days.

Corneal Ulcers: Apply every 15 minutes for 6 hours, then apply every 30 minutes for the remainder of day 1, then apply every 1 hour on day 2, then apply every 4 hours on days 3–14, maximum duration of treatment 21 days, to be administered throughout the day and night in both Adult and Children.

Side Effects: Corneal deposits, ear pain, eye burning, stinging, conjunctival hyperemia.

Caution: Hypersensitivity to quinolones, risk of anaphylaxis. Remove contact lenses during treatment.

LIGNOCAINE HYDROCHLORIDE

Presentation: Eye drops containing 4% Lignocaine hydrochloride, fluorescein sodium 0.25%.

Indications: Short-acting local anaesthesia of cornea and conjunctiva.

Administration: *Adult and Child*: Local anaesthesia 1 drop by instillation into the eye.

Side effects: Burning, stinging, redness; rarely, allergic reactions may occur.

Caution: Avoid prolonged use (cause of severe keratitis, permanent corneal opacification, scarring, delayed corneal healing); protect the eye from dust and bacterial contamination until sensation fully restored.

OFLOXACIN EYE DROPS

Presentation: Eye drops containing 0.3% solution (3 mg/ml) Ofloxacin.

Indications: Treatment of only bacterial eye infections. It does not work for other types of eye infections. Unnecessary use or overuse of any antibiotic can lead to its decreased effectiveness

Administration: *Bacterial Conjunctivitis*; Days 1 – 2: 1 - 2 drops in the affected eye every 2 – 4 hours; then days 2-7: 1-2 drops 4 times daily.

Side effects: This medication may temporarily sting or burn your eyes for a minute or two when applied. Temporary blurred vision, eye discomfort, itching, redness, dryness, tearing, feeling as if something is in your eye, or sensitivity to light may occur. If any of these effects persist or worsen, notify your doctor or pharmacist promptly.

Contraindications: Hypersensitivity reactions
Caution: Serious and occasionally fatal hypersensitivity (anaphylactic) reactions

POVIDONE EYE DROPS

Presentation: Eye drops containing 5% in 0.4 mls unit dose.

Indications: Indicated for cutaneous peri-ocular and conjunctival antisepsis before ocular surgery to support post-operative infection control. Dry eye conditions

Administration: Apply 4 times daily or as required. Gently instill 2 to 3 drops of the solution onto the eye/eyes. Allow the solution to spread, by asking the patient to close their eyes and roll their eyes around. Leave the drops on the eye/eyes for two minutes before rinsing.

Side effects: Consult your pharmacist or physician

Caution: Consult your pharmacist or physician

Contraindications: Hypersensitivity to iodinated povidone, to iodine or any of the excipients.

NATAMYCIN EYE SUSPENSION

Presentation: 5% sterile suspension for topical ophthalmic administration. Each ml of the suspension contains: Active: Natamycin 5% (50mg)

Indications: Treatment of fungal blepharitis, conjunctivitis, and keratitis caused by susceptible organisms including *Fusarium solani* keratitis

Administration: The preferred initial dosage in fungal keratitis is one drop of Natamycin ophthalmic suspension 5% instilled in the conjunctival sac at hourly or two-hourly intervals. Frequency of application can usually be reduced to one drop 6 to 8 times daily after the first 3 to 4 days. Therapy should generally be continued for 14 to 21 days or until there is a resolution of active fungal keratitis. In many cases, it may be helpful to reduce the dosage gradually at 4 to 7-day intervals to assure that the replicating organism has been eliminated. Less frequent initial dosage (4 to 6 daily applications) may be sufficient in fungal blepharitis and conjunctivitis.

Side effects: Allergic reaction, change in vision, chest pain, corneal opacity, dyspnea, eye discomfort, eye oedema, eye hyperemia, eye irritation, eye pain, foreign body sensation, paresthesia, and tearing.

Contraindications: Contraindicated in individuals with a history of hypersensitivity to any of its components.

Caution: Failure of improvement of keratitis following 7-10 days of administration of the drug suggests that the infection may be caused by a microorganism not susceptible to natamycin.

AZITHROMYCIN EYE DROPS

Presentation: 2.5 ml of a 1% sterile topical ophthalmic solution

Indications: Treatment of bacterial conjunctivitis caused by susceptible isolates of the following microorganisms: *Haemophilus influenzae, Staphylococcus aureus, Streptococcus mitis group, Streptococcus pneumonia*.

Administration: Instill 1 drop in the affected eye(s) twice daily, eight to twelve hours apart for the first two days and then instil 1 drop in the affected eye(s) once daily for the next five days

Side effects: Eye irritation, blurred vision, burning, stinging and irritation upon instillation, contact dermatitis, corneal erosion, dry eye, eye pain, itching, ocular discharge, punctate keratitis, visual acuity reduction) and non-ocular reactions (dysgeusia, facial swelling, hives, nasal congestion, periocular swelling, rash, sinusitis, urticaria).

Contraindications: Hypersensitivity to any component of this product.

Caution: Topical Ophthalmic Use Only

CHLORAMPHENICOL + DEXAMETHASONE EYE DROPS

Presentation: Solution containing 1% Chloramphenicol + 0.5% Dexamethasone, 5 ml

Indications: For steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where bacterial infection or a risk of bacterial ocular infection exists.

Administration: 1 or 2 drops is instilled into the affected eyes every 3 or 4 hours, or more frequently if deemed advisable by the prescribing physician. The administration should be continued day and night for the first 48 hours, after which the interval between applications may be increased. Treatment should be continued for at least 48 hours after the eye appears normal.

Side effects: Adverse reactions seen with Chloramphenicol are transient ocular burning or discomfort. Other reported reactions include stinging, redness, itching, conjunctivitis/ keratitis, periocular/facial oedema, foreign body sensation, photophobia, blurred vision, tearing, dryness and eye pain.

Contraindications: It is contraindicated in fungal, viral, tuberculous and other infections of the eye and glaucoma. It is also contraindicated in patients hypersensitive to any component of this product. The use of anti-infective and steroid is always contraindicated after uncomplicated removal of a corneal foreign body.

Caution: Dexamethasone and Chloramphenicol

Eye drops must be used under strict medical supervision because of the possibility of inducing corneal abscess, fungal keratopathy or glaucoma. The patient should be referred to an ophthalmologist if the eye has not responded within 48 hours.

LATANOPROST EYE DROPS

Presentation: Eye drops containing 50mcg/ ml of Latanoprost.

Indications: Treatment of high pressure inside the eye due to glaucoma (open-angle type) or other eye diseases (e.g., ocular hypertension). It is similar to a natural chemical in the body (prostaglandin) and works by regulating the flow of fluid within the eye which results in lower pressure. Lowering high pressure inside the eye helps to prevent blindness.

Administration: Apply this medication in the affected eye(s) usually once daily in the evening, or as directed by your doctor. Do not use this medication more frequently than prescribed; using more can decrease effectiveness.

Side effects: Burning/stinging/itching/redness of the eye, feeling as if something is in the eye, changes in eyelash number/colour/length/ thickness, eyelid changes, skin darkening, dry eye, lid crusting/discomfort, or increased sensitivity to light may occur.

Contraindications: Some products that may interact with this drug are: eyelash treatment (such as topically applied bimatoprost).

Caution: Vision may be temporarily blurred or unstable after applying this drug. Do not drive, use machinery, or do any activity that requires clear vision until you are sure you can perform such activities safely.

DIPIVEFRINE EYE DROPS

Presentation: Ophthalmic Solution, USP 0.1% sterile

Indications: Indicated as initial therapy for the control of intraocular pressure in chronic open-angle glaucoma.

Administration: One drop in the eye(s) every 12 hours.

Side effects: Arrhythmias and hypertension have been reported with ocular administration of epinephrine, eye pain, mydriasis, blurry vision, eye pruritus, headache and allergic reaction.

Contraindications: Should not be used in patients with narrow angles since any dilation of the pupil may predispose the patient to an attack of angle-closure glaucoma. Contraindicated in patients who are hypersensitive to any of its components. **Caution:** Macular oedema has been shown to occur in up to 30% of aphakic patients treated with epinephrine. Discontinuation of epinephrine generally results in reversal of the maculopathy.

HYPROMELLOSE EYE DROPS

Presentation: Eye drops containing 0.3% w/v Hypromellose.

Indications: Treatment of keratoconjunctivitis sicca accompanying rheumatoid arthritis, xerophthalmias or keratitis or during gonioscopy procedures. It is also used to moisten hard contact lenses and to lubricate artificial eyes and also used to relieve dry, irritated eyes.

Administration: One or two drops topically instilled into the eye three times daily as needed, or as directed by a physician.

Side effects: Vision blurred, eye pain, foreign body sensation in eyes, eye irritation and redness of the eye.

Contraindications: Hypersensitivity to the active substance, Hypromellose or any of the excipients.

Caution: Do not drive, use machinery, or do any activity that requires clear vision until you are sure you can perform such activities safely.

MANNITOL SOLUTION

Presentation: Solution in water containing 20% Mannitol.

Indications: Used to reduce swelling and pressure inside the eye

Administration: 100 ml of 20% Mannitol is given by i.v between 30 and 60 minutes before surgery.

Side effects: Allergic reaction: hives; difficult breathing; swelling of your face, lips, tongue, or throat, increased thirst or urination, confusion, vomiting, constipation, muscle pain or weakness, leg cramps, bone pain, lack of energy, irregular heartbeats, tingly feeling.

Contraindications: Contra-indicated in the first 24 hours following head trauma.

Caution: Avoid using within 24 hours following head injuries

11 Blood Products

11.1 Anti-coagulants

Anticoagulants are of little value in the prevention of arterial thrombosis. However, they are useful in the management of venous thromboembolism. Anticoagulant therapy carries the risk of haemorrhage which is increased in the following circumstance: severely ill patients taking other medicines such as phenylbutazone, aspirin, salicylates and clofibrate concomitantly. Care should be taken with patients who are also taking glutethimide or phenobarbitone, as these Medicines accelerate the degradation of the anticoagulants and the dose needs to be re-adjusted if they are withdrawn.

HEPARIN

Presentation: Injection containing Heparin 1000, 5000, 25000 units/ml.

Indications: Disseminated intravascular coagulation, prevention of postoperative thrombosis, deep-vein thrombosis.

Administration: *Adults:*

By intravenous injection; loading dose of 5000 units followed by continuous infusion of 1000 units every hour over 24 hours.

By subcutaneous injection;

Prophylaxis of deep-vein thrombosis, 5 000 units 2 hours before surgery, then every 8 to 12 hours until the patient is ambulant.

In pregnancy; 10 000 units every 12 hours.

Treatment of deep vein thrombosis; initially 10 000 to 20 000 units every 12 hours or 2500 units/10kg every 12 hours, adjusted daily by laboratory monitoring.

Children:

Treatment of deep-vein thrombosis and pulmonary embolism, by IV injection:

Neonate to Child 1 year: initially 75 units/kg (50 units/kg if < 35 weeks corrected age), then *by continuous IV infusion*, 25 units/kg/hour, adjusted according to APTT or anti-Factor Xa.

1–12 years: initially 75 units/kg, then *by continuous IV infusion* 20 units/kg/hour, adjusted according to APTT or anti-Factor Xa.

By SC injection:

1 month–12 years: 250 units/kg every 12 hours adjusted according to APTT or anti-Factor Xa.

Prophylaxis in general surgery, *by SC injection:*

1 month–12 years: 100 units/kg (maximum 5000 units) twice daily, adjusted according to APTT or anti-Factor Xa.

Side effects: Haemorrhage, thrombocytopenia, hyper sensitisation, osteoporosis after prolonged use, alopecia.

Caution: Partial thromboplastin time should be monitored, care is necessary for patients with severe hypertension or recent history of cerebral thrombosis.

Contraindications: Haemophilia and other haemorrhagic disorders, peptic ulcer, severe hypertension, severe liver disease.

ENOXAPARIN

Presentation: Injection containing 100 mg/ml Enoxaparin sodium

Indications: Treatment of thromboembolism in pregnance, (BNF), Prophylaxis of Deep Vein Thrombosis and Treatment of Acute Deep Vein Thrombosis

Administration: 40 mg by subcutaneous injection once a day (with the initial dose given 2 hours before surgery) in patients undergoing abdominal surgery who are at risk for thromboembolic complications. The usual duration of administration is 7 to 10 days.

Deep vein thrombosis with or without pulmonary embolism, SC injection: 1 mg/kg every 12 hours.

Children:
Specialist use only

Side effects: Upset stomach, fever, irritation or burning at the site of injection, bleeding, anaemia (not having enough healthy red blood cells) swelling in your legs

Caution: Used with care in patients with a bleeding diathesis, uncontrolled arterial hypertension or a history of recent gastrointestinal ulceration, diabetic retinopathy, renal dysfunction and haemorrhage.

WARFARIN SODIUM

Presentation: Tablet containing 1mg, 3 mg,4mg and

5mg Warfarin sodium.

Indications: Prophylaxis and treatment of venous thrombosis and thromboembolism in rhematic heart disease

Administration: Initially 5 –10mg depending on prothrombin time reported as INR, maintenance doses according to prothrombin time.

Children (under specialist advice):
200 micrograms/kg (maximum 10 mg) as a single dose on day 1, then 100 micrograms/kg (maximum 5 mg) once daily.

Side effects: Urticaria, haemorrhage from any organ in the body.

Contraindications: Early and late pregnancy, peptic ulcer, severe hypertension.

Caution: Hepatic or renal disease, monitor prothrombin time.

To consider other enoxaparin like products

11.2 Anti-haemorrhagics

AMINO-CAPROIC ACID

Presentation: Tablet containing 500mg Aminocaproic acid. Syrup containing 250/500mg/ml Aminocaproic acid. An injection containing 5g/20ml per dilution and 24g/96ml for infusion.

Indications: Treatment and prophylaxis of haemorrhage due to excessive fibrinolysis

Administration: Oral or slow intravenous infusion; 4 – 5g initially followed by 1 – 1.25g every hour for up to 8 hours. If treatment is necessary for more than 8 hours then the total dose should not exceed 30g over 24 hours. Dosage should be reduced in patients with renal impairment

Side effects: Gastrointestinal disturbances (dose-related), dizziness, tinnitus, headache, generalized thrombosis, nasal and conjunctival congestion and skin rashes. Hypotension, bradycardia and arrhythmias may occur when aminocaproic acid is given by rapid intravenous injection or infusion

Caution: Renal or cardiac impairment, when treatment is prolonged, it is advisable to monitor creatine phosphokinase value for signs of muscle damage. Oral contraceptives increase the probability of hypercoagulability.

ETAMSYLATE

Presentation: Tablet containing 250mg and 500 mg; Injection containing 250mg/2ml Etamsylate.

Indications: Hemorrhage, menorrhagia and treatment and prevention of periventricular hemorrhage in low birth neonates.

Administration:

Menorrhagia - The recommended dose is 500 mg 4 times/day during menstruation.

Control of hemorrhage after surgery - The recommended dose is 250-500 mg 4-6 hourly as needed.

Presurgical: 250-500mg IV/IM 1 hour before surgery.

Peri-surgical: 250-500mg IV. Repeat the dosage if necessary.

Postsurgical: 250-500mg IV/IM every 4-6 hours as long as the risk of bleeding persists.

Emergency cases: according to the severity of the case: 250-500mg IV/IM every 4-6 hours as long as the bleeding risk persists.

Children:
12.5mg/kg every 6hrs

Side effects: Nausea, headache, transient hypotension,

Contraindications: Hypersensitivity and porphyria.

Caution: Exclude structural or histological causes of menorrhagia, or fibroids causing distortion of the uterine

cavity, before initiating treatment.

TRANEXAMIC ACID (TXA)

Presentation: Solution for injection containing Tranexamic acid 100 mg/ml; Tablet containing 250mg and 500mg Tranexamic Acid.

Indication: Short-term use to reduce or prevent haemorrhage; It is indicated for women of reproductive age and is not indicated for use in premenarchal females.

Administration:

Dental extraction:

10mg/kg IV immediately before surgery or 10mg/kg IV every 6-8hr 1 day before surgery, then 10 mg/kg IV 3 or 4 times daily for 2 to 8 days.

OR 25mg/kg PO every 6-8 hr 1-day presurgery and 2-8 days postsurgery.

Menorrhagia

500-1000 mg PO three times daily for a maximum of 5 days during monthly menstruation. Do not exceed 3 doses in 24 hours or take for more than 5 days per menstrual cycle.

Local fibrinolysis, Epistaxis:

500-1500 mg PO three times daily for a maximum of 7 days.

Postpartum Hemorrhage (PPH):

If oxytocin and other uterotonics fail to stop the bleeding or if it is thought that the bleeding may be partly due to trauma, give 1 g IV slowly over 10 minutes, repaeat after 30 minutes if bleeding continues.

Give in all cases of PPH, regardless of whether the bleeding is due to genital tract trauma or other causes within 3 hours and as early as possible after onset of PPH; Fixed dose of 1 g in 10 ml (100 mg/ml) IV at 1 ml per minute (i.e., administered over 10 minutes) Second dose of 1 g IV if bleeding continues after 30 minutes or if bleeding restarts within 24 hours of completing the first dose.

Side effects: Visual abnormalities, hypotension (with rapid administration)**,** Nausea, vomiting, diarrhea, allergic dermatitis and giddiness.

Contraindications: Tranexamic acid is contraindicated in patients with known tranexamic acid hypersensitivity, Acquired defective color vision, subarachnoid hemorrhage and active intravascular clotting.

Cautions: Tablets should be swallowed whole and not chewed or broken apart. To avoid hypotension, administer at a rate not to exceed 100 mg (1 ml) per minute. May be administered together with replacement therapy. Prepare the same day the solution is to be used; discard any remaining solution after single-use. May be mixed with most solutions for infusion such as electrolyte, carbohydrate, amino acid, and dextran solutions. Use with caution in renal impairment, subarachnoid hemorrhage, DIC.

FIBRINOGEN

Presentation: Dry or freeze-dried powder for reconstitution containing fibrinogen concentrate alone or in combination with other factors such as Human factor III, thrombin or human albumin. When reconstituted the preparation will contain not less than 60g/ litre of clottable protein. **Indications:** Control of haemorrhage associated with low blood fibrinogen concentration.

Administration: Consult Haematologist.

Side effects: Chills, cough, headache, hypersensitivity, pallor, skin reactions, vomiting, asthma, dizziness, embolism and thrombosis, feeling hot, night sweats, tinnitus cautions, risk of thrombosis, vaccination against hepatitis A and hepatitis B may be required.

HUMAN ANTI-HAEMOPHILIAC FRACTION (FACTOR VIII)

Presentation: Freeze-dried concentrate containing 3 units/ml and not less than 0.1 units/mg of total protein when dissolved. It is also available in 250IU, 750IU, 1000IU, 3000IU, and 6000IU.

Indications: Control of haemorrhage in haemophilia A including those undergoing surgery such as dental or general surgery.

Administration: *Adult and Children:*

Treatment of bleeding; administer every 8, 12 or 24 hours. Start treatment as soon as possible (optimimally within 2 hourss): 20-30 IU/kg (1-2 days in case unsatisfactory), 25IU/kg for dental extraction once before a procedure.

Bleeding to lower wall oral cavity and to the neck, GIT, or surgical procedure; 40-50 IU/kg for 1-7 days after onset of bleeding. For long term use, 25-30IU/kg every 48 hours.

Dose (in units) = weight (kg) x 0.5 x % desired increase of (normal) plasma concentration of factor VIII.

Children: same dose/administration as in adults.

Side effects: Headache, tachycadia, chills, blurred vision, samnolence. Allergic reactions including chills and fever. Hyperfibrinogenaemia may occur after massive doses with factor VIII products. This is less likely with newer products whose fibrinogen content has been reduced.

Contraindications: Hypersensitivity

Caution: Intravascular haemolysis may occur with large or frequently repeated doses in patients with blood group A, B, or AB. This is less likely to occur with high potency concentrates. Administer at a rate <10ml/ minute, watch out thrombolytic events.

FACTOR IX FREEZE DRIED CONCENTRATE

Presentation: Powder for solution for infusion available in 250IU, 500IU, 1000 IU.

Indications: Haemophilia B

Administration: ***Adults & Children***

Modereate to severe Hemophilia B; Treatment of bleeding; administer every 12, 18 or 24 hours. The dose may vary also depending on the site involved;

Bleeding to joints and/or muscle, epistaxis, gingiva: 40-60 IU/kg for 1-2 days. Higher doses of 60-80 IU/kg are required for bleeding to lower wall of oral cavity and neck; GIT.

Only 40IU/kg once before dental extraction.

For long term prophylaxis treatment 25-50 IU/ kg 2-3 times a week.

Side effects: Allergic reactions, including chills, fever, back pain, nausea, dizziness, rash, taste perversion, IV site cellulitis, dry cough, renal infarct.

Contraindications: Disseminated vascular coagulation, Hypersensitivity to products or its excipients and signs of fibrinolysis.

Caution: Risk of thrombosis, hypersensitivity reactions including anaphylaxis, nephrotic syndrome, thromboembolic complications

PHYTOMENADIONE (VITAMIN K)

Presentation: Injection containing 10mg/ml Phytomenadione. Tablet (sugar-coated) containing 10mg Phytomenadione.

Indications: Vitamin K deficiency particularly in neonates and also in liver disease. Reversal of effects of anti-coagulants.

Administration: ***Adults:***

Antagonist to warfarin, no bleeding or minor bleeding: 500 mcg IV; OR up to 5 mg orally.

Moderate haemorrhage: 10–20 mg PO/IM

Severe haemorrhage, by slow IV injection: 5–10 mg.

Liver disease: 1-2mg repeated as desired.

Children:

Neonatal prophylaxis: 1mg IV immediately after birth.

Reversal of warfarin anticoagulation if no significant bleeding:

15–30 micrograms/kg IV (max. per dose 1 mg) for 1 dose, repeated as necessary.

Significant bleeding:

250–300 micrograms/kg IV (max. per dose 10 mg) for 1 dose.

Side effects: Shock-like reactions, cyanosis, bronchospasm, rapid pulse, pain and swelling at the injection site.

Caution: Pregnancy, store in the dark, do not use if the separation has occurred or oil droplets have appeared. To be given it slowly.

PROTAMINE SULPHATE

Presentation: Injection containing 10mg/ml Protamine sulphate.

Indications: To counteract the anticoagulant effect in heparin overdosage.

Administration: By intravenous injection over 10 minutes: 1mg neutralises 100 units heparin when given within 15 minutes. Maximum dose 50mg.

Side effects: Flushing, hypotension, bradycardia, dyspnoea

Caution: Those at increased risk of allergy to protamine including previous treatment with protamine insulin, allergy to fish, infertile male or those who have had a vasectomy.

11.3 Thrombolytic Medicines

ALTEPLASE

Presentation: Powder for injection containing 50 mg Alteplase.
Indications: Acute myocardial infarction.
Administration: ***Adults****:*

Acute myocardial infarction**,** IV injection: 10mg to be initiated within 6–12 hours of symptom onset, followed by (by IV infusion) 50 mg, to be given over 60 minutes, then (by intravenous infusion) 10 mg for 4 infusions. Each 10mg infusion dose to be given over 30 minutes, total dose of 100mg over 3 hours; maximum 1.5 mg/kg in patients less than 65kg.

Acute myocardial infarction, accelerated regimen, IV injection:

Body weight up to 65 kg: Initially 15 mg, to be initiated within 6 hours of symptom onset, followed by (by intravenous infusion) 0.75 mg/kg, over 30 minutes, then 0.5 mg/kg, to be given over 60 minutes, maximum total dose of 100mg administered over 90 minutes.
Body weight 65 kg and above: Initially 15 mg, to be initiated within 6 hours of symptom onset, followed by (by intravenous infusion) 50 mg to be given over 30 minutes, then 35mg over 60 minutes, maximum total dose of 100mg administered over 90 minutes.

Children:

Limited data available for acute myocardial infarction.

Side effects: Hypotension, Intracranial hemorrhage, Pulmonary embolism, Pulmonary edema, Arterial embolism, Bruising, Hypotension, DVT, Intracranial haemorrhage.

Contraindications: Recent delivery, history of hypersensitivity to gentamicin (residue from manufacturing process). Active internal bleeding, history of recent stroke, ischemic stroke within 3 months except when within 4.5 hr, bleeding diathesis, aortic dissection, current severe uncontrolled hypertension, Recent (within 3 months) brain injury or facial trauma intracranial or intraspinal surgery or serious head trauma, presence of aneurysms, current severe uncontrolled hypertension, prior intracranial haemorrhage.
Cautions: Concurrent use with other anticoagulants should be avoided. Use caution in recent major surgery, severe hepatic/renal dysfunction acute pericarditis, hemostatic defects, severe thrombophlebitis, cerebrovascular disease, hypertension.

RALTEPLASE

Presentation: Powder for injection containing 18mg/10 ml.

Indications: Acute Myocardial Infarction

Administration: *Adults:*

Acute Myocardial Infarction, IV injection: 10units IV bolus (over 2 minutes), followed by a second dose given 30 minutes after first (for total cumulative dose of 20 units). Treatment should be initiated after onset of acute myocardial infarction. Give each bolus injection via an intravenous line in which no other medication is being simultaneously injected or infused.

Children:
No information available.

Side effects: Anemia, cholesterol embolization, gastrointestinal bleeding, Cardiogenic shock, pain intracranial hemorrhage, cardiac reinfarction
Contraindications: Hypersensitivity, recent cardiovascular event, uncontrolled hypertension, bleeding, recent intracranial or intraspinal surgery or trauma, intracranial neoplasm.

Cautions: recent major surgery, cute pericarditis, hemostatic defects, severe thrombophlebitis, patients on oral anticoagulants, diabetic hemorrhagic retinopathy. elderly
Hepatic impairment: Avoid use in severe dysfunction.

Renal impairment: Use with caution in <10 GFR (ml/min).
Pregnancy: Use with caution, if benefits outweighs the risk.
Breastfeeding: Limited information. Not known whether drug crosses into breast milk.

TENECTEPLASE

Presentation: Injection containing 10,000 units (50 mg) tenecteplase with diluent in pre-flled syringe containing 10ml water for injection.

Indications: Acute MI with persistent ST elevation or recent left bundle branch block.

Administration: ***Adult***

By IV injection*:* 30–50 mg (max. per dose 50 mg, i.e., 10,000 units), dose to be given over 10 seconds and initiated within 6 hours of symptom onset according to body weight.

Children:
No or insufcient experience in children and adolescents, therefore its use is not recommended.

Side effects: Anaphylaxis, drowsiness, hemiparesis, venous thrombosis, haemorrhage, reperfusion arrhythmias, embolism, epistaxis, ecchymosis, hypotension, angina, recurrent ischaemia, cardiac failure, MI, cardiogenic shock, pericarditis, pulmonary oedema, cardiac arrest, mitral valve incompetence, pericardial efusion, cardiac tamponade, myocardial rupture, pulmonary embolism.

Contraindications: Hypersensitivity to tenecteplase or any of its excipients or gentamicin (a trace residue from the manufacturing process),Signifcant bleeding disorder either at present or within the past 6 months, Patients receiving oral anticoagulant treatment, any history of CNS neoplasm, aneurysm, known bleeding diathesis,

severe uncontrolled hypertension, major surgery, biopsy of a parenchymal organ, or signifcant trauma within the past 2 months (this includes any trauma associated with the current AMI), Prolonged cardiopulmonary resuscitation (> 2 minutes) within the past 2 weeks, Acute pericarditis and/or subacute bacterial endocarditis, Acute pancreatitis, Severe hepatic dysfunction, active peptic ulceration, Arterial aneurysm and known arterial/venous malformation, neoplasm with increased bleeding risk, any known history of haemorrhagic stroke or stroke of unknown origin, known history of ischaemic stroke or transient ischaemic attack in the preceding 6 months, dementia.

Cautions: Advanced age, i.e., over 75 years. In the following conditions, the risk of tenecteplase therapy may be increased and should be weighed against theanticipated benefts: Systolic blood pressure > 160 mm Hg, Cerebrovascular disease, Recent GI or genitourinary bleeding (within the past 10 days), High likelihood of left heart thrombus, e.g., mitral stenosis with atrial fibrillation, any known recent (within the past 2 days) IM injection, Low body weight < 60 kg, Patients receiving oral anticoagulants. Breastfeeding: Avoid breastfeeding for 24 hours after dose (express and discard milk during this time).

11.4 Antiplatelets

ACETYLSALICYLIC ACID (ASPIRIN)

Presentation: Tablet containing 75mg Acetylsalicylic acid.

Indication: Prophylaxis of cerebrovascular disease or myocardial infarction.

Administration: A low dose of aspirin is used for secondary prevention of thrombotic cerebrovascular or cardiovascular disease. 150-300mg is given after myocardial infarction and 300mg is given after ischaemic (not haemorrhagic) stroke. The initial dose is followed by maintenance treatment with Acetylsalicylic acid 75 – 300mg daily. A low dose of aspirin is also of benefit in the primary prevention of vascular events when the estimated 10-year coronary heart disease risk is 15% or greater and provided that blood pressure is controlled. A low dose of aspirin (75100mg) is also given following coronary bypass surgery.

Side effects: Bronchospasm; gastro-intestinal haemorrhage (occasionally major).

Contraindications: children under 12 years, first trimester pregnancy, and in breastfeeding, active peptic ulceration, haemophilia and other bleeding disorders.

Caution: Asthma; uncontrolled hypertension; pregnancy.

CLOPIDOGREL

Presentation: Tablet containing 75mg Clopidogrel.

Indications: Prevention of atherothrombotic events in percutaneous coronary intervention, in peripheral arterial disease, MI, in acute coronary syndrome, in atrial fibrillation, in risk of a vascular event (usually as an adjunct to Aspirin); also, in Transient ischaemic attack and in acute ischaemic stroke for patients with aspirin hypersensitivity.

Administration: ***Adult***

Usual Dose: 75mg once daily.

Prevention of atherothrombotic events in percutaneous
coronary intervention (adjunct with aspirin):
Loading dose 300 mg, to be taken prior to the procedure; alternatively loading dose 600 mg; higher
dose may produce greater and more rapid inhibition of platelet aggregation.

Prevention of atherothrombotic events in acute coronary syndrome without ST-segment elevation (given with aspirin):

Initially 300 mg, then 75 mg daily for up to 12 months.

Prevention of atherothrombotic events in acute MI with ST-segment elevation (given with aspirin), oral:

18–75 years: Initially 300 mg, then 75 mg for at least 4 weeks.

76 years and over: 75 mg daily for at least 4 weeks.

Children:
No or insufcient experience in children and adolescents, therefore its use is not recommended.

Side effects: GI disturbance, GI and duodenal ulceration, Haemorrhage (e.g., GI, intracranial), skin reactions, SCARs, thrombocytopenia, Acquired **Contraindications:** Active bleeding.

Cautions: Discontinue 7 days before elective surgery if antiplatelet efect not desirable, patients at risk of increased bleeding from trauma, surgery, or other pathological conditions, elderly with concurrent signifcant bleeding risk. Use with caution in hepatic impairment, renal impairment, pregnancy and breastfeeding.

RIVAROXABAN

Presentation: Tablet containing 10 mg, 15 mg, 20 mg Rivaroxaban.

Indications: Treatment and prevention of recurrent deep vein thrombosis and pulmonary embolism.

Administration: ***Adult:***

Treatment and prevention of recurrent deep vein thrombosis and pulmonary embolism, oral: Day 1–21, 15mg twice daily, then day 22 onward 20 mg once daily.

Prevention of recurrent DVT and PE, following completion of at least 6 months of therapy for DVT or PE, oral: 10-20mg once daily.

Atrial fibrillation: oral: 20 mg once daily

Children:
Treatment of venous thromboembolism/ Prophylaxis of recurrent venous thromboembolism
Body weight 2.6–2.9 kg: 0.8 mg 3 times a day for at least 3 months.
Body weight 3–3.9 kg: 0.9 mg 3 times a day for at least 3 months
Body weight 4–4.9 kg: 1.4 mg 3 times a day for at least 3 months
Body weight 5-6.9kg: 1.6 mg 3 times a day for at least 3 months
Body weight 7-7.9 kg: 1.8 mg 3 times a day for at least 3 months
Body weight 8 - 8.9 kg: 2.4 mg 3 times a day
Body weight 9- 9.9 kg: 2.8 mg 3 times a day
Body weight 10-11.9 kg: 3 mg 3 times a day
Body weight 12-29.9 kg: 5 mg twice daily
Body weight 30-49.9 kg: 15 mg once daily
Body weight 50 kg and above:20 mg once daily

Side Effects: Anaemia, asthenia, constipation, diarrhoea, dizziness, fever, gastrointestinal, discomfort, haemorrhage, headache, hypotension, menorrhagia, nausea, oedema, pain in extremity, post procedural anaemia. renal impairment. skin reactions, tachycardia, vomiting, wound complications, angioedema, dry mouth, hepatic disorders, hypersensitivity, intracranial haemorrhage, malaise, syncope, thrombocytopenia, thrombocytosis, severe cutaneous adverse reactions.

Contraindications: Hypersensitivity to the active substance or to any of the excipients. Active clinically signifcant bleeding. Lesion or condition, if considered to be a signifcant risk for major bleeding. This may include current or recent GI ulceration, presence of malignant neoplasms at high risk of bleeding, recent major surgery, recent intracranial haemorrhage, known or suspected oesophageal varices, arteriovenous malformations. Concomitant treatment with any other anticoagulants, hepatic disease associated with coagulopathy.

Cautions: The product may contain inactive ingredients that may cause allergic reactions. History of hepatic or renal disease, blood disorders, bleeding disorders including anaemia, haemophilia and thrombocytopenia. Avoid in hepatic impairment, pregnancy and breastfeeding.

DABIGATRAN ETEXILATE

Presentation: Capsule 75mg, 110mg and 150mg

Indications: Prophylaxis of venous thromboembolism following major orthopaedic surgery, treatment and prophylaxis of (recurrent) deep-vein thrombosis and pulmonary embolism.

Administration: ***Adult:***

Prophylaxis of venous thromboembolism following major orthopaedic surgery:

18–74 years*:* 110 mg, to be taken 1–4 hours after surgery, followed by 220 mg once daily.

75 years and over*:* 75 mg, to be taken 1–4 hours after surgery, followed by 150 mg once daily.

Treatment of deep-vein thrombosis/treatment of pulmonary embolism/Prophylaxis of recurrent deep vein thrombosis/Prophylaxis of recurrent pulmonary embolism. following at least 5 days treatment with a parenteral anticoagulant

18–74 years: 150 mg twice daily

75–79 years*:* 110–150 mg twice daily

80 years and over*:* 110 mg twice daily

Children:

Following at least 5 days treatment with a parenteral anticoagulant:

Body weight 11–12 kg: 75 mg twice daily

Body weight 13–20 kg: 110 mg twice daily

Body weight 21–30 kg: 150 mg twice daily

Body weight 31–40 kg: 185 mg twice daily

Body weight 41–50 kg: 220 mg twice daily

Body weight 51–60 kg: 260 mg twice daily

Body weight 61 kg and above: 300 mg twice daily

Side effects: Hepatic function abnormal, anaemia, diarrhoea, haemorrhage, hyperbilirubinaemia, nausea, post procedural complications, vomiting, wound complications, angioedema, dysphagia, gastrointestinal discomfort, gastrointestinal disorders, intracranial haemorrhage, post procedural drainage skin reactions, thrombocytopenia, wound drainage

Contraindications: Active bleeding, antiphospholipid syndrome (increased risk of recurrent thrombotic events), do not use as anticoagulant for prosthetic heart valve, malignant neoplasms, oesophageal varices, recent brain surgery, recent gastro-intestinal ulcer, recent intracranial haemorrhage, recent ophthalmic surgery, recent spine surgery, significant risk of major bleeding, vascular aneurysm.

Cautions: Bacterial endocarditis, bleeding disorders, body-weight less than 50kg, elderly, gastritis, gastro-oesophageal reflux, oesophagitis, recent biopsy, recent major trauma, thrombocytopenia.

Pregnancy: Manufacturer advises avoid unless essential—toxicity in animal studies.

Breast feeding: Manufacturer advises avoid—no information available.

FONDAPARINUX SODIUM

Presentation: Solution for injection containing 2.5mg/0.5ml, 5mg/0.4ml, 7.5mg/0.6ml, 10mg/0.8ml Fondaparinux.

Indications: Prophylaxis of venous thromboembolism following surgery and in immobilised patients, treatment of superficial-vein thrombosis, in unstable angina and myocardial infarction, treatment of deep vein thrombosis and pulmonary embolism.

Administration: ***Adult****:*

Prophylaxis of venous thromboembolism in patients after undergoing major orthopaedic surgery of the hip or leg, or abdominal surgery:

Initially 2.5 mg, dose to be given 6 hours after surgery, then 2.5 mg once daily.

Prophylaxis of venous thromboembolism in medical patients immobilised because of acute illness

2.5 mg once daily subcutaneously

Treatment of superficial-vein thrombosis

50 kg and above: 2.5 mg once daily subcutaneously for at least 30 days (max. 45 days if high risk of thromboembolic complications). Treatment should be stopped 24 hours before surgery and restarted at least 6 hours post operatively.

Treatment of unstable angina and non-ST-segment elevation myocardial infarction

2.5 mg once daily for up to 8 days (or until hospital discharge if sooner), treatment should be stopped 24 hours before coronary artery bypass graft surgery (where possible) and restarted 48 hours post operatively.

Treatment of ST-segment elevation myocardial infarction

Initially by intravenous injection, or by intravenous

infusion**:** Initially 2.5 mg daily for the first day, then (by

subcutaneous injection) 2.5 mg once daily for up to 8 days (or until hospital discharge if sooner), treatment should be stopped 24 hours before coronary artery bypass graft surgery (where possible) and restarted 48 hours post operatively

Treatment of deep - vein thrombosis and pulmonary embolism: an oral anticoagulant (usually warfarin) is started at the same time as fondaparinux (fondaparinux should be continued for at least 5 days and until INR is 2 for at least 24 hours)

Weight up to 50kg: 5mg every 24 hours

50– 100kg: 7.5 mg every 24 hours

101kg and above: 10mg every 24 hours

Side effects: Anaemia, haemorrhage, chest pain, coagulation disorder, dyspnoea, fever, hepatic function abnormal, nausea, oedema, platelet abnormalities, skin reactions, thrombocytopenia, vomiting, wound secretion, anxiety, confusion, constipation, cough, diarrhoea, dizziness, drowsiness, fatigue, gastritis, gastrointestinal discomfort, genital oedema, headache, hyperbilirubinaemia, hypersensitivity, hypokalaemia, hypotension, leg pain.

Contraindications: Active bleeding, bacterial endocarditis, renal impairment CrCl<30ml/min, history of hypersensitivity reaction, thrombocytopenia.

Caution: Elderly>75yrs (prolonged half-life), active gastro-intestinal ulcer disease, bleeding disorders, brain surgery, low bodyweight, ophthalmic surgery, recent intracranial haemorrhage, risk of catheter thrombus during percutaneous coronary intervention, spinal or epidural anaesthesia (risk of spinal haematoma avoid if using treatment doses), spinal surgery.

11.5 Haematopoietics

IRON

Haemopeotics should not be given until an accurate diagnosis has been made. They should be introduced singly. A response is shown by a rise in reticulocyte count in a week. If a patient with apparent iron deficiency anaemia fails to respond to treatment with either oral or parental iron preparations, the diagnosis should be reviewed.

FERROUS SULPHATE

Presentation: Tablet containing 200mg Ferrous sulphate. A paediatric mixture containing 60mg/5ml Ferrous sulphate.

Indications: Treatment and prevention of iron deficiency anaemia.

Administration: *Adult*; 600 – 800mg daily in three divided doses. Maintenance; 200 – 400mg daily. Take after food.

Children:
Up to 1 year: 5ml well diluted with water three times daily.
1–5 years: 10ml well diluted with water three times daily.

Side effects: Gastro-intestinal disturbances.

Contraindications: Aplastic anaemia and megaloblastic anaemia.

Caution: Do not use with tetracycline, could be poisonous to children.

FERROUS GLUCONATE

Presentation: Tablet containing Ferrous gluconate 300mg (35mg iron).

Indications: Iron-deficiency anaemia.

Administration: *Prophylacxis:* 2 tablets daily before food.

Therapeutic: 4-6 tablets daily in divided doses before food.

Children:
6-12 years: prophylactic and therapeutic 1 – 3 tablets daily.

Side effects: Gastrointestinal irritation may occur with iron salts, nausea and epigastric pain, constipation or diarrhoea.

Caution: Pregnancy.

FERROUS FUMERATE

Presentation: Tablet containing 322mg (100mg) Iron

Indications: Iron-deficiency anaemia.

Administration: *prophylaxis* 1 tablet daily; *therapeutic* 1 tablet twice daily.

Side effects: See Ferrous Gluconate above.

Caution: Pregnancy

FERROUS GLYCINE SULPHATE

Presentation: Syrup containing ferrous glycine sulphate equivalent to 25mg Iron per 5ml

Indications: Iron-deficiency anaemia

Administration: 5 – 10mls 3 times daily.

Children: 2.5 – 5mls 1-3 times daily according to age.

Side effects: See Ferrous Gluconate above.

Caution: Pregnancy

FOLIC ACID

Presentation: Tablet containing 0.4mg and 5mg folic acid

Indications: Prevention and treatment of folic acid deficiency

Administration: *Adult:* 0.4–20mg daily.

Children:
Folate deficiency, megaloblastic anaemia, *oral*

Neonate to 1 year: Initially 500 mcg/kg (maximum 5 mg) once daily for up to 4 months; up to 10 mg once daily may be required in malabsorption states.

Over 1 year: 5 mg daily for 4 months; up to 15 mg daily may be required in malabsorption states

Haemolytic anaemia, *oral*

1 month–12 years: 2.5–5 mg once daily

Contraindications: Subacute combined degeneration of the spinal cord.

HYDROXOCOBALAMIN (VITAMIN B_{12})

Presentation: Injection containing 1mg/ml hydroxocobalamin

Indications: Pernicious anaemia

Administration: Initially 1mg intramuscularly repeated 5 times at intervals of 2-3 days.

Maintenance dose 1mg every three months.

Children: as for adult.

Caution: Should not be given before diagnosis is fully established

IRON DEXTRAN

Presentation: Injectable solution containing 50 mg of elemental Iron/ml

Indications: Treatment of patients with documented iron deficiency or anaemia in whom oral administration is unsatisfactory or impossible.

Administration: 25–100mg IV or deep IM, max dose not to exceed 100mg (2ml)/day.

Note: dose calculated based on iron deficiency formula.

Side effects: Abdominal pain, diarrhoea, nausea, vomiting, arthralgia, metallic taste, inflammation at the injection site.

IRON SUCROSE

Presentation: Injectable solution containing 20mg/ml of Iron.

Indications: Used in treatment of Iron Deficiency Anaemia and in CKD

Administration: ***Adults***

Iron-deficiency anaemia: Doses calculated according to body weight and iron deficit. For intermittent IV infusion, dilute to a concentration of 1 mg/ml with sodium chloride 0.9%.

Haemodialysis-dependent CKD – 100 mg elemental iron IV (injection or infusion over 2-5 minutes) per dialysis session not to exceed total cumulative dose of 1000mg divided in 3 doses/week.

Non-dialysis-dependent CKD – 200 mg IV for 5 doses in over 14 days (cumulative 1000 mg in 14-day period).

Peritoneal dialysis-dependent CKD – 300 mg IV infusion (1.5 hour) for 2 doses 14 days apart, then 400 mg IV infusion (2.5 hours) 14 days later (cumulative dose of 1000 mg divided in 3 doses/month).

Children

Less than 2 years: safety and efficacy not established.

2 years:

Haemodialysis-dependent – 0.5 mg/kg IV once in 2 weeks for 12 weeks (not to exceed 100 mg/dose)

Non-dialysis dependent or peritoneal dependent (on erythropoietin) – 0.5 mg/kg IV once in 4 weeks for 12 weeks (not to exceed 100 mg/dose).

Side effects: Common include hypotension, muscle cramps, headache, nausea. Less common include Dizziness, fatigue, arthralgia, back pain, hypertension, fluid overload, peripheral oedema, cough, vomiting, diarrhoea, constipation and pruritus.

Contraindications: Hypersensitivity, Anaemia not caused by iron deficiency and iron overload.

Caution: Risk of hypotension, withhold therapy in Iron overload and hypersensitivity reactions.

ERYTHROPOIETIN (EPOIETIN)

Presentation: Injectable solution (prefilled syringe) 2000 to 4000 units/ml

Indications: CKD-associated anaemia, Zidovudine-related anaemia, chemotherapy-related anaemia and in reduction of Allogeneic red Blood Cell transfusions in Patients undergoing elective, non-cardiac, non-vascular surgery.

Administration: **Adult**

Patients with CKD on dialysis, by IV or SC injection*:* 50 to 100 units/kg 3 times weekly initially; treatment initiated when haemoglobin level is <10g/dL; reduce or interrupt dose if haemoglobin level approaches or is > 11g/dL

Patients with CKD NOT on dialysis

Treatment is initiated only when the haemoglobin level is <10g/dL. Dose is reduced or interrupted, and lowest dose of epoetin sufficient to reduce the need for red blood cell transfusions is used if haemoglobin is >10g/dL.

Children:

< 1 month: Safety and efficacy not established.

>1 month: 50 units/kg 3 times weekly initially; If patient on dialysis, IV route is recommended

Treatment should be initiated when haemoglobin level is <10g/dL; reduce or interrupt dose if haemoglobin level approaches or exceeds >11g/dL

Zidovudine- associated anaemia, by IV or SC injection:

< 8 months: Safety and efficacy not established

8 months–17 years: 50 to 400units/kg 2 to 3 times weekly

Chemotherapy related anaemia, by IV injection:

< 5 years: Safety and efficacy not established

5–18 years: 600 units/kg (Maximum: 40000units) once. Dose is reduced by 25% if haemoglobin increases >1g/dL in any two-week period OR reaches a level to avoid red blood cell transfusion.

Dose is withheld if haemoglobin exceeds level needed to avoid red blood cell transfusion and initiated at 75% the initial dose when haemoglobin approaches a level where red blood cell transfusions may be required

Dose is increased to 900 units/kg weekly (Maximum 60000 units) after initial 4 weeks of treatment if haemoglobin increases by <1g/dL and remains <10g/dL

Treatment is discontinued if no response after 8 weeks or if red blood cell transfusions are required.

Side effects: Common - Arthralgia, embolism, thrombosis, headache, hypertension (dose-dependent), influenza like illness, skin reactions, stroke. Uncommon - Hypertensive crisis (in isolated patients with normal or low blood pressure), respiratory tract congestion, seizure.

Contraindications: Patients unable to receive thromboprophylaxis, pure red cell aplasia following erythropoietin therapy and uncontrolled hypertension.

Caution: Aluminium toxicity (can impair the response to erythropoietin) and concurrent infection (can impair the response to erythropoietin).

12 Nutrition

12.1 Vitamins, minerals and dietary supplements

Vitamins are used for the prevention and treatment of specific deficiency states or where the diet is inadequate. They may be prescribed to prevent or treat deficiency but not as a dietary supplement.

RETINOL (VITAMIN A)

Retinol (Vitamin) A is a fat-soluble vitamin and essential for growth, development and maintenance of epithelial tissue and vision. Deficiency state develops with inadequate dietary intake. This is common in children.

Effects of deficiency: Night blindness, xerophthalmia, xeromalacia, abnormal bone and teeth formation, dry skin and mucous membrane, retarded growth, decreased resistance to infections, significantly increased risk of child mortality.

Effects of overdose: Drying and cracking of the skin, pain in long bones, sparse hair growth, growth retardations, increased intracranial pressure.

Natural sources: Dietary vitamin is derived from two sources, namely animal and plan. Animal sources include liver, kidney, dried fish, oils, whole milk, egg yolk. Plant sources include carrots, whole grain, yellow fruits, dry/ dark green or yellow vegetables.

Presentation: Capsule containing 50,000 i.u., 100,000 i.u., 200,000 i.u. vitamin A

Indications: Night blindness, xerophthalmia, xeromalacia. Adjunct treatment in measles, diarrhoea, malnutrition and primary biliary cirrhosis.

Administration:

Therapeutic dose: 50,000 i.u daily.

Primary biliary cirrhosis

IV doses of 10,000 units every 2 to 4 months

Children:

Physiological requirements:

Up to 1 year; 1500 i.u. daily.

1–12 years; 2000 – 4500 i.u. daily.

Over 12 years; 5000 – 8000 i.u. daily.

In deficient populations children should receive a high dose supplement every 6 months as follows; 6 – 11 months, 100,000 i.u. 1 – 6 years 200,000 i.u. ***Xerophthalmia*:**

Over 1 year of age 200,000 units by mouth immediately on diagnosis.

6–12 months 100,000 units

Less than 6 months: 50,000 units given by mouth immediately on diagnosis, then on the following day and repeated 2 weeks later.

Side effects: Excessive amounts may lead to hypervitaminosis A, raised intracranial pressure, tinnitus, visual disturbances, acute vitamin A intoxication.

Caution: Destroyed by exposure to strong sunlight. Pregnancy, women of child-bearing age and breastfeeding. Resistant to usual cooking temperatures.

Vitamin B-Group

The Vitamin B-Group comprises the following substances Vitamin B_1 (Thiamine), Vitamin B_2 (Riboflavin), Vitamin B_6 (pyridoxine and derivatives) and Vitamin B_{12} (cobalamines). To these are added nicotinic acid and derivatives, folic acid and pantothenic acid.

The term vitamin B complex is a term generally used when individual Vitamin B substances and other components are commercially prepared. The ingredients and doses are according to the manufacturers' instructions.

Indications, side effects and caution areas for the individual components of the formulation. The presentation of the Vitamin B complex is in form of tablets, capsules, elixir and injection.

THIAMINE (VITAMIN B_1)

This is a water-soluble vitamin. It is essential in carbohydrate metabolism. Its deficiency leads to a syndrome known as beriberi.

Natural sources: Liver, meats, milk, legumes, cereals and nuts.

Presentation: Tablet containing 25mg, 50mg, 100mg, 300mg thiamine hydrochloride. In high potency vitamin B Co. injections containing 25mg/ ml (intravenous), 50mg/ ml (intramuscular) **Indications:** Treatment of thiamine deficiency, beriberi, adjunct in the treatment of alcohol abuse.

Administration: ***Adult:***

Physiological requirements: *Adult and Over 12 years*; 1.5mg daily

Mild deficiency: 25 – 100mg orally.

In severe cases, up to 300mg orally in divided doses. Higher doses acceptable in Wernicke-Korsakoff syndrome by intravenous route.

Beriberi: 5-30 mg IM three times daily; then 5-30 mg P.O three times daily for 1 month.

Children:

Physiological requirements:

Up to 1 year; 200 – 500mcg daily.

1 – 12 years; 500mcg – 1.3mg.

Maple syrup urine disease: 5 mg/kg P.O daily

Metabolic disorders and Congenital lactic acidosis:

≤1 month: 50–200 mg IV/PO once daily

>1 month: 100–300 mg IV/PO once daily. It may be divided in one to two divided doses.

Beriberi:10-25 mg IV/IM daily or 10-50 mg/dose PO daily for at least 2 weeks, then 5-10 mg/day PO for 1 month*Rapid therapy of severe depletion/malabsorption of water-soluble vitamins B and C, especially in alcoholism, where a severe depletion of thiamine can lead to Wernicke's encephalopathy, IV*:

<6 years: quarter of the adult dose

6–10 years: third of the adult dose

10–14 years: half to two thirds of the adult dose

14 years and over: as for the adult dose

Side effects: In overdose-sudden death with injection. Hypersensitivity reactions which may be fatal.

Caution: Destroyed by normal cooking heat. Because of the possibility of a potentially serious allergic reaction, use by injection should be restricted to those patients in whom parenteral treatment is essential, the intravenous injection should be given slowly (over 10 minutes).

RIBOFLAVIN (VITAMIN B_2)

It is a water-soluble vitamin. It is used as a coenzyme in the various metabolic reactions. It is also necessary for the normal functioning of pyridoxine and nicotinic

acid. Riboflavin deficiency mainly results from insufficient intake. The deficiency state is called ariboflavinosis. In addition, there may also be normocytic anaemia and some ocular symptoms. It may also occur in other deficiency states with other B vitamins

Natural sources: Milk, cheese, liver, meat, eggs, fish, green vegetables, whole grain.

Presentation: Tablet containing 5mg riboflavin.

Indications: Aviboflavinosis characterized by conditions such as glossitis, stomatitis, photophobia and blurred vision, metabolic diseases.

Administration: ***Adult:***

Physiological requirements: 1.3mg – 1.5mg daily.

Metabolic Disease: 5 – 10mg daily.

Riboflavin disease: 6-30 mg/day PO in divided doses.

Children:

Physiological requirements:

Up to 1 year; 400 – 600mcg.

1–12years; 600mcg – 3mg.

Over 12 years; 1.3mg – 1.5mg daily.

Metabolic disease: 50–100 mg 1–2 times a day.

Riboflavin disease *≥12 years:* 6-30 mg/day PO in divided doses.

3-12 years: 3-10 mg/day PO in divided doses.

Side effects: Urine discolouration

Contraindications: Hypersensitivity

Caution: Ensure Recommended Dietary Allowances in Pregnacy are maintained.

NICOTINAMIDE (VITAMIN B_3)

Naturally occurs as a water-soluble vitamin B substance which is converted to nicotinamide adenine dinucleotide (NADP). These co-enzymes play a major role in electron transfer reactions in the respiratory chain. Their deficiency leads to a syndrome of pellagra which is characterised by skin lesions especially to areas exposed to sunlight with hyperpigmentation and hyperkeratinisation. Nicotinic acid deficiency may occur in association with other Vitamin B complex deficiency states e.g. in alcoholism.

Effects of deficiency: Pellagra.

Natural sources: Milk, fish, poultry, liver, whole grain, green vegetables and groundnuts.

Presentation: Tablet containing 50mg Nicotinamide

Indications: Pellagra, especially in alcoholism.

Administration: Daily requirements are not known but a daily human requirement is required for optimum amounts of nicotinic acid to be absorbed.

Side effects: Vasodilation, dryness of the skin, pruritus hyperpigmentation, abdominal cramps, peptic ulcer disease, amblyopia, jaundice, impaired liver function, decrease in glucose tolerance, hyperglycaemia, hyperuricaemia.

Caution: Peptic ulcer disease, diabetes mellitus, gout or impaired liver function.

PYRIDOXINE (VITAMIN B_6)

A water-soluble vitamin involved principally in amino acid, carbohydrate and fat metabolism and also required for haemoglobin formation. Deficiency is rare but may occur during drug therapy e.g. isoniazid therapy. Deficiency causes sideroblastic anaemia, dermatitis, cheilosis and neurologic symptoms such as peripheral neuritis, convulsions, especially in neonates.

Effects of deficiency: Irritability, convulsions especially in neonates, hypochromic anaemia, polyneuritis.

Natural sources: Meat, liver, kidney, whole grain, groundnuts and soya beans.

Presentation: Tablet containing 10mg, 25mg, 50mg pyridoxine hydrochloride.

Indications: Pyridoxine deficiency such as may occur in isoniazid therapy or metabolic

disorders e.g. hyperoxaluria, in sideroblastic anaemia, peripheral neuropathy.

Administration: ***Adult:***

Physiological requirements: 1.2 – 1.8mg daily.

Isoniazid neuropathy:

Prophylaxis: 10mg daily Therapeutic dose; 50mg 3 times daily.

Idiopathic sideroblastic anaemia; 100 – 400mg daily in divided doses

Children:

Physiological requirements:

Up to 1 year; 200 – 400mcg.

1–12 years; 500mcg.

Over 12 years; 1.2 – 1.8mg daily.

Deficiency states; 50 – 150mg daily in divided doses.

Prophylaxis of isoniazid neuropathy:

1 month–11 years: 5–10 mg daily.

12–17 years: 10 mg daily.

Side effects: Large dose and long-term therapy leads to severe peripheral neuritis (neuropathies).

Caution: Destroyed by heat, intestinal synthesis occurs.

VITAMIN B_{12}

This is a water-soluble vitamin. It occurs in various forms of cobalamins. Deficiency is commoner in those strict vegetarians who do not ingest any animal and dairy products. It is also common in patients after gastrectomy or ileal resection. Deficiency causes megaloblastic anaemia, demyelination and other neurological damage.

Presentation: Tablet containing 500 mcg; Injection containing 1000mcg/ml of cyanocobalamin/hydroxo cobalamin.

Indications: Cyanide poisoning, Pernicious anaemia and other macrocytic anaemia.

Administration: *Pernicious anaemia and other macrocytic anaemia without neurological involvement*: IM cyanocobalamin and hydroxocobalamin 250-1000mcg on alternate days for one to two weeks. Then 250mcg weekly until blood levels are normal.

Maintenance dose: 1000mcg cyanocobalamin monthly or 1000 mcg hydroxycobalamin every 2 to 3 months.

Prophylaxis for Vitamin B_{12} deficiency following gastrectomy or malabsorption syndromes: IM cyanocobalamin 250–100mcg monthly and intramuscular hydroxocobalamin 100mcg every 2 to 3 months.

For vitamin B_{12} deficiency of dietary origin – oral cyanocobalamin Adult:50 – 150 mcg daily in between meals.

Poisoning with cyanides: Initially 5g, to be given over 15 minutes, then 5 g if required, this second dose can be given over 15 minutes–2 hours depending on severity of poisoning and patient stability.

Children:

Pernicious anaemia and other macrocytic anaemia:

30-50 mcg IM/SC once daily for 2 weeks. Administer concomitantly with 1 mg/day of folic acid for 1 month.

Maintenance dose: 100 mcg IM/SC monthly

For vitamin B_{12} deficiency of dietary origin*, oral:* 50–105 mcg daily in 1–3 divided doses.

***Poisoning with cyanides*:**

Body weight 5 kg and above: Initially 70 mg/kg (max. per dose 5g), to be given over 15 minutes, then 70 mg/kg (max. per dose 5 g) if required, this second dose can be given over 15 minutes–2 hours dependingon severity of poisoning and patient stability.

Side effects: Allergic hypersensitivity following parenteral administration, arrhythmias secondary to hypokalaemia.

Caution: Avoid use in herbs disease or tobacco amblyopia since these optic neuropathies may degenerate further. Diagnosis of Vitamin B12 deficiency should be confirmed before giving hydroxocobalamin. Interactions: (see Appendix II) absorption of Vitamin B_{12} is

reduced when administered together with neomycin, aminosalicylic acid, H^2 receptor antagonist, and colchicines

ASCORBIC ACID (VITAMIN C)

Presentation: Tablet containing 50mg, 100mg, 200mg, Ascorbic acid. Effervescent tablet containing 1g Ascorbic acid. An injection containing Ascorbic acid 100mg/ml.

Indications: Supplementation and deficient states (irritability, slow growth, decreased resistance to infections, haemorrhagic tendencies, poor wound healing due to deficeiency), prevention and treatment of Scurvy.

Administration*: Adult:*

Treatment of scurvy, Oral: 1 to 2 g for the first 2 days then 500 mg daily for a week. Alternative dose: 250mg four times daily for a week.

Prophylaxis of scurvy, Oral: Recommended daily intake Males: 90mg/day

Females: 75mg/day

Pregnancy: 85mg/day; not to exceed 2000mg/day (80mg if less than 18years old; not to exceed 1800mg/day).

Children:

Treatment of scurvy, Oral

Not less than 250 mg daily in 1–2 divided doses until clinical signs of scurvy disappear.

Prophylaxis of scurvy, Oral

25–75 mg daily.

Side effects: Large doses cause diarrhoea, other GIT disturbances, hyperoxaluria, renal calcium, oxalate calculi, haemolysis in patients with G6PD deficiency.

Caution: Destroyed by usual cooking temperatures, hyperoxaluria, deficiency of G6PD.

ERGOCALCIFEROL (VITAMIN D_2)

Vitamin D comprises compounds used in the treatment and prevention of rickets. The margin of safety between therapeutic and toxicity concentration is narrow. Therefore, vitamin D dietary supplementation may be detrimental in patients already receiving adequate dietary intake. Furthermore, Vitamin D is the most likely of all vitamins to cause toxicity.

Presentation: Tablet/capsule containing 10,000 units (250mcg), 50,000 units (1.25mg) ergocalciferol. An injection containing 300,000 units/ml ergocalciferol in oil.

Indications: Vitamin D deficiency including that caused by intestinal malabsorption, chronic liver disease, hypoparathyroidism.

Administration: *Therapeutic dose* – deficiency due to malabsorption or liver disease – up to 40000 units daily.

Hypocalcaemia due to hypothyroidism – doses up to 100,000 units daily. Monitor calcium levels initially weekly then every 2 to 4 weeks to optimize clinical response and avoid hypercalcaemia.

Effects of deficiency: Rickets and osteomalacia.

Physiological requirements: *Child*; 400i.u. daily. *Adult*; 100 i.u. daily

Therapeutic dose*:* 40,000 – 100,000 units daily

Natural sources: Milk, fish, liver, oil, sunlight.

Side effects: Excess leads to hypercalcaemia, hypercalciuria, renal damage and cardiovascular damage.

Contraindications: Hypercalcaemia

Caution: Infants, renal and heart disease, hypercalcaemia. Infants breastfed by mothers taking therapeutic doses of vitamin D.

COLECALCIFEROL (VITAMIN D) WITH CALCIUM CARBONATE

Presenetation: Tablet containing 250mg, 500mg, 600mg/100iu, 200iu, 400iu, 600iu, 800iu Colecalciferol; Oral suspenstion 325mg.

Indication: Calcium and vitamin D deficiency, prevention and treatment of calcium and vitamin D deficiency especially in the elderly.

Administration: Dosed according to the deficit or daily maintenance requirements. Daily dietary reference intake for calcium and vitamin D:

19-50 years: 1000 mg + 600 IU daily

≥51-70 years (males): 1000 mg + 600 IU

≥51 years (females): 1200 mg + 600 IU

≥70 years (males): 1200 mg + 800 IU

Pregnancy and breastfeeding: 1000mg + 600IU

Osteoporosis prevention in adults ≥50 years, oral: Vitamin D intake may need to be increased to 800-1000 mg.

Side effects: Hypersensitivity reactions including pruritus, wheezing, urticaria and oropharyngeal swelling. Mild gastro-intestinal disturbances, such as constipation, flatulence, nausea, gastric pain, diarrhea, occasional skin rash, Hypercalciuria, and in rare cases hypercalcaemia have been seen with long term treatment at high dosages.

Contraindications: Hypersensitivity to the active substance or to any of the excipients, hypercalcaemia, bone metastases or other malignant bone disease, sarcoidosis; primary hyperparathyroidism and vitamin-D overdosage, Severe renal failure, hypercalcemia, hypervitaminosis D, osteoporosis due to prolonged immobilisation, renal stones, severe hypercalciuria.

Cautions: Monographs for calcium and vitamin D combinations vary.

CALCIUM CARBONATE

Presentation: Tablet containing 500mg Calcium
Indications: Phosphate binding in renal failure and hyperphosphataemia; Calcium deficiency

Administration:

Adult *Adjunctive therapy in osteoporosis and Prevention and treatment of calcium deficiency, oral:* 2 to 3 tablets daily. *Phosphate binder:* Dose as required by the individual patient depending on serum phosphate level.

Children:

Phosphate binding in renal failure and hyperphosphataemia, *Oral:*

1–11 months: 120 mg 3–4 times a day, dose to be adjusted as necessary, to be taken with feeds
1–5 years: 300 mg 3–4 times a day, dose to be adjusted as necessary, to be taken prior to or with meals
6–11 years: 600 mg 3–4 times a day, dose to be adjusted as necessary, to be taken prior to or with meals
12–17 years: 1.25 g 3–4 times a day, dose to be adjusted as necessary, to be taken prior to or with meals.

Calcium deficiency, *Oral:*

Neonate: 0.25 mmol/kg 4 times a day, adjusted according to response.
1 month–4 years: 0.25 mmol/kg 4 times a day, adjusted according to response
5–11 years: 0.2 mmol/kg 4 times a day, adjusted according to response
12–17 years: 10 mmol 4 times a day, adjusted according to response

Side effects: Hypercalciuria**,** Flatulence, GI discomfort, milk-alkali syndrome, skin reactions.

Contraindications: Diseases and/or conditions resulting in hypercalcaemia and/or hypercalciuria, for example in hyperparathyroidism, vitamin D overdosage, decalcifying tumours such as plasmacytoma and skeletal metastases, in severe renal failure untreated by renal dialysis and in osteoporosis due to immobilisation. Renal calculi (nephrolithiasis).

Cautions: History of nephrolithiasis, Sarcoidosis, Renal impairment.

Multivitamin Tablets and Syrups

These are available in different formulations.

The constituents and dose are according to the manufacturer's instructions. Indications and side effects are as for the constituents mentioned above.

HYDROLYZED PROTEIN

Presentation: Powder containing lactose-free protein without vitamins and minerals

Indications: Lactose intolerance (e.g. in kwashiorkor) and protein supplementation.

Administration: ***Adults:*** 1 – 2 teaspoonfuls 3 times daily.

Children: Use as milk.

Caution: Use for short a period as necessary.

HIGH ENERGY PROTEIN SUPPLEMENT (HEPS)

Presentation: Powder containing dried skimmed milk, corn, soy, milk and sugar.

Indications: Prevention and treatment of protein-calorie malnutrition, expectant mothers in the third trimester, during breastfeeding.

Administration: 3 tablespoons mixed with 2 tablespoons of oil in boiled water or mixed with porridge three timed daily.

12.2 Electrolyte and water replacement

Fluid and electrolyte therapy should be considered as replacement therapy and maintenance therapy.

Replacement therapy

Dehydration may result from either inadequate intake (thirst or fasting) or excessive loss (diarrhoea or vomiting). Rehydration fluid should replace sodium bicarbonate, potassium and water in amounts roughly equivalent to the loss and should contain glucose. (See rehydration chart in 2.3.4.).

Maintenance therapy

Any patient deprived of normal dietary intake requires water and electrolytes to replace obligatory losses in urine, stool, sweat and evaporation in exhaled air. Protein and calories are also required, but complete parenteral replacement is difficult and rarely essential if therapy is required for a limited period. The water, sodium and potassium requirements for normal maintenance therapy are 115ml, 3MEQ, 2.5MEQ respectively for every 100 calories metabolised. Supplemental therapy is needed where the loss of fluid and electrolyte are specific. Inappropriate use may lead to fluid and electrolyte imbalance.

12.2.1 Oral administration

ORAL REHYDRATION SALTS (ORS)

Presentation: WHO formula containing 3.5g/l sodium chloride, trisodium citrate 2.9g/l, potassium chloride 1.5g/l, glucose (anhydrous) 20.00g/l.

Indications: Correction or maintenance of fluid and electrolyte balance

Administration: ***Adult***

Fluid and electrolyte loss in acute diarrhoea, oral: 200–400 ml solution after every loose motion. Frequency and dose may be adjusted according to clinical condition of the patient.

Children: WHO Recommends Plans A, B and C, see below

Plan A: No dehydration; Nutritional advice, increased fluid intake (e.g., unsalted soup, unsalted rice water, yoghurt or plain water), at least one fluid that normally contains salt (e.g., ORS solution, salted drinks including salted rice water and vegetable or chicken soup with salt) and zinc supplementation at home are usually sufficient. The aim is to give as much nutrient-rich food as the child will accept. Breastfeeding should always be continued to reduce the risk of diminishing supply. Give as much fluid as the child wants until diarrhoea stops and, as a guide, after each loose stool give:

Under 2 years: 50–100 ml (a quarter to half a large cup) of fluid.

2–10 years: 100–200 ml (a half to one large cup)

Older than 10 years: as much fluid as the child wants.

Parents should be advised about circumstances in which they should seek further advice.

Plan B: Moderate dehydration: whatever the child's age, a 4-hour treatment plan is applied to avoid short-term problems. It is recommended that parents are shown how to give approximately 75 ml/kg of oral rehydration solution over a 4-hour period, and it is suggested that parents should be watched to see how they cope at the beginning of the treatment. A larger amount of solution (up to 20 ml/kg/hour and maximum 750 ml/hour) can be given if the child continues to have frequent stools or if the child wants more than the estimated amount of ORS solution, and there are no signs of overhydration (e.g., oedematous eyelids). In case of vomiting, rehydration must be discontinued for 10 minutes and then resumed at a slower rate. In younger children, breastfeeding should be continued on demand and the mother should be encouraged to do so, older children should receive milk and nutritious food as normal after completing the 4 hours of oral rehydration. The child's status must be reassessed after 4 hours to decide on the most appropriate subsequent treatment. If signs of dehydration worsen, shift to treatment.

Plan C: Severe dehydration, IV rehydration should be started as per treatment plan C. Zinc supplementation should begin as soon as the child can eat and has completed 4 hours of rehydration. Oral rehydration solution should continue to be offered once dehydration has been controlled, for as long as the child continues to have diarrhoea. In severe dehydration, hospitalization is necessary, but the most urgent priority is to start rehydration. The preferred treatment for children with severe dehydration is rapid IV rehydration. In hospital (or elsewhere), if the child can drink, oral rehydration solution should be given during the IV rehydration (20 ml/kg/hour oral before infusion, then 5 ml/kg/hour oral during IV rehydration). For IV rehydration, it is recommended that compound solution of sodium lactate (or, if this is unavailable, sodium chloride 0.9% IV infusion) is administered at a rate adapted to the child's age. IV rehydration using compound sodium lactate solution or sodium chloride 0.9% infusion IV: ***Infant:*** 30 ml/kg over 1 hour, then 14 ml/kg/hour for 5 hours.

Child: 30 ml/kg over 30 minutes, then 28 ml/kg/hour for 2.5 hours. If the IV route is unavailable, a nasogastric tube is also suitable for administering oral rehydration solution.

Nasogastric rehydration using oral rehydration solution:

Infant or Child: 20 ml/kg/hour for 6 hours (total 120 ml/kg). If the child vomits, the rate of administration of the oral solution should be reduced. Reassess the child's status after 3 hours (6 hours for infants) and continue treatment as appropriate with plan A, B or C.

Side effects: Vomiting (may indicate too rapid administration), hypernatraemia and hyperkalaemia (may result from overdose in renal impairment or administration of too concentrated a solution).

Cautions: Renal impairment.

ZINC SULPHATE

Presentation: Tablet (dispersible) containing 20 mg of Zinc.

Indications: Zinc deficiency, Adjunct in management of diarrhoea.

Administration: ***Adult***

Zinc deficiency or supplementation in zinc-losing conditions: (body-weight 31 kg and above): 45 mg 1–3 times a day, dose to be adjusted as necessary, to be dissolved in water and taken after food, dose expressed as elemental zinc.

For Adjunct in management of diarrhoea: 20 mg of zinc daily for 10–14 days.

Children:

Zinc deficiency or supplementation in zinc-losing conditions:

≤ 28 days: 1 mg/kg daily, dose expressed as elemental zinc, to be dissolved in water and taken after food.

Body-weight up to 10 kg: 22.5 mg daily, dose to be adjusted as necessary, to be dissolved in water and taken after food, dose expressed as elemental zinc.

Body-weight 10–30 kg: 22.5 mg 1–3 times a day, dose to be adjusted as necessary, to be dissolved in water and taken after food, dose expressed as elemental zinc.

Body-weight 31 kg and above: 45 mg 1–3 times a day, dose to be adjusted as necessary, to be dissolved in water and taken after food, dose expressed as elemental zinc.

For Adjunct in management of diarrhoea:

≤6 months: 10 mg (elemental zinc) daily for 10–14 days.

≥6 months–5 years: 20 mg (elemental zinc) daily for 10–14 days.

Sideeffects: Abdominalpain,dyspepsia,nausea, vomiting, diarrhoea, gastric irritation, gastritis, irritability, headache, lethargy.

Cautions: Acute renal failure (may accumulate). Zinc is likely safe when taken in the RDA but may be harmful when taken in high amounts. Renal impairment.

SODIUM POLYSTYRENE SULFONATE

Presentation: Available in oral formulation as powder for suspension as 450mg, Oral suspension 15g/60ml

Indications: Treatment of hyperkalaemia; to remove resin from colon.

Administration: Adult: 15 g 3–4 times a day.

By rectum: 30 g, retain for 9 hours followed by irrigation to remove resin from colon.

Children:

PO: 1 mg/kg every 6 hours or use exchange ratio of 1 mEq K + 1g of resin for lower dose. Oral use not recommended in patients < 1 month old.

Rectal: 1g/kg every 2-6 hours.

Side effects: Appetite decreased, bezoar, constipation (discontinue avoid magnesium-containing laxatives), diarrhea, electrolyte imbalance, epigastric discomfort.

Contraindication: Obstructive bowel disease.

Caution: Congestive heart failure, hypertension, oedema.

POTASSIUM CHLORIDE

Potassium is an essential electrolyte.

Presentation: Tablet containing 600mg potassium chloride. 15% potassium chloride injection in 10mls ampoules.

Indications: Prevention and treatment of potassium deficiency or hypokalaemia and prevention of diuretic-induced hypokalaemia.

Administration: 1,200 – 3,600mg daily in three divided doses. Swallow whole with fluid in an upright position. Up to 50 mmol daily orally. In severe acute hypokalaemia give an infusion containing 20mmol of potassium in 500ml over 2-3 hours under ECG control. Max; dose 2-3mmol potassium/kg/body weight in 24 hours

Side effects: After oral administration, nausea, vomiting, diarrhoea, abdominal cramps, gastric ulcer perforation and GIT bleeding may also occur. Hyperkalaemia especially in renal impairment, cardiac toxicity especially after intravenous administration.

Contraindications: Hyperkalaemia.

Caution: Avoid in renal failure, ensure adequate fluid intake, intestinal stricture, history of peptic ulcer, cardiac disease.

12.2.2 Intravenous administration

DEXTROSE (GLUCOSE)

Presentation: Solution containing 2.5% glucose in water (200ml), 5% glucose in water (1 litre), 10% glucose in water (1 litre), 50% glucose in water (100ml), 5% glucose in normal saline (1 litre).

Indications: Fluid replacement, provision of energy, hypoglycaemia.

Administration: Depends on the clinical condition of patient

Side effects: Injection especially if hypertonic may cause venous irritation and thrombophlebitis.

Caution: Diabetes mellitus and insipidus, 50% dextrose should be given into a large vein.

POTASSIUM CHLORIDE

(Refer to Potassium Chloride above under 12.2.1)

SODIUM BICARBONATE

Presentation: Solution containing 4.2% sodium bicarbonate, 50ml, 500ml. A capsule containing sodium bicarbonate 500mg.

Indications: Correction of metabolic acidosis, cardiac arrest, chronic acidotic states such as uraemic acidosis or renal tubular acidosis, to make ph of the urine alkaline.

Administration: ***Slow intravenous injection or continuous intravenous infusion according to requirements.***

Acidosis: 3 – 5mEq/kg.

In cardiac arrest larger doses are required. 500ml vials must be diluted in the ratio of 2 parts of bicarbonate to 5 parts of dextrose 5%.

Orally

Correction of metabolic acidosis: 4.8g daily (8 tablets).

Alkalinisation of urine, relief of discomfort in mild urinary-tract infections: 3 g P.O every 2 hours until urinary pH exceeds 7. To be dissolved in water.

Maintenance of alkaline urine: 5–10 g P.O daily, to be dissolved in water.

Children:

Chronic acidotic states such as uraemic acidosis or renal tubular acidosis.

Initially 1–2 mmol/kg P.O daily in divided doses, adjusted according to response.

Metabolic acidosis

Administer an amount appropriate to the body base deficit, to be given by slow intravenous injection of a strong solution (up to 8.4%), or by continuous intravenous infusion of a weaker solution (usually 1.26%)

Renal hyperkalaemia: 1 mmol/kg daily.

Persistent cyanotic spell in a child with congenital heart disease despite optimal use of 100% oxygen and propranolol:

1 mmol/kg IV, dose given to correct acidosis (or dose calculated according to arterial blood gas results), sodium bicarbonate 4.2% intravenous infusion is appropriate for a child under 1 year and sodium bicarbonate 8.4% intravenous infusion in children over 1 year.

Side effects: Alkalosis. Most serious side effects are due to hypernatraemia. This may lead to pulmonary and peripheral oedema and dehydration of the brain. GIT effects are nausea, vomiting, diarrhoea and abdominal cramps.

Contraindications: Routine use of intravenous sodium bicarbonate.

Caution: Cardiac failure, hypertension, renal failure, peripheral and pulmonary oedema and toxaemia of pregnancy.

SODIUM CHLORIDE (NORMAL SALINE)

Presentation: Solution containing 0.9% sodium chloride, 200ml, 1 litre packs, 500ml packs of sodium chloride.

Indications: Correction of electrolyte imbalance. Sterile irrigation in eye, bladder, general skin or wound cleansing.

Administration: *Replacement therapy*; 8-10mcg/kg body weight.

In severe sodium depletion: 2-3 litres of 0.9% solution over 2-3 hours, thereafter a slower rate.

Maintenance therapy; 2.5mcg/kg body weight.

Side effects: Sodium accumulation (electrolyte imbalance) and oedema. Hypernatraemia if large doses are administered and oedema.

Caution: Restrict intake in renal, cardiac impairment, hypertension, peripheral and pulmonary oedema and toxaemia of pregnancy.

SODIUM LACTATE AND GLUCOSE

Presentation: Full strength and half-strength solution containing sodium chloride and potassium bicarbonate. Half strength also contains dextrose 2.5%.

Indications: Dehydration

Administration: *Mild dehydration*; 50ml/kg body weight.

Moderate dehydration; 70 – 100mg/kg body weight.

Severe dehydration; 120 – 150ml/kg body weight.

Side effects: Fluid overload and electrolyte imbalance.

SODIUM LACTATE COMPOUND (RINGER-LACTATE SOLUTION)

Presentation: Solution containing sodium chloride 0.6%. sodium lactate 0.25%. potassium chloride 0.04%. calcium chloride 0.027%, 500ml, 1000ml packs

Indications: Diabetic coma, severe dehydration due to acute diarrhoea and burns.

Administration: *Acidosis*; 60ml/kg body weight.

Alkalinisation of urine; 30ml/kg body weight.

Severe dehydration; 30ml/kg body weight per hour.

The dose may be adjusted according to patients needs.

Side effects: Salt and water overload

WATER FOR INJECTION

Presentation: Available in 1ml, 2ml, 5ml, 10ml, 20ml, 50ml of water.

Indications: For reconstitution of injections.

Presentation: Solution containing dextran 70 in 5% dextrose or in 0.9% sodium chloride in 500ml packs.

Indications: Predominantly for blood volume expansion in shock arising from conditions such as burns or septicaemia and following acute haemorrhage.

Administration: ***Adult:*** *By intravenous infusion*

Shock: No more than 20ml/kg during first 24hours; then 10ml/kg/day

Acute haemorrhage or in the shock phase of burns injury: (initial 48 hours), 500ml to 1000ml rapidly, followed by 500ml later if necessary, given slowly. The total dose and rate of flow will depend on the clinical state of the patient.

Children:

Shock, IV infusion: Initial dose 10ml/kg infused rapidly, no more than 20ml/kg/24hours, then no more than 10ml/kg/day, for not more than 5days.

Side effects: Urticarial and other hypersensitivity reactions, fluid overload.

Contraindications: Severe congestive heart failure, renal failure.

Caution: Congestive heart failure, renal impairment, coagulation defects, blood samples should be taken before infusion, as dextran 70 may interfere with blood group cross-matching or other biochemical measurements.

GELATIN

Presentation: Solution containing gelatin polygeline, 500ml.

Indications: Low blood volume

Administration: *By IV infusion;* initially 500 – 1000ml of a 3.5–4% solution.

Children:

Initially 10–20 ml/kg IV. Use 3.5–4% solution.

Side effects: See under Dextran above (12.2.3.), increased risk of hypersensitivity reactions.

Caution: See under Dextran above (12.2.3.),

Contraindications: See under Dextran above (12.2.3.).

13 Medicines acting on the Skin

Dermatological preparations for several conditions are available in various suitable vehicles. The choice of vehicle i.e. creams, lotion, application, the aqueous or oily base is important as the vehicle may affect the degree of hydration of the skin or aid the penetration of the active drug in the preparation and thereby affect the treatment outcome.

Some additives in topical preparations may be associated with sensitization. These include wool fat, some fragrances, propylene glycol etc.

Preparations containing an antibacterial should be avoided unless a bacterial infection is present. The choice of such medicines should be limited to those not used systematically.

13.1 Antiprutitics

CALAMINE

Presentation: Lotion containing calamine 15% and zinc oxide 5%. An ointment containing calamine 15% in white soft paraffin.

Indications: Pruritis.

Administration: Adult:

Mild pruritus caused by sunburn and other minor skin conditions: Apply liberally to the entire affected area 3–4 times daily with a pad of cotton wool.

Children:
Mild pruritus caused by sunburn and other minor skin conditions: Apply liberally 3–4 times daily with a pad of cotton wool.

13.2 Topical corticosteroids

For the treatment of inflammation of the skin, particularly eczematous disorders. Corticosteroids are only for the relief of symptoms and suppression of signs. They are of no use in the treatment of infections and urticaria. They are contraindicated in rosacea and ulcerative conditions as they worsen the condition. They should not be used indiscriminately in pruritis. Systemic or potent corticosteroids should be avoided or given only under specialist supervision.

The most potent topical corticosteroids should be reserved for recalcitrant dermatoses. Use in children should be avoided or, if necessary should be used with great care and only for short periods.

HYDROCORTISONE

Presentation: Cream containing 0.5% and 1% hydrocortisone, ointment containing 0.5% and 1% hydrocortisone.

Indications: Mild inflammatory skin disorders such as eczema.

Administration: Apply thinly 2 – 3 times daily, reducing frequency as the condition responds.

Side effects: Thinning of skin with prolonged use, increased hair growth, peri-oral dermatitis, acne at the site of application, mild pigmentation and vellus hair.

Contraindications: Untreated bacterial, fungal or viral infections.

BETAMETHASONE

Presentation: Cream containing betamethasone valerate 0.05% and 0.1 % in water-miscible base, ointment containing betamethasone valerate 0.05% and 0.1.% in anhydrous paraffin base, lotion containing betamethasone valerate 0.05% - 0.1%. Scalp application containing betamethasone valerate 0.1%.

Indications: Severe inflammatory skin disorders such as eczema unresponsive to less potent corticosteroids; psoriasis.

Administration: Apply thinly 2 – 3 times daily reducing frequency as the condition responds.

Side effects: Severe pituitary-adrenal-axis suppression and hypercorticism and immunosuppression on prolonged use.

Contraindications: See hydrocortisone above. Do not use in infants and children.

CLOBETASOL

Presentation: Cream, Ointment, Scalp application containing 0.05% clobetasol propionate.

Indications: Short term treatment of severe resistant inflammatory skin disorders such as recalcitrant eczema unresponsive to less potent corticosteroids, psoriasis.

Administration: Apply thinly 1 – 2 times daily for up to 4 weeks reducing frequency as the condition responds.

Side effects: See hydrocortisone above.

Contraindications: See hydrocortisone above.

Caution: This is a high potent corticosteroid.

FLUOCINOLONE

Presentation: Cream, an ointment containing 0.025% fluocinolone acetonide.

Indications: Inflammatory skin disorders such as eczema, psoriasis.

Administration: Apply thinly 2 – 3 times daily reducing frequency as the condition responds.

Side effects: See hydrocortisone above.

Contraindications: See hydrocortisone above

13.3 Preparations for Eczema and Psoriasis

13.3.1 Eczema

Eczema (dermatitis) is due to a particular type of epidermal inflammation. Where possible the causative factor should be established and removed before commencing medication. Emollients and preparations containing zinc oxide and calamine may be sufficient to treat dry, fissured, scaly lesions. Chronic eczematous conditions where there is marked thickening of the skin and pronounced scaling may require treatment with other substances like keratolytic.

TACROLIMUS

Presentation: Ointment containing 0.03% or 0.1% of Tacrolimus

Indications: moderate to severe atopic eczema, facial, flexural, or genital psoriasis

Administration: *Treatmen*t- Apply twice daily until lesion clears (consider other treatment if eczema worsens or no improvement after 6 weeks). Initially 0.1% ointment to be applied thinly, reduce frequency to once daily or strength of ointment to 0.03% if condition allows.

Prophylaxis- Apply twice weekly, 0.1% ointment to be applied thinly, with an interval of 2–3 days between applications.

Side effects: Alcohol intolerance, increased risk of infection, abnormal sensation, skin reactions, lymphadenopathy.

Contraindications: Malignant or potentially malignant skin lesions, congenital epidermal barrier defects, generalised erythroderma, immunodeficiency, infection at treatment site.

Caution: Pregnancy, breastfeeding, hypersensitivity, hepatic impairment.

COAL TAR

Presentation: Ointment, lotion, cream containing Coal tar extract 1%, 5% or 10%. Also available in combination with calamine and zinc oxide.

Indications: Chronic eczema and psoriasis.

Administration: 1 – 3 times daily starting with low strength preparation.

Side effects: Skin irritation and acne-like eruptions, photosensitivity, stains skin, hair and fabric.

Caution: Avoid eyes and broken or inflamed skin.

SALICYLIC ACID

Presentation: Ointment containing salicylic acid 2% in wool alcohol ointment; A paste containing salicylic acid 2% and zinc oxide 24%.

Indications: Chronic eczema

Administration: Apply twice daily.

Side effects: Irritant contact sensitivity, systemic effects if used extensively, excessive drying of the skin.

Caution: Avoid broken or inflamed skin.

13.3.2 Psoriasis

Psoriasis is characterized by epidermal thickening and scaling. Preparations containing coal tar, salicylic acid and dithranol are commonly used to treat psoriasis. Some patients are intolerant to dithranol even in low concentrations. Fair skin is more sensitive than dark skin. It is important to recognise the problem of intolerance early in treatment.

CYCLOSPORIN

Cyclosporin may be used, under specialist supervision, in severe resistant psoriasis. Corticosteroids should be avoided and if used specialist supervision is necessary. Only weaker corticosteroids like hydrocortisone should be used and only for short periods.

TAZAROTENE

Presentation: Cream or Gel containing 0.05-0.1% of Tazarotene

Indications: Mild to moderate plaque psoriasis, Acne Vulgaris and wrinkles

Administration: Apply once daily usually for up to 12 weeks, apply in the evening

Side effects: Contact dermatitis, paraesthesia, pain, folliculitis, skin atrophy, excoriations and rash.

Contraindications: Pregnancy

Cautions: Avoid contact with eczematous skin, avoid contact with eyes, avoid contact with face, avoid contact with hair covered scalp, avoid contact with inflamed skin, avoid contact with intertriginous areas.

DITHRANOL

Presentation: Ointment containing 0.1%, 2% and 5% dithranol.

Indications: Subacute and chronic psoriasis

Administration: Apply to the lesion, cover with a dressing and leave for an hour. It is preferable to leave the application overnight but short contact applications are also effective.

Side effects: Local burning, sensitization and irritation, stains skins, hair and fabrics.

Caution: Intolerance in some patients, wash hands thoroughly after use, avoid use near eyes.

SALICYLIC ACID

Presentation: See 13.3.1 under eczema

Indications: Psoriasis

Administration: Apply twice daily

Side effects: See 13.3.1 under Eczema

Caution: See 13.3.1 under eczema

13.4 Preparations for acne

Treatment involves removing follicular plugs and reducing skin flora. The skin should be cleaned regularly with detergent solutions. Antiseptics and keratolytics are applied after cleansing. Topical antibiotics may also be used for mild to moderately severe acne.

Preparations are those containing erythromycin (refer to systemic anti-infectives), tetracycline or clindamycin. Topical neomycin is unsuitable owing to sensitization.

Topical corticosteroids should not be used in acne.

Thick, greasy preparations should not be used.

BENZOYL PEROXIDE

Presentation: Gel containing 2.5%, 5% benzoyl peroxide in the aqueous-alcoholic base, cream containing 5% benzoyl peroxide in a non- greasy basis, lotion containing 5% benzoyl peroxide in a non-greasy basis.

Indications: Acne vulgaris

Administration: Apply 1 – 2 times daily to clean skin, starting with lower strength preparations.

Side effects: Skin irritation which subsides with continued treatment.

Caution: Avoid contact with eyes, mouth, mucous membranes. May bleach fabrics.

CLINDAMYCIN CREAM/GEL

Presentation: Topical cream or gel containing 1% of Clindamycin.

Indications: Acne Vulgaris

Administration: ***Adult*** **-**Apply twice daily, to be applied thinly.

Children:
Apply twice daily, to be applied thinly.

Side effects: Skin dryness, oiliness, erythema, peeling, burning/itching.

Contraindication: Hypersensitivity to clindamycin.

SALICYLIC ACID

Presentation: Topical solution containing 2% salicylic acid in a detergent base.

Indications: Acne vulgaris

Administration: Use up to 3 times daily. See also 13.3.1 under eczema.

Side effects: See 13.3.1 under eczema

Caution: Avoid contact with mouth, eyes, mucous membranes.

13.5 Preparations for Warts

SALICYLIC ACID

Warts are usually self-limiting and so the least destructive method of treatment should be used. Keratolytics are the preferred method of treatment.

Presentations: Ointment containing 50% Salicylic acid in paraffin basis. Ointment containing 25% salicylic acid, 20% podophyllum resin, Paint containing 16.7% Salicylic acid. 16.7% lactic acid in flexible collodion, application containing 26% salicylic acid.

Indications: Removal of warts.

Administration: Apply directly to the wart. Remove dead skin by gentle rubbing with pumice stone then cover with plaster (unless in collodion basis).

Side effects: Skin irritation. See 13.3.1 under eczema.

Contraindications: Preparation containing podophyllum contraindicated in pregnancy.

Caution: Protect surrounding skin and avoid broken skin; not suitable for application to the face, anogenital region or large areas.

PODOPHYLLIN

Presentation: Ointment containing podophyllum resin 15% in compound benzoin tincture.

Indications: External genital warts

Administration: Apply directly to the wart and allow to stay for no longer than 6 hours. Then wash off. Avoid splashing surrounding skin during application.

Side effects: Irritation of treated area, severe toxicity on excessive application.

Contraindications: Pregnancy, breastfeeding and in children.

Caution: Avoid in normal skin and open wounds. Keep away from the face, very irritant to the eyes. Cover surrounding skin with soft paraffin as protection. Treat only a few warts at a time where there are many as severe toxicity caused by absorption of podophyllin has been reported.

13.6 Anti-infective skin preparations

This section includes antibacterial, antifungal and antiviral preparations.

Some infections particularly if they are widespread, may require systemic treatment, as topical applications may not achieve adequate penetration.

13.6.1 Anti-Bacterial Preparations

Antibacterial Medicines should only be considered in skin conditions involving infection by a sensitive organism. To minimize the development of resistant organisms, topical preparations should, as far as possible, contain medicines that are not used systemically.

NEOMYCIN SULPHATE

Presentation: Cream containing Neomycin sulphate 0.5%.

Indications: Skin infections due to sensitive organism. **Administration:** Apply up to 3 times daily; maximum 60g daily for 3 weeks. Do not repeat for at least 3 months.

Side effects: Allergic hypersensitivity, ototoxicity, nephrotoxicity with prolonged use.

Contraindications: Hypersensitivity to neomycin, cross-sensitisation with aminoglycosides.

FUSIDIC ACID

Presentation: Cream or gel containing Fusidic acid 2%, ointment containing Sodium fusidate 2%.

Indications: Staphylococcal skin infections.

Administration: Apply 3 – 4 times daily.

Side effects: Local hypersensitivity reactions.

13.6.2 Antifungal preparations

These are available as lotions, ointments and dusting powders. Lotions are preferred for application to large and hairy areas. Ointments are best avoided on moist surfaces because of their occlusive properties. Dusting powders are not effective and may cause skin irritation.

BENZOIC ACID

Presentations: Ointment containing benzoic acid 6% and salicylic acid 3%.

Indications: Ringworm (tinea).

Administration: Apply twice daily.

CLOTRIMAZOLE

Presentation: Cream or powder containing 1% Clotrimazole.

Indications: Fungal skin infections.

Administration: Apply once daily until a few days after the disappearance of all symptoms.

Side effects: Occasional skin irritation or sensitivity.

Contraindications: Hypersensitivity to clotrimazole.

KETOCONAZOLE CREAM

Presentation: Cream or shampoo containing 1% or 2% Ketoconazole.

Indications: Tinea pedis, other fungal skin infections, seborrhoeic dermatitis and dandruff, treatment and prophylaxis of pityriasis versicolor.

Administration: *Cream* - Apply 1-2 times daily for 2-4 weeks.

Shampoo - Apply twice weekly for 2–4 weeks, leave preparation on for 3–5 minutes before rinsing.

Side effects: Skin reactions, alopecia, angioedema, folliculitis, abnormal hair texture.

Contraindications: Broken skin, hypersensitivity.

MICONAZOLE NITRATE

Presentation*:* Cream containing Miconazole nitrate 2%, a lotion containing Miconazole nitrate 2%.

Indications: Fungal infections of skin, hair and nails. **Administration:** Apply twice daily and continue for 10 days after lesions have healed.

For nail infections: apply daily under occlusive dressing.

Side effects: Occasional skin irritation or sensitivity.

Contraindications: Hypersensitivity to miconazole.

GRISEOFULVIN TABLETS

Presentation: Tablet containing 125mg, 250mg or 500mg Griseofulvin.

Indications: Tinea Infections.

Administration: ***Adult*** – 500mg once daily for at least 2 weeks up to a maximum of 6 months depending on site of infection.

Children:
7-11mg/kg/day for 2 weeks to 6 months depending on site of infection.

Side effects: Rash, urticaria, headache, fatigue, dizziness, oral thrush, diarrhoea, nausea, vomiting, insomnia, hepatotoxicity, photosensitivity.

Contraindications: Pregnancy, Hepatic Impairment and hypersensitivity.

Cautions: Risk for SJS.

TERBINAFINE

Presentation: Cream containing 1% Terbinafine; Tablet containing 250mg Terbinafine.

Indications: Tinea Infections, dermatophyte infections of the nails, cutaneous candidiasis/ pityriasis versicolor

Administration: *Cream:* Apply 1–2 times a day for up to 1–2 weeks, to be applied thinly, review treatment after 2 weeks.

Tablet: 250 mg once daily for 2 weeks – 3 months.

Side effects: With oral use: altered taste, decreased appetite, athralgia, diarrhea, nausea, abdominal pain, skin reactions. With topical use: burning, dryness, exfoliation, itchiness, rash.

Contraindication: Hypersensitivity, active or chronic liver disease.

SELENIUM

Presentation: Shampoo or lotion containing 1-2.5% of Selenium

Indications: Seborrhoeic dermatitis/Dandruff, Pityriasis versicolor

Administration: *Seborrhoeic dermatitis:* Apply twice weekly for 2 weeks, then apply once weekly for 2 weeks, then apply as required.

Pityriasis versicolor- Apply once daily for 7 days, apply to the affected area and leave on for 10 minutes before rinsing off.

The course may be repeated if necessary. Diluting with a small amount of water prior to application can reduce irritation.

Side effects: Skin irritation, alopecia, itching, unusual dryness or oiliness of the scalp.

Contraindication: Hypersensitivity to selenium.

Caution: Avoid contact with mucus membranes.

13.6.3 Antiviral preparation

Topical preparations are not effective for the treatment of buccal or vaginal infections. Systemic preparations should be used in these cases. Herpes Zoster also requires systemic treatment.

ACYCLOVIR

Presentation: Cream containing 5% aciclovir
Indications: Initial and recurrent labial and genital herpes simplex infections.

Administration: Start treatment at the first sign of attack, apply to lesions every 4 hours (5 times daily) for 5 days. Continue up to 10 days if necessary.

Side effects: Transient stinging or burning, occasionally erythema or drying of the skin.

Contraindications: Hypersensitivity to acyclovir.

Caution: Avoid contact with eyes and mucous membranes, pregnancy

13.7 Parasiticidal Preparations

To effectively treat parasitic infections like scabies, all members of the affected household should be treated. The itching of scabies may persist for days after the infection has been eliminated. Antipruritic treatment may be administered.

BENZYL BENZOATE

Presentation: Emulsion containing Benzyl benzoate 25%.

Indications: Scabies.

Administration: Apply over the whole body (omit head and neck), repeat without bathing on the following day. Wash off on the third day. A third application may be required.

Side effects: Skin irritation, burning sensation especially on genitalia and excoriation, occasionally rashes, may cause convulsions when ingested.

Caution: Avoid in children, avoid contact with eyes and mucous membrane, pregnancy and breastfeeding.

MALATHION

Presentation: Lotion containing Malathion 0.5% in alcoholic base or liquid containing Malathion 0.5% in aqueous base.

Indications: Crab lice, head lice and scabies.

Administration: *Pediculosis* – rub lotion into dry hair, scalp, and affected area, comb, allow to dry naturally, remove by washing after 12 hours.

Scabies – apply liquid preparation over the whole body, omitting head and neck, and wash off after 24 hours.

Side effects: Skin irritation.

Caution: Avoid contact with eyes, alcoholic lotions not recommended for pediculosis in asthmatics or small children, or scabies or crab lice. Do not use lotion for more than once a week for 3 weeks at a time; medical supervision required when used in children under six months.

PERMETHRIN

Presentation: Cream rinse containing permethrin 1%. Dermal cream containing permethrin 5%.

Indications: (Cream rinse) head lice and (dermal cream) scabies.

Administration: *Cream Rinse (Head lice):* Apply to clean damp hair, leave on for 10 minutes, rinse and dry.

Dermal Cream (Scabies) – Apply over the whole body (excluding head in adults) and wash off after 8 – 24 hours.

Children:
Apply over the whole body, including face, neck, scalp and ears. If hands are washed with soap within 8 hours of application, the cream should be re-applied.

Side effects: Pruritus, erythema, and stinging; rarely: rashes and oedema.

Caution: Avoid contact with eyes, pregnancy and breastfeeding; children under 6 months: medical supervision required for cream rinse; children aged 2 months – 2 years: medical supervision required for dermal cream.

13.8 Surgical Antiseptics

Some of these preparations are used in minor burns and abrasions while others are used for general cleansing of skin and wounds. Preparations containing camphor and sulphonamides should be avoided.

CETRIMIDE

Presentation: Cream containing cetrimide 0.5% in water-miscible basis. A solution containing cetrimide 0.15% and chlorhexidine 0.015%.

Indications: Used in minor burns and abrasions, for cleansing and disinfecting wounds and burn.

ALCOHOL

Presentation: As surgical spirit or industrial methylated spirit.

Indications: Skin preparation before injection.

Administration: Apply as required.

Caution: Flammable, avoid using on broken skin.

SODIUM CHLORIDE

Presentation: Solution containing sodium chloride 0.9%.

Indications: General cleansing of skin and wounds.

CHLORHEXIDENE

Presentation: Solution containing chlorhexidine gluconate 0.05%.

Indications: For cleansing and disinfecting wounds and burns.

BENZALKONIUM CHLORIDE

Presentation: Solution containing benzalkonium chloride 1%.

Indications: Skin disinfection as pre-operative skin preparation.

Caution: Avoid contact with eyes.

IODINE COMPOUNDS

Presentation: Antiseptic solution containing povidone-iodine 10% in aqueous solution, antiseptic paint containing povidone-iodine 10%.

Indications: For disinfecting minor wounds and infections.

Side effects: Rarely sensitivity, may interfere with thyroid function tests.

Contraindications: Avoid regular use in patients with thyroid disorders or those receiving lithium therapy.

Caution: Pregnancy, breastfeeding, broken skin. Application to large wounds or severe burns may produce systemic adverse effects such as metabolic acidosis, hypernatremia and impairment of renal function.

CRYSTAL VIOLET (GENTIAN VIOLET)

Presentation: Paint containing crystal violet 0.5% in purified water.

Indications: Impetigo

Side effects: Mucosal ulceration

Caution: Stains skin and clothes. Not recommended for application to the mucous membrane or open wounds.

POTASSIUM PERMANGANATE

Presentation: Solution containing potassium permanganate 0.1% in water.

Indications: Cleansing and deodorizing suppurating eczematous reactions and wounds.

Administration: Wet dressing, or baths, approximately 0.01%.

Caution: Irritant to the mucous membrane, stains clothes and skin.

SODIUM DICHLORISOCYANURATE SOLUTION

Produce a rapid-acting wide spectrum disinfectant solution effective against vegetative bacteria, fungi, viruses and bacterial spores.

Presentation: Tablet containing Sodium Dichlorisocyanurate 0.5g, 2.5g, 5.0g and Granules 500g.

Indication: For disinfection of working surfaces, utensils, glassware and equipment in maternity units, nurseries, surgeries and laboratories, together with general hospital disinfection.

Caution: Warning! Do not use together with other products. May release dangerous gases (chlorine). If swallowed, wash mouth out thoroughly with water and drink plenty (500mg) of water or milk. Do not immerse animal fibres such as wool or silk due to strong proteolytic action. Avoid prolonged contact with stainless steel items. Do not form sprays or aerosols. Contact with combustible material may cause a fire. Avoid contact with skin and eyes. Thoroughly rinse eyes with water if need be.

Note: - Granules can be sprinkled onto spillage resulting in the hazard being rapidly solidified and made safe for disposal.

SODIUM HYPOCHLORITE

Presentation: A stabilized solution containing sodium hypochlorite 1%.

Indications: Disinfection of hard surfaces, food utensils, feeding bottles and teats.

Administration: Immense for 3 hours.

Caution: Dilute before use.

CHLOROXYLENOL

Presentation: Liquid containing chloroxylenol 4.8%.

Indications: General antisepsis and disinfectant.

Caution: Dilute with water.

14 Medicines used in the Treatment of Diseases of the Ear, Nose and Oropharynx

14.1 Medicines acting on the ear

OTITIS EXTERNA

Otitis externa is an inflammation of the external ear. Chronic otitis media must be excluded before commencing treatment. Many cases respond to a thorough cleansing of the external ear canal by suction, dry mopping or gentle syringing.

If an infection is present, an appropriate non-systemic anti-infective e.g. neomycin may be applied for only about a week. Sensitivity to some anti-infectives and solvents may occur, therefore caution is advised e.g. propylene glycol in chloramphenicol ear drops.

Where infection is present with inflammation and eczema, preparations containing an antiinfective and a corticosteroid may be used. Avoid the use of preparations containing aminoglycosides or polymyxins if the eardrum is suspected to be broken. Acute infection may cause severe pain and a systemic antibiotic is required with a simple analgesic e.g. paracetamol.

Eczema of the pinna may be treated with topical corticosteroids but prolonged use should be avoided.

OTITIS MEDIA

Otitis media is inflammation of the inner ear. Acute otitis media is the commonest cause of severe ear pain in small children and infants. Otitis media with effusions should be referred to hospital.

Local treatment of acute otitis media is ineffective and there is no place for local anaesthetic drops. Many attacks are viral in origin. Simple analgesics to relieve pain may be the only treatment required. The bacterial infection should be treated with systemic antibiotics. In some cases, thorough cleansing with an aural suction tube may completely control the infection. Refer to chapter 4.

14.1.1 Anti-inflammatory preparations

BETAMETHASONE SODIUM PHOSPHATE

Presentation: Eye/ear/nose drops containing 0.1% betamethasone sodium phosphate. Eye/ ear/ nose drops containing 0.1% betamethasone sodium phosphate plus 0.5% neomycin sulphate.

Indications: Eczematous inflammation in otitis externa (see notes above under 14.1).

Administration: *Ears:* 2 – 3 drops in the ear every 2 – 4 hours, reduce frequency when relief is obtained.

Eye, nose - see relevant sections

Side effects: Local sensitivity reactions.

Contraindications: Untreated infection.

Caution: Avoid prolonged use.

DEXAMETHASONE SODIUM PHOSPHATE

Presentation: Eye/ear drops containing 0.1% Dexamethasone sodium phosphate.

Indications: Inflammation in otitis externa with eczema present; short term treatment.

Administration: Instil 2-3 drops every 2-3 hours; reduce frequency when relief is obtained.

Contraindications: Untreated infection.

Caution: Use under expert supervision, avoid prolonged use.

HYDROCORTISONE

Presentation: Ear drops containing 1% Hydrocortisone acetate plus 0.3% Gentamycin sulphate. Eye/ear drops containing 1.5% Hydrocortisone acetate plus 0.5% Neomycin sulphate. Eye/ear ointment containing 1.5% Hydrocortisone acetate plus 0.5% Neomycin sulphate.

Indications: Eczematous inflammation in otitis externa (see notes above under 14.1)

Administration: *Eardrops*; 2 – 4 drops in the ear every 6 – 8 hours

Side effects: Local sensitivity reactions.

Contraindications: Untreated infection.

Caution: Avoid prolonged use

14.1.2 Anti-infective preparations

CHLORAMPHENICOL

Presentation: Eardrops containing 5% chloramphenicol in propylene glycol

Indications: Bacterial infection in otitis externa (refer to notes above).

Administration: Instil 2-3 drops into the ear 2-3 times a day.

Side effects: Sensitivity to propylene glycol

Contraindications: Perforated tympanic membrane.

Caution: Avoid prolonged use.

GENTAMYCIN

Presentation: Eye/Ear drops containing Gentamycin sulphate 0.3%.

Indications: Bacterial infection in otitis externa.

Administration: Instil 2-4 drops in the ear 3-4 times daily and at night.

Side effects: Local sensitivity.

Contraindications: Perforated tympanic membrane.

Caution: Avoid prolonged use.

CIPROFLOXACIN

Presentation: Ear drops containing ciprofloxacin 0.3%. **Indications:** Acute localised and chronic otitis externa.

Administration: Adult and Children 1-17 years: apply 0.25ml twice daily for 7 days.

Side effects: Ear pruritus

Contraindications: Perforated tympanic membrane.

Caution: Avoid prolonged use.

CLOTRIMAZOLE

Presentation: Ear drops containing clotrimazole 1% solution.

Indications: Otomycosis (Fungal infection of the ear).

Administration: ***Adult and Children:*** Apply 2–3 times a day; continue for at least 14 days after disappearance of infection.

Side effects: Hypersensitivity, oedema, pain, paraesthesia, skin reactions.

Contraindications: Hypersensitivity.

NEOMYCIN SULPHATE See under 14.1.1.

Systemic Antibiotics:

For severe otitis externa.

Amoxicillin: 25 mg/kg three times daily for 5-7 days. If penicillin-hypersensitive: **Erythromycin:** 10-20 mg/kg orally twice daily

Cephalexin: 6.25 mg/kg orally every 6 hours;

Ciprofloxacin: 10mg/kg orally every 12 hours,

(Refer to antibiotics under Section 4)

14.1.3 Wax softeners

Earwax protects the meatal skin and needs only be removed if it causes deafness or interferes with a proper view of the eardrum. As a general rule syringing is best avoided in patients with a history of recurring otitis externa, a perforated eardrum or previous ear surgery.

Wax may be removed by syringing with warm water. If necessary, wax can be softened with simple remedies such as vegetable oil.

SODIUM BICARBONATE

Presentation: Eardrops containing sodium bicarbonate 5%.

Indications: Excessive ear wax.

Administration: Instil 3-4 drops in the ear. Keep ear uppermost for 5-10 minutes. A syringe with warm water.

Caution: The drops should be recently prepared.

VEGETABLE OIL

Presentation: Eardrops

Indications: Earwax

Dose: Warm to body temperature and instil 4 -5 drops into the ear, wait 5-10 minutes with ear upwards and then syringe with warm water.

Caution: Hypersensitivity to oil reported.

14.2 Medicines acting on the Nose

14.2.1 Medicines used in nasal allergy

Oral antihistamines and systemic nasal decongestants are used to control mild cases. Topical corticosteroids and sodium cromoglycate may be used in severe cases. (see section 6).

14.2.2 Topical nasal decongestants

The common cold has no effective treatment at the moment and the temptation to use nasal drops should be resisted. Sodium chloride 0.9% given as nasal drops may relieve nasal congestion by liquifying mucus secretions.

SODIUM CHLORIDE

Presentation: Solution containing 0.9% sodium chloride administered as nasal drops

Indications: Nasal congestion

Administration: Use as required.

XYLOMETAZOLINE HYDROCHLORIDE

Presentation: 0.05% nasal spray/drops

Indications: Nasal congestion

Administration: ***Adults:*** 2–3 drops 2–3 times a day for a maximum of 7 days.

Children:
6–11 years: 1–2 drops 1–2 times a day for a maximum of 5 days
12–17 years: 2–3 drops 2–3 times a day for a maximum of 7 days.

Side effects: Cardiovascular effects, headache, hypersensitivity, nasal dryness, nausea, paraesthesia, visual impairment.

Contraindications: Decongestants in infants and children under 6 years has been associated with agitated psychosis, ataxia, hallucinations, and even death: Avoid; pregnancy.

Cautions: Angle-closure glaucoma, avoid excessive or prolonged use, cardiovascular disease (in children), diabetes mellitus, elderly, hypertension, hyperthyroidism, ischaemic heart disease (in adults), prostatic hypertrophy, (risk of acute retention) (in adults), rebound congestion.

FLUTICASONE

Presentation: Nasal spray containing 27.5mcg/spray and 50mcg/spray

Indications: For prophylaxis and treatment of seasonal allergic or perennial rhinitis.

Administration: ***Adults****:* 100 mcg once daily, increased to 100 mcg twice daily if necessary.

Children:

4–11 years: 50 mcg once daily, increased to 50 mcg twice daily if necessary.

12–17 years: 100 mcg once daily, increased to 100 mcg twice daily if necessary.

Side effects: Adrenal suppression, nasal ulceration occurs commonly with nasal preparations containing fluticasone furoate.

Contraindications: Hypersensitivity to fluticasone or ingredients.

Cautions: May mask acute infection, including fungal infection, exacerbate viral infections or limit response to vaccines; not for use in untreated localized infection involving nasal mucosa; administer antimicrobial therapy if bacterial infection of sinuses suspected or confirmed; respiratory tract fungal or bacterial infections, parasitic infections, ocular herpes simplex may occur.

MOMETASONE FUROATE

Presentation: Nasal spray containing 50mcg/ dose.

Indications: For prophylaxis and treatment of seasonal allergic or perennial rhinitis

Administration: ***Adults:*** 100 mcg daily, increased to 200 mcg if necessary.

Children:

3–11 years: 50 mcg daily, sprayed into each nostril.

12–17 years: 100 mcg daily, increased to 200 mcg if necessary.

Side effects: Nasal ulceration occurs commonly with preparations containing mometasone furoate, nose/throat dryness or irritation, blood tinged mucus/phlegm, and nose bleeds may occur.

Contraindications: Hypersensitivity.

Caution: Glaucoma, cataracts, infection, recent nose bleeds.

LORATIDINE

Presentation: Oral solution containing 1mg/ ml and tablet containing 5mg and 10mg Loratidine.

Indications: Nasal congestion, allergic rhinitis.

Administration: ***Adults****:* 10mg once daily or 5my every 12 hour. Do not exceed 10mg a day.

Children:

< 2years: Not recommended

2-6 years: 5 mg PO once daily

>6 years: 10 mg PO once daily; not to exceed 10 mg a day.

Side effects: Headache, Somnolence, Drowsiness, Nervousness, Fatigue, Dry mouth, Hyperkinesia, Conjunctivitis, Dysphonia, Malaise, URTI, Abdominal pain.

Contraindications: Hypersensitivity

Cautions: Renal and hepatic impairment.

CETIRIZINE

Presentation: Tablets containing 5mg and 10mg, oral solution containing 1mg/ml.

Indications: Symptomatic relief of allergy such as hay fever, chronic idiopathic urticaria, atopic dermatitis.

Administration: ***Adult:*** 10 mg once daily

Children:

2–5 years: 2.5 mg twice daily.

6–11 years: 5 mg twice daily.

12–17 years: 10 mg once daily.

Side effects: Agitation, asthenia, diarrhea, malaise, paraesthesia, skin reactions, aggression, angioedema, confusion, depression, hallucination, hepatic function abnormal, insomnia, movement disorders, oculogyration, oedema, seizure, syncope, tachycardia, taste altered, thrombocytopeniatic, tremor, urinary disorders, vision disorders, weight increased,

abdominal pain, appetite increased, dizziness, drowsiness, dry mouth, headache, memory loss, nausea, pharyngitis, suicidal ideation, vertigo.

Contraindications: Avoid in severe renal impairment, hypersensitivity to cetirizine hydrochloride or any of its ingredients levocetirizine, or hydroxyzine.

Cautions: Avoid alcohol, sedatives, and tranquilizers, due to increased risk of drowsiness. May cause CNS depression; avoid activities requiring mental alertness until accustomed to medication.

14.3 Medicines acting on the Oropharynx

14.3.1 Medicines for Oral Ulceration and Inflammation

Ulceration of the oral mucosa may be caused by trauma (physical or chemical), recurrent aphthae, infection, carcinoma, dermatological disorders, nutritional deficiencies, gastrointestinal disease, haematopoietic disorders and drug therapy. It is important to establish the diagnosis in each case as the majority of these lesions require specific management in addition to local treatment. Patients with unexplained mouth ulcers of more than three weeks duration require urgent referral to hospital for further diagnosis to exclude other more serious conditions such as oral cancer. Local treatment is aimed at protecting the ulcerated area, relieving pain and reducing inflammation.

14.3.1.1 Mouthwashes, Gargles and Dentifrices

Simple Mouthwashes

A saline or compound thymol glycerine mouth wash may relieve pain.

SODIUM CHLORIDE

Presentation: Mouth wash containing sodium bicarbonate 1%, sodium chloride 1.5% in a suitable vehicle with peppermint flavour.

Indications: Oral hygiene.

Administration: Rinse or gargle 10 ml twice daily (rinse or gargle for about 1 minute).

THYMOL

Presentation*:* Mouth wash containing glycerol 10%, thymol 0.05% with colouring and flavouring (compound thymol glycerine B.P. 1988); mouth wash solution tablets which may contain antimicrobial, colouring and flavouring agents in a suitable effervescent basis to make a mouth wash suitable for dental purposes.

Indications: Oral hygiene (see notes above)

Administration: *Mouth wash;* To be used undiluted or diluted with 3 volumes of warm water as necessary.

Mouth wash solution tablets; dissolve 1 tablet in a glass of warm water and rinse when necessary.

CARBENOXOLONE SODIUM

Presentation: Mouth gargle containing carbenoxolone sodium 1% (20mg/sachet). A Gel containing 2% carbenoxolone sodium in adhesive base.

Indications: Mild oral and perioral lesions.

Administration: *For mouth ulcers:* dissolve 1 sachet in 30-50ml of warm water and rinse 3 times a day and at bedtime. *Gel:* Apply after meals and at bedtime.

Side effects: May produce sodium and water retention and hypokalaemia.

Caution: Contraindicated in patients with hypokalaemia.

Antiseptic mouthwashes

Use of a chlorhexidine mouth wash is often beneficial in any mucosal ulceration with secondary bacterial infection and healing of aphthae is often accelerated. There is evidence that chlorhexidine has a specific effect inhibiting the formation of plaque on the teeth.

Mouthwashes have a mechanical cleansing action and freshen the mouth. Those containing an oxidising agent may be useful in the treatment of acute ulcerative gingivitis.

CETYLPYRIDINIUM CHLORIDE

Presentation: Solution containing cetylpyridinium chloride 0.5%

Indications: Oral hygiene.

Administration: Use undiluted or diluted with an equal volume of water.

Chlorhexidine Gluconate

Presentation: Solution containing chlorhexidine gluconate 0.1%, 0.12%, 0.2%, 0.5%. Dental gel containing 0.1% chlorhexidine gluconate. Oral spray containing 0.2% chlorhexidine gluconate.

Indications: Oral hygiene. Plaque inhibition.

Administration: Rinse mouth with 10 - 15ml for 30 seconds to 1 minute, 2 to 3 times a day.

Brush teeth with gel once or twice a day.

Spray teeth and gingival surfaces using up to 12 actuations twice a day.

Caution: Chlorhexidine gluconate may be incompatible with some ingredients in toothpaste; an interval of at least 30 minutes should be left between using toothpaste and chlorhexidine mouth wash.

HEXETIDINE

Presentation: Mouth wash or gargle containing 0.1% hexetidine.

Indications: Oral hygiene

Administration: Use 15ml undiluted 2 – 3 times a day.

Oxidising Agents

HYDROGEN PEROXIDE

Presentation: Mouth wash containing 6% hydrogen peroxide

Indications: Oral hygiene (see notes above).

Administration: Rinse the mouth for 2 -3 minutes with 15ml in half a glass of warm water 2 - 3 times a day.

POVIDONE IODINE

Presentation: Mouth wash or gargle containing 1% povidone-iodine.

Indications: Oral hygiene.

Administration: ***Adults and children over 6 years;*** Up to 10ml undiluted or diluted with an equal volume of warm water for up to 30 seconds, up to 4 times a day for up to 14 days.

Side effects: Idiosyncratic mucosal irritation and hypersensitivity reactions may interfere with the thyroid function tests and with tests for occult blood.

Contraindications: Avoid regular use in patients with thyroid disorders or those receiving lithium therapy.

Caution: Pregnancy, breastfeeding.

Mechanical Protection

Some gelatin-based pastes such as carmellose gelatin gel relieve discomfort by protecting the ulcer site through adhering to the mucosa.

CARMELLOSE SODIUM

Presentation: Oral paste containing carmellose sodium 16.5% in gelatin base. Powder containing carmellose sodium, pectin and gelatin in equal parts.

Indications: Mechanical protection of oral, and perioral lesions.

Administration: *Paste;* apply a thin layer on the lesion when necessary after meals.

Powder; sprinkle on the affected area when necessary.

Side effects: Occasional exacerbation of local infection.

CHOLINE SALICYLATE

Presentation: Oral gel containing choline salicylate 8.7% in a flavoured gel base.

Indications: Mild oral and perioral lesions.

Administration: Apply 1.25cm of gel with gentle massage not more often than every 3 hours.

Children:
Over 4 months old; apply 0.60cm of gel not more often than every 3 hours. Maximum 6 applications a day.

14.3.1.2 Corticosteroids

Some forms of oral ulcerations respond to corticosteroid therapy. Aphthous ulcers especially in the prodromal phase appear to respond well to this kind of therapy. Thrush and other types of candidiasis are recognised complications of corticosteroid treatment.

Triamcinolone dental paste is made in such a way that the paste is in contact with the mucosa for long enough to allow penetration of the lesion by the corticosteroid. However, application of the paste is not easy for some patients.

TRIAMCINOLONE ACETONIDE

Presentation: Oral paste containing triamcinolone acetonide 0.1% in adhesive base.

Indications: Oral and perioral lesions.

Administration: Apply a thin layer 2 - 4 times a day; do not rub in; use should be limited to 5 days in children and short-term treatment is also advised in adults.

Side effects: Occasional exacerbation of local infection.

14.3.1.3 Local Anaesthetics

Because of their relatively short duration of action when applied topically, local anaesthetics have a limited role in the management of oral ulcers. They may be useful in relieving the pain of intractable oral ulceration particularly that of major aphthae. Lignocaine 5% ointment or lozenges may be applied to the ulcer. Care should be taken to avoid anaesthesia of the pharynx, especially before meals as this may lead to choking.

Presentation: Ointments, gels, mouthwashes, sprays and lozenges.

Indications: Relief of pain in oral lesions.

Caution: Avoid prolonged use.

14.3.1.4 Oropharyngeal anti-infective Medicines

The commonest cause of sore throat is viral infection which does not benefit from antibiotic treatment. Streptococcal sore throats require systemic penicillin therapy (see section 4.). Systemic metronidazole is used in acute ulcerative gingivitis (see section 4.). Dental surgery and local treatment of periodontal diseases include administration of gels of metronidazole and of minocycline.

Oral antifungal Medicines

Oral thrush may be caused by *candida Albicans* and sometimes even other forms of stomatitis which may be a sequel to the use of broad-spectrum antibiotics or cytotoxics. Usually, withdrawal of the causative drug may lead to resolution of the condition; otherwise, an antifungal drug may be effective.

Of the antifungal Medicines used for infections of the oral cavity, amphotericin and nystatin are not absorbed from the gastrointestinal tract and are used by the local application in the mouth. Fluconazole and itraconazole are absorbed when taken orally and are available for administration by mouth for oropharyngeal candidiasis (see section 4.4.).

AMPHOTERICIN

Presentation: Lozenges containing 10mg Amphotericin-B sugar-free suspension containing 100mg/ml amphoterin B, 12ml supplied with a pipette.

Indications: Oral and perioral fungal infections.

Administration: *Lozenges*; dissolve 1 lozenge slowly in the mouth 4 times a day. May require 10 – 15 days of treatment. Continue for 48 hours after lesions have resolved. Increase the dose to 8 times daily if the infection is severe.

Oral suspension; place 1ml in the mouth after food and retain near lesions 4 times daily for 14 days. Continue for 48 hours after lesions have resolved.

Side effects: Local irritation, pruritis.

MICONAZOLE

Presentation: Sugar-free oral gel containing 24mg/ml Miconazole.

Indications: Prevention and treatment of oral fungal infection.

Administration: ***Adult*;** place 5 – 10ml in the mouth after food and retain near lesions 4 times daily.

Children:
Under 2 years; 2.5ml twice a day.
2- 6 years; 5ml twice a day.
Over 6 years; 5ml 4 times a day.
Continue treatment for 48 hours after lesions have resolved.

Side effects: Nausea, vomiting, diarrhoea and rarely allergic reactions.

Contraindications: Hepatic impairment.

Caution: Pregnancy and breast-feeding, avoid in porphyria.

NYSTATIN

Presentation: Pastilles containing Nystatin 100,000 units/ml. Oral suspension (sugar free) containing nystatin 100,000 units/ml.

Indications: Oral and perioral fungal infections.

Administration: *Pastilles/suspension;* 100,000 units 4 times a day after food for 7 days. Continue for 48 hours after lesions have resolved.

Note: Immunosuppressed patients may require higher doses e.g. 500,000 units 4 times a day.

Side effects: Nausea, oral irritation and sensitisation.

ITRACONAZOLE

Presentation: Oral solution containing 50mg/5ml; Capsule containing 100mg, 200mg Itraconazole.

Indication: Oral candidiasis

Administration: ***Adult:*** 100-200 mg P.O daily for 14 days.

Children:
1 month–11 years: 3–5 mg/kg P.O once daily for 15 days.
12–17 years: 100 mg P.O once daily for 15 days.

Viral Infection

Herpes infections of the mouth may be managed by a soft diet, adequate fluid intake, analgesics as required and use of chlorhexidine mouthwash to control plaque accumulation if tooth brushing is painful. In the case of severe herpetic stomatitis, systemic acyclovir is required (see section 4.).

Lozenges and Sprays

There is no convincing evidence that antiseptic lozenges and sprays have a beneficial action. They sometimes irritate and cause sore tongue and sore lips. Some of these products also contain local anaesthetics, which relieve pain but may cause sensitisation.

14.3.2 Treatment of Dry Mouth

Dry mouth (xerostomia) may be caused by Medicines' antimuscarinic (anticholinergic) side effects e.g. antispasmodics, tricyclic antidepressants and some antipsychotics; by irradiation of the head or neck region or by damage to or disease of the salivary glands. Patients with a persistently dry mouth may develop a burning or scalding sensation and have poor oral hygiene, they develop increased dental caries, periodontal diseases, intolerance of dentures and oral infections (particularly candidiasis). Dry mouth may be relieved in many patients by simple measures such as frequent sips of cool drinks or sucking pieces of ice or sugar-free pastilles. Artificial saliva can provide useful relief of dry mouth. Properly balanced artificial saliva should be of a neutral pH and contain electrolytes (including fluoride) to correspond approximately to the composition of saliva. Pilocarpine tablets are restricted to use in xerostomia following irradiation for head and neck cancer. They are effective only in patients who have some residual salivary gland functions and therefore should be withdrawn if there is no response.

PILOCARPINE HYDROCHLORIDE

Presentation: Tablets (film-coated) containing Pilocarpine hydrochloride 5mg.

Indications: Salivary glands hypofunction in xerostomia following irradiation for head and neck cancer (see also notes above under 14.3.2).

Administration: 5mg 3 times a day with or immediately after meals (last dose always with an evening meal); if the dose is tolerated but if the response is not sufficient after 4 - 8 weeks, dose may be increased to maximum 50mg daily in divided doses (but associated with increased side effects); Discontinue if no improvement after 3 months.

Children:
Not recommended in children.

Side effects: Sweating, chills, diarrhoea, nausea, vomiting, lacrimation, abdominal pain, amblyopia, hypertension, constipation, abnormal vision, dizziness, rhinitis, asthma, increased urinary frequency, headache, dyspepsia, vasodilation, flushing.

Contraindications: Uncontrolled asthma and chronic obstructive pulmonary disease (increased bronchial secretion and increased airway glaucoma).

Caution: Close medical supervision in asthma (avoid if uncontrolled) and in cardiovascular disease, biliary tract disease, peptic ulcer, hepatic impairment, there is a risk of increased urethral smooth tone and renal colic, eye examination before treatment (decreased visual acuity more likely at night and in patients with central lens changes); maintain adequate fluid intake to avoid dehydration associated with excessive seating; cognitive or psychiatric disturbances.

15 Medicines used in the treatment of Musculoskeletal Disorders

15.1 Rheumatic disease

Most rheumatic diseases require symptomatic treatment to relieve pain and stiffness. Non-steroidal anti-inflammatory medicines (NSAIDs) are commonly used and in certain circumstances, corticosteroids may be required to suppress inflammation.

Medicines are available which may affect the disease process itself and favourably influence the outcome of rheumatoid arthritis. These include penicillamine, gold salts, antimalarials, immunosuppressants and sulphasalazine.

15.1.1 Non-steroidal Anti-Inflammatory Drugs (NSAIDs)

In single-dose, NSAIDs have analgesic activity comparable to that of paracetamol and can therefore be taken on demand for mild or intermittent pain.

In full dosage, they have an analgesic and an anti-inflammatory effect which is long-lasting and therefore makes them suitable for use in inflammatory conditions such as rheumatoid arthritis and some cases of advanced osteoarthritis.

The differences in anti-inflammatory activity between different NSAIDs are small but there are considerable differences in the incidence and type of side effects. The prescriber should, therefore, weigh efficacy against possible side-effects.

A feature of NSAIDs is the considerable variation in individual patient response. It is, therefore, often necessary to change from one NSAID to another until a suitable one is found for a particular patient.

Most NSAIDs produce an effect within a few days. If no response is obtained, then the drug should be changed – after one week if used for analgesia alone, after 3 weeks if used for its anti-inflammatory action.

ACETYL SALICYLIC ACID

Presentation: Tablet containing Acetylsalicylic acid 300mg, dispersible tablets containing Acetylsalicylic acid 300mg.

Indications: Acute pain and inflammation in rheumatic disease (e.g. rheumatoid arthritis, osteoarthritis) and other musculoskeletal disorders including juvenile arthritis. Not recommended for use in minor illness and in children under 12 years.

Administration: 0.3 – 1g every 4 hours, maximum in acute conditions 8g daily

Children:
Under 12 years: Not recommended.
Juvenile arthritis: up to 80mg/kg body weight daily in 5 – 6 divided doses, increased in an acute exacerbation to 130mg/kg body weight. Doses should be taken after food.

Side effects: Common with anti-inflammatory doses; gastrointestinal discomfort or nausea, ulceration with occult bleeding and occasionally major haemorrhage, other

haemorrhages e.g. subconjunctival, tinnitus, vertigo, mental confusion, hypersensitivity reactions (angioedema, bronchospasm and rashes), increased bleeding time rate. Rare side effects include oedema, myocarditis, blood disorders particularly thrombocytopenia.

Contraindications: Gastro-intestinal ulceration, children under 12 years (except for juvenile arthritis) due to association with Reye's syndrome, breastfeeding haemophilia and other bleeding disorders, not for treatment of gout; history of hypersensitivity to aspirin and other NSAIDs includes those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or other NSAIDs.

Caution: Asthma, allergic disease, uncontrolled hypertension, hepatic or renal impairment (avoid if severe), may worsen these conditions, dehydration, pregnancy particularly at term, elderly, G6PD deficiency.

IBUPROFEN

Presentation: Film-coated, sugar-coated tablet containing 200mg and 400mg Ibuprofen; syrup containing Ibuprofen 100mg/5ml, gel/cream containing Ibuprofen 5%.

Indications: Pain and inflammation in rheumatic diseases (including juvenile arthritis) and other musculoskeletal disorders.

Administration: *Oral:* 1.2 – 1.8g daily in 3 – 4 divided doses, with food or milk, increased if necessary to a maximum of 2.4 g daily; maintenance dose of 0.6 – 1.2g daily.

Cream/gel; Apply up to 3 times daily – apply with a gentle massage.

Children:

Not recommended for children under 7kg.

>7kg: 20mg/kg body weight daily in divided doses (juvenile arthritis, up to 40mg/kg body weight daily).

Side effects: Has fewer side effects than other NSAIDs and is usually well tolerated. Side effects include gastrointestinal discomfort, nausea, diarrhoea, occasionally bleeding and ulceration; hypersensitivity reactions (angioedema, bronchospasm, rashes) headache, dizziness, vertigo, hearing disturbances e.g. tinnitus, haematuria, blood disorders, fluid retention (rarely precipitating congestive heart failure in elderly patients); a reversible acute renal failure in patients with pre-existing renal impairment.

Contraindications: Patients with a history of hypersensitivity to aspirin or other NSAIDs include those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAIDs; patients with active peptic ulceration.

Caution: Elderly, allergic disorders, patients with renal, cardiac or hepatic impairment since the use of NSAIDs may result in deterioration of renal function, asthma. Gel/cream; avoid contact with eyes, mucous membranes, inflamed or broken skin.

DICLOFENAC

Presentation: Enteric-coated tablet containing Diclofenac sodium 25mg, 50mg, modified-release tablet containing diclofenac sodium 75mg, 100mg. Injection 3ml ampoules containing diclofenac sodium 25mg/ml. Suppositories containing diclofenac sodium 12.5mg, 100mg. A gel containing diclofenac diethyl ammonium salt 1.16% (equivalent to diclofenac sodium 1%).

Indications: Pain and inflammation in rheumatic diseases (including juvenile arthritis) and other musculoskeletal disorders, acute gout.

Administration: *Orally;* 75 – 150mg daily in 2-3 divided doses, after food.

By deep IM injection into the gluteal muscle, acute exacerbations and post-operative; 75 mg once daily (twice daily in severe cases) for a maximum of 2 days.

Ureteric colic; 75mg, then a further 75mg after 30 minutes if necessary.

Rectally (suppositories); 100mg usually at night.

Gel; Apply 3 – 4 times daily with gentle massage (not suitable for children). Maximum total daily dose by any route 150mg.

Children: *Juvenile arthritis*

1 year or over; orally or rectally:

1–3mg//kg body weight daily in divided doses (25mg enteric-coated tablets or 12.5mg suppositories only).

Side effects: See under Ibuprofen above.

Contraindications: Porphyria, see under Ibuprofen above.

Caution: See under Ibuprofen above. Pain may occur at the injection site (occasionally tissue damage occurs), suppositories may cause rectal irritation.

NAPROXEN

Presentation: Tablet containing 250mg, 500mg Naproxen; A suspension containing naproxen 125mg/5ml. Suppositories containing naproxen 500mg.

Indications: Pain and inflammation in rheumatic disease (including juvenile arthritis) and other musculoskeletal disorders; acute gout.

Administration: *Orally* with food; 0.5 – 1g daily in 2 divided doses or 1g once daily.

Acute musculoskeletal disorders; 500mg initially, then 250mg every 6 - 8 hours as required, maximum dose after first day 1.25g daily.

Acute gout: 750mg initially, then 250mg every 8 hours until the attack has passed. rectally (suppositories); 500mg at bedtime, if necessary 500mg in the morning as well.

Children:

(over 5 years) juvenile arthritis; 10mg/kg body weight daily in 2 divided doses.

Side effects: See under ibuprofen above, has a lower incidence of side effects.

Contraindications: See under Ibuprofen above.

Caution: See under Ibuprofen above. Suppositories may cause rectal irritation and occasional bleeding.

INDOMETHACIN

Presentation: Capsule or tablet containing Indomethacin 25mg, 50mg. A suspension containing Indomethacin 25mg/5ml. Suppositories containing Indomethacin 100mg.

Indications: Pain and moderate to severe inflammation in rheumatic disease and other acute musculoskeletal disorders, acute gout.

Administration: *Orally;*

Rheumatoid arthritis; 50 – 200mg daily in 3 divided doses with food.

Acute gout; 150 – 200mg daily in 3 divided doses.

Rectally in suppositories; 100mg at night and in the morning if required.

Combined oral and rectal treatment; maximum total daily dose 150 – 200mg.

Side effects: High incidence of side effects, frequently gastrointestinal disturbances (including diarrhoea) headache, dizziness, and lightheadedness, gastrointestinal ulceration and bleeding, rarely, drowsiness, confusion, insomnia, convulsions, psychiatric disturbances, depression, syncope, thrombocytopenia, hypertension, hyperglycaemia, blurred vision, corneal deposit, peripheral neuropathy. Suppositories may cause pruritus, discomfort, bleeding.

Contraindications: See under ibuprofen above.

Caution: See under ibuprofen above, breastfeeding, epilepsy, parkinsonism, psychiatric disturbances; during prolonged therapy ophthalmic and blood examination are particularly advisable, avoid rectal administration in proctitis and haemorrhoids. Dizziness may affect the performance of skilled tasks e.g. driving.

PIROXICAM

Presentation: Capsule or tablet containing piroxicam 10mg, 20mg. An injection containing piroxicam 20mg/ml. Suppositories containing piroxicam 20mg. A gel containing piroxicam 0.5%.

Indications: Pain and inflammation in rheumatic disease (including juvenile arthritis) and other musculoskeletal disorders, acute gout.

Administration: *Orally or rectally,*

Rheumatic disease; initially 20mg daily with food, maintenance 10 – 30mg daily in single or divided doses.

Acute musculoskeletal disorders; 40mg daily in single or divided doses for 2 days, then 20mg daily for 7 – 14 days.

Acute gout; 40mg initially, then 40mg daily in single or divided doses for 4 – 6 days.

By deep intramuscular injection into the gluteal muscle, for initial treatment of acute conditions, as a dose by mouth (on short term basis).

Children Over 6 years*:* orally, juvenile arthritis;
L*ess than 15kg*; 5mg daily.
16- 25 kg; 10mg daily.
26–45kg; 15mg daily.
Over 46kg; 20mg daily.

Side effects: See under Ibuprofen above, pain at the injection site (occasionally tissue damage occurs), pancreatitis.

Contraindications: See under ibuprofen above.

Caution: See under ibuprofen above, avoid in porphyria.

MELOXICAM

Presentation: Tablet containing 7.5mg and 15mg. Oral suspension containing 7.5mg/5ml Meloxicam.

Indications: Exacerbation of osteoarthritis, pain and inflammation in rheumatic disease, ankylosing spondylitis, relief of pain and inflammation in juvenile idiopathic arthritis and other musculoskeletal disorders in children.

Administration: ***Adult:***

Exacerbation of osteoarthritis: 7.5 mg once daily, then increased, if necessary, up to 15 mg once daily.

Pain and inflammation in rheumatic disease, Ankylosing spondylitis: 15 mg once daily, then reduced to 7.5 mg once daily if required (7.5 mg once daily in the elderly).

Children:
Exacerbation of osteoarthritis:
16–17 years: 7.5 mg once daily, then increased, if necessary, up to 15 mg once daily
Pain and inflammation in rheumatic disease, Ankylosing spondylitis
16–17 years: 15 mg once daily, then reduced to 7.5 mg once daily if required.
Relief of pain and inflammation in juvenile idiopathic arthritis and other musculoskeletal disorders in children intolerant to other NSAIDs
12–17 years (body weight up to 50 kg): 7.5 mg once daily
12–17 years (body weight 50 kg and above): 15 mg once daily

Side effects: Constipation, diarrhoea, gastrointestinal discomfort, gastrointestinal disorders, headache, nausea, vomiting, anaemia, angioedema, burping, dizziness, drowsiness, electrolyte imbalance, fluid retention, hepatic disorders, hypersensitivity, oedema, skin reactions, stomatitis, vertigo, acte kidney injury, asthma, thrombocytopenia, conjunctivitis, leucopenia, altered mood, nightnares, palpitations, severe cutaneous adverse reactions, tinnitus, vision disorders, agranulocytosis, confusion.

Contraindications: Active gastro-intestinal bleeding, active gastro-intestinal ulceration, history of gastro-intestinal bleeding related to previous NSAID therapy history of gastro-intestinal perforation related to previous NSAID therapy, history of recurrent gastro-intestinal haemorrhage, history of recurrent gastro-intestinal ulceration severe heart failure.

Cautions: Allergic disorders, cardiac impairment (NSAIDs may impair renal function), cerebrovascular disease, coagulation

defects, connective-tissue disorders, dehydration, elderly, heart failure, history of gastro-intestinal disorders, peripheral arterial disease, uncontrolled hypertension.

CELECOXIB

Presentation: Capsule containing 50 mg, 100mg, 200mg and 400mg. Oral suspension containing 25mg/ml Celecoxib.

Indications: Pain and inflammation in osteoarthritis, pain and inflammation in rheumatoid arthritis, ankylosing spondylitis, migraine and dysmenorrhoea.

Administration: ***Adult:***

Pain and inflammation in osteoarthritis:

200 mg daily in 1–2 divided doses, then increased if necessary to 200 mg 12 hourly, discontinue if no improvement after 2 weeks on maximum dose.

Pain and inflammation in rheumatoid arthritis:

100 mg twice daily, then increased if necessary to 200 mg twice daily, discontinue if no improvement after 2 weeks on maximum dose.

Ankylosing spondylitis:

200 mg daily in 1–2 divided doses, then increased if necessary to 400 mg daily in 1–2 divided doses, discontinue if no improvement after 2 weeks on maximum dose.

Dysmenoeehoea:

400 mg PO initially, then 200 mg PRN on first day; 200 mg 12hourly PRN on subsequent days.

Migraine:

120 mg PO once daily

Children

NOT Recommended for children less than 2 years

≥2 years and >25 kg: 100 mg PO 12 hourly

≥2 years and 10-25 kg: 50 mg PO 12 hourly

Side effects: Angina pectoris, benign prostatic Hyperplasia, cough, diarrhoea, dizziness, dysphagia Dyspnoea, fluid retention, gastrointestinal discomfort gastrointestinal disorders, headache, hypersensitivity hypertension, increased risk of infection, influenza like illness, injury, insomnia, irritable bowel syndrome, muscle tone increased, myocardial infarction, nausea, nephrolithiasis, oedema, skin reactions, vomiting, weight increased, Anaemia, anxiety, arrhythmias, breast tenderness, burping, cerebral infarction, chest pain, conjunctivitis, constipation, depression, drowsiness, dysphonia, electrolyte imbalance, embolism and thrombosis, fatigue, tinnitus, haemorrhage, hearing impairment, paraesthesia, heart failure, hepatic disorders, lipoma, lower limb fracture, muscle complaints, nocturia, oral disorders palpitations, respiratory disorders.

Contraindications: Patients with a history of hypersensitivity to aspirin or any other NSAID which includes those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAID. Contra-indicated in patients with sulfonamide sensitivity. Active gastro-intestinal bleeding, active gastro-intestinal ulceration, cerebrovascular disease, inflammatory bowel disease, ischaemic heart disease, mild to severe heart failure, peripheral arterial disease.

Cautions: Allergic disorders, cardiac impairment NSAIDs may impair renal function, coagulation defects, connective-tissue disorders, dehydration (risk of renal impairment), elderly history of cardiac failure history of gastrointestinal disorders, hypertension, left ventricular dysfunction.

15.1.2 Corticosteroids

Corticosteroids should only be used in rheumatic diseases for specific indications. They can be used when other anti-inflammatory medicines are unsuccessful and in severe life-threatening situations to induce remission.

Polymyalgia rheumatica and temporal (grant cells) arteritis are always treated with corticosteroids. Polyarthritis nodosa and polymyositis are usually treated with

corticosteroids. Systemic lupus erythematosus is also treated with corticosteroids when necessary. Ankylosing spondylitis should not be treated with long-term corticosteroids through pulse doses that do not respond to conventional treatment.

Local corticosteroids injections are given to relieve pain, relieve inflammation, increase mobility and reduce deformity in joints. In rheumatoid arthritis such as tennis or golfer's elbow or compression neuropathies, they are injected directly into soft tissue. In tendinitis, they are injected into the tendon sheath (except the Achilles tendon which should not be injected as it has no true tendon sheath).

PREDNISOLONE

Presentation: Tablet containing prednisolone 1mg, 5mg, 25mg.

Indications: Suppression of inflammation in rheumatic disease when other Medicines are unsuccessful, polymyalgia rheumatic, temporal (giant cell) arteritis, polyarthritis nodosa, polymyositis, systemic lupus erythematosus.

Administration: *Polymyositis rheumatic;* initially 10 –15mg daily.

Temporal arteritis; 40 - 60mg daily. Treatment should be continued until remission occurs, then the dose gradually reduced to a maintenance dose of 7.5 – 10mg.

Polyarthritis nodosa, polymyositis, systemic lupus erythematosus; initially 60mg daily, reduce to a maintenance dose of 10 – 15mg daily.

Side effects: Cushing's syndrome, diabetes, osteoporosis, at high doses avascular necrosis, mental disturbances, euphoria, muscle wasting, peptic ulceration, suppression of clinical symptoms of infection leading to spread of infection, growth suppression in children, adrenal suppression (so dosage should be gradually reduced), risk of steroids cataract (75%) if more than 15mg prednisolone is given daily for several years, acne.

Contraindications: Viral infection e.g. herpes simplex, herpes zoster, measles, chickenpox; septicaemia, tuberculosis.

Caution: Should not be withdrawn abruptly as this may lead to acute adrenal insufficiency, hypotension and death. Other withdrawal symptoms rhinitis, conjunctivitis, loss of weight, arthralgia, painful and itchy skin nodules.

METHYLPREDNISOLONE

Presentation: Injection powder for reconstitution containing methylprednisolone as sodium succinate 40mg, 125mg, 200mg, 1g, 2g or injection, aqueous suspension containing methylprednisolone acetate 40mg/ml.

Indications: Sodium succinate preparation; suppression of highly active inflammatory disease while longer-term and slower acting medication is being started.

Acetate preparation; local inflammatory of joints and soft tissue.

Administration: *Sodium succinate preparation*; by slow intravenous injection or infusion: up to 1g on 3 consecutive days.

Acetate preparation; by intra-articular or soft tissue injection: 4–80mg according to size, where appropriate may be repeated at intervals of 7 – 35 days.

Side effects: See under prednisolone; flushing may occur with intra-articular injections.

Contraindications: See under Prednisolone.

Caution: See under prednisolone, full aseptic preCaution should be observed, rapid intravenous administration of large doses has been associated with cardiovascular collapse.

HYDROCORTISONE

Presentation: Injection (aqueous suspension) containing hydrocortisone acetate 25mg/ml.

Indications: Local inflammation of joints and soft tissues.

Administration: By intra-articular or soft-tissue injection; 5 – 50mg according to size, where appropriate may be repeated at intervals of 21 days. Not more than 3 joints should be treated on any one day.

Children:
5 – 30mg daily (divided).

Side effects: See under prednisolone, flushing may occur with intra-articular injection of corticosteroids.

Contraindications: Avoid infected areas.

Caution: See under prednisolone; full aseptic preCaution should be observed.

DEXAMETHASONE

Presentation: Injection containing dexamethasone sodium phosphate 5mg/ml. An injection containing dexamethasone phosphate 4mg/ml.

Indications: See under prednisolone.

Administration: 0.4 – 4 mg according to size, where appropriate may be repeated at intervals of 3 – 21 days according to the response by intra-articular or soft tissue injection.

Side effects: See under prednisolone.

Caution: See under prednisolone.

Contraindications: See under prednisolone.

TRIAMCINOLONE ACETONIDE

Presentation: Solution for injection containing 40mg.

Indication: Local inflammation of joint and soft tissue.

Administration: ***Adult****:* 5 to 40mg (max 80mg) intra-articular injection.

Children:
6-12 years: 0.03-0.2 mg/kg IM every 1-7 days.
>12 years: 60 mg IM every 6 weeks; may be supplemented by additional 20-100 mg IM PRN

Side effects: Joint swellings, contusions, sinusitis, cough, acne, arrhythmia, adrenal suppression, anaphylaxis, arthralgia, thromboembolism, delayed wound healing, euphoria, cataracts, hypertrichosis.

Contraindications: Systemic fungal infection, except as intra-articular injection for localized joint conditions, documented hypersensitivity to corticosteroids or any components of the product, IM corticosteroids contraindicated for idiopathic thrombocytopaenic purpura, administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids.

Caution: Triamcinolone acetonide injectable suspension is for intra-articular or intralesional use only. Rare instances of anaphylaxis have been reported in individuals receiving triamcinolone acetonide injection, regardless of the route of administration.

15.1.3 Rheumatic Disease Process Suppressants

Certain Medicines may suppress the disease process in rheumatic arthritis (gold, penicillamine hydroxychloroquine, chloroquine, immunosuppressants and sulphasalazine) and psoriatic arthritis (gold, immunosuppressants). These Medicines should only be used on expert advice. Full therapeutic response is produced after 4 – 6 months of treatment. If no response is seen within 6 months, the drug should be discontinued.

These Medicines are used when treatment with NSAIDs has been unsuccessful and if there is evidence of disease progression, treatment should be initiated before joint damage becomes irreversible.

Penicillamine has a similar action to gold and more patients can continue treatment than with gold. Chloroquine and hydroxychloroquine have similar action to and are better tolerated than gold or penicillamine. Immunosuppressants have similar action to gold and are alternatives where the response has not been obtained with gold, penicillamine, chloroquine or hydroxychloroquine.

PENICILLAMINE

Presentation: Tablet containing Penicillamine 50mg, 125mg, 250mg.

Indications: Severe active rheumatoid arthritis including juvenile arthritis, palindromic rheumatism.

Administration: ***Adult;*** initially 125 – 250mg daily before food for 1 month, increased by a similar amount at intervals of not less than 4 weeks to the usual maintenance dose of 500 – 750mg daily. The maximum dose, 1.5g daily. ***Elderly*****;** initially 50 – 125mg daily before food increased at intervals of not less than 4 weeks, to a maximum of 1g daily.

Children:
Initially 50mg daily before food for 1 month increased at intervals of not less than 4 weeks to the maintenance of 15 – 20mg/kg daily.

Side effects: Nausea, transient loss of taste, rashes which may necessitate discontinuation of treatment, anorexia, fever, blood disorders (thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia), proteinuria, haematuria, haemolytic anaemia, nephrotic syndrome, lupus erythematosus like syndrome, myasthenia gravis-like syndrome, pemphigus, Goodpasture's syndrome, Steven-Johnson syndrome.

Contraindications: Hypersensitivity, lupus erythematosus.

Caution: Renal impairment, pregnancy; avoid concurrent treatment with gold, chloroquine, hydroxychloroquine, or immunosuppressive treatment, avoid oral iron preparations within 2 hours of a dose, blood counts including platelets and urine examinations should be done every 1 or 2 weeks in the first 2 months then every 4 weeks to detect blood disorders and protein-urea.

CHLOROQUINE

Presentation: Tablet containing Chloroquine phosphate 250mg (150mg base), chloroquine sulphate 200mg (150mg base), syrup containing chloroquine sulphate 68mg/5ml (base 50mg/5ml), injection containing chloroquine sulphate 54.5mg/ ml (base 40mg/ml).

Indications: Active rheumatoid arthritis (including juvenile, arthritis) discoid lupus erythematosus.

Administration: Chloroquine base 150 mg daily, a maximum of 2.5 mg/kg body weight daily (lean body weight).

Children: Up to 3mg/kg body weight daily.

Side effects: Gastrointestinal disturbances, headache, visual disturbances, irreversible retinal damage, corneal opacities, depigmentation or loss of hair, skin reactions, ECG changes; rarely blood disorders.

Contraindications: Psoriatic arthritis.

Caution: Hepatic and renal impairment, pregnancy, porphyria, may exacerbate psoriasis, neurological disorders (especially epilepsy) may aggravate myasthenia gravis, severe gastrointestinal disorders, G6PD deficiency, elderly; avoid concurrent hepatotoxic Medicines; examine eyes before starting treatment and monitor once monthly for visual disturbance.

HYDROXYCHLOROQUINE

Presentation: Tablet containing 200mg Hydroxychloroquine.

Indications: Active rheumatoid arthritis, Systemic and discoid lupus erythematosus, Dermatological conditions caused or aggravated by sunlight, Malaria prophylaxis.

Administration: **Adult:**

Malaria prophylaxis

400 mg (310 mg base) PO weekly, starting 2 weeks before exposure and continued for 4 weeks after departure from endemic area

Active rheumatoid arthritis, Systemic and discoid lupus erythematosus, Dermatological conditions caused or aggravated by sunlight: 200–400 mg daily, maximum 6.5mg/kg/day.

Systemic Lupus Erythematosus

200-400 mg/day (155-310 mg base/day) PO as a single daily dose or in two divided doses.

Doses >400 mg/day are not recommended

Children:

Malaria prophylaxis

6.5 mg/kg (5 mg/kg base) PO once weekly, not to exceed 400 mg (310 mg base), starting 2 weeks before exposure and continued for 4 weeks after leaving the endemic area

Active rheumatoid arthritis, Systemic and discoid lupus erythematosus, Dermatological conditions caused or aggravated by sunlight

6.5 mg/kg per day

Side effects: Abdominal pain, appetite decreased, diarrhea, emotional lability, headache, nausea, skin reactions, vision disorders, vomiting, Alopecia, corneal oedema, dizziness, eye disorders, hair colour changes, nervousness, neuromuscular dysfunction, retinopathy, seizure, tinnitus, vertigo, Acute hepatic failure, agranulocytosis, anaemia, angioedema, bone marrow disorders, bronchospasm, cardiac conduction disorders, cardiomyopathy, hearing loss, hypoglycaemia, leucopenia, movement disorders, muscle weakness, myopathy, photosensitivity reaction, psychosis, overdose: Hydroxychloroquine is very toxic in overdosage; overdosage is extremely hazardous and difficult to treat. Life-threatening features include arrhythmias (which can have a very rapid onset) andconvulsions (which can be intractable).

Contraindications: Hypersensitivity to 4-aminoquinoline derivatives.

Cautions: Acute porphyrias, diabetes, G6PD deficiency, maculopathy, may aggravate myasthenia gravis, may exacerbate psoriasis, neurological disorders (especially in those with a history of epilepsy—may lower seizure threshold), severe gastrointestinal disorders.

AZATHIOPRINE

Presentation: Tablet containing azathioprine 25mg, 50mg; Injection, powder for reconstitution containing azathioprine (as sodium salt) 50mg.

Indications: Rheumatoid arthritis when no response is obtained with gold, penicillamine, chloroquine, hydroxychloroquine.

Administration: 1.5 to 2.5mg/kg daily in divided doses.

Side effects: Irritation at the injection site; myelosuppression, hepatic toxicity, nausea, vomiting, diarrhoea.

Contraindications: Psoriatic arthritis, hypersensitivity to azathioprine, pregnancy

Caution: Reduce dose when given concurrently with allopurinol, blood counts should be done every 4 weeks to detect possible neutropenia and/ or thrombocytopenia, patients will be prone to atypical infections, herpes zoster infections may occur; reduce dose in severe hepatic or renal impairment.

INFLIXIMAB

Presentation: Solution for injection containing 100mg per vial.

Indications: Rheumatoid arthritis, psoriatic arthritis, plague psoriasis, crohns disease, ulcerative colitis, reducing signs and symptoms in patients with active ankylosing spondylitis.

Administration: ***Adult:***

Moderate to severely active Rheumatoid Arthritis in combination with methotrexate

3 mg/kg IV at 0, 2, and 6 weeks, then once every 8 weeks thereafter. If incomplete response is noted, dose may be increased to 10 mg/kg OR increasing the dosing frequency to every 4 weeks.

Psoriatic Arthritis

5 mg/kg IV at 0, 2, and 6 weeks, then every 8 weeks thereafter. May be used with methotrexate.

Plaque Psoriasis

5 mg/kg IV at 0, 2, and 6 weeks, then every 8 weeks thereafter. Can be used with or without methotrexate.

Crohn Disease

5 mg/kg IV at 0, 2, and 6 weeks, then every 8 weeks thereafter.

For adult patients who respond and then lose

their response, consideration may be given to treatment with 10 mg/kg

Patients who do not respond by week 14 are unlikely to respond with continued dosing and consideration should be given to discontinue.

Ulcerative Colitis

5 mg/kg IV at 0, 2, and 6 weeks, then every 8 weeks SC.

Ankylosing Spondylitis

5 mg/kg IV at 0, 2, and 6 weeks, THEN every 6 Weeks thereafter

Children:
<6 years: safety not established.
≥6 to 17 years: 5 mg/kg IV at 0, 2, and 6 weeks, then every 8 weeks thereafter

Side effects: Development of antinuclear antibodies, Infection, Upper respiratory tract infection, Abdominal pain, Nausea Infusion-related reaction, Headache, respiratory tract infection, Diarrhea, elevated liver enzymes, leukopenia, neutropenia.

Contraindications: Active serious infections, documented hypersensitivity.

Cautions: Demyelinating disorders (risk of exacerbation), dermatomyositis, development of malignancy.

GLUCOSAMINE /CHONDROITIN

Presentation: Tablet containing 1500mg glucosamine only. Also tablet containging 500mg glucosamine, 267mg chondroitin and 50mg vitamin C. Also tablet containing 375mg glucosamine and 300mg chondroitin.

Indications: Symptomatic relief of mild to moderate osteoarthritis of the knee.

Administration: ***Adult:*** 1500 mg once daily, review treatment if no benefit after 2–3 months.

Side effects: Constipation, diarrhoea, fatigue, gastrointestinal discomfort, headache, nausea, flushing, skin reactions, jaundice, angioedema, asthma, diabetes mellitus, dizziness, hypercholesterolaemia, oedema, vomiting.

Cautions: Asthma, impaired glucose tolerance, predisposition to cardiovascular disease.

Contraindications: Pregnancy, breastfeeding, hypersensitivity, hypersensitivity to shellfish.

15.2 Gout

It is important to distinguish medicines used for the treatment of acute attacks of gout from those used in the long-term control of the disease. The latter exacerbate and prolong the acute manifestations if started during an attack.

Acute attacks of gout are treated with high dose NSAIDs or with colchicine. Aspirin should not be used for gout.

Allopurinol is not effective in treating acute attacks of gout and may prolong the attack if started during the acute episode. Long term treatment with allopurinol reduces the formation of uric acid. Initial treatment with allopurinol may precipitate an acute attack of gout and the patient should therefore be given colchicine or an anti-inflammatory analgesic for about three months.

15.2.1 Non-Steroidal Anti-Imflammatory Drugs

See under Rheumatic Disease section 15.1.1

15.2.2 Colchicum Alkaloids

Colchicine is as effective as NSAIDs but its toxicity at higher doses limits its usefulness. However, it is of value in patients with heart failure as it does not induce fluid retention like NSAIDs. It is also useful in patients receiving anticoagulants.

COLCHICINE

Presentation: Tablet containing Colchicine 500 mcg.

Indications: Acute gout, short term prophylaxis during initial therapy with allopurinol, pregnancy, breastfeeding.

Administration: *Acute gout*; 1mg initially, then 500 mcg every 2 – 3 hours until the pain is relieved or vomiting or diarrhoea occurs or until a total of 10mg has been reached. Do not repeat the course within 3 days.

Prevention of attacks during initial treatment with allopurinol: 500 mcg 2 – 3 times daily.

Side effects: Nausea, vomiting, diarrhoea, abdominal pain, excessive doses may cause profuse diarrhoea, gastro-intestinal haemorrhage, rashes and renal damage. Rarely peripheral neuritis, alopecia, on prolonged treatment blood disorders.

Caution: Gastro-intestinal disease, renal impairment.

15.2.3 Xanthine Oxidase Inhibitors

These include Allopurinol and Febuxostat.

Allopurinol is especially useful in patients with renal impairment or urate stones where uricosuric medicines cannot be used. It is usually given once daily but doses over 300mg daily should be divided.

ALLOPURINOL

Presentation: Tablet containing Allopurinol 100mg, 300mg.

Indications: Prophylaxis of gout and uric acid and calcium oxalate renal stones.

Administration: Initially 100 mg daily as a single dose, after food, gradually increased over 1 – 3 weeks according to plasma or urinary uric acid concentration, to about 300mg daily; usual maintenance dose 200 – 600 mg, rarely 900 mg daily divided into 300mg doses.

Side effects: Rashes (withdraw therapy), skin reactions, fever, lymphadenopathy, arthralgia, eosinophilia, gastro-intestinal disorders, rarely malaise, headache, vertigo, drowsiness, taste disturbances, hypertension, symptomless xanthine deposits in muscle, alopecia, hepatotoxicity, paraesthesia, neuropathy.

Contraindication: Not for the treatment of acute gout.

Caution: Give prophylactic colchicine or NSAIDs (not aspirin or salicylates) until at least 1 month after hyperuricaemia is corrected, ensure adequate fluid intake (2 litres per day), hepatic and renal impairment.

FEBUXOSTAT

Presentation: Tablet containing 40 mg and 80 mg.

Indications: Treatment of chronic hyperuricaemia in gout, prophylaxis and treatment of acute hyperuricaemia with initial chemotherapy for haematological malignancies.

Administration: **Adult**:

Treatment of chronic hyperuricaemia in gout: Initially 80 mg once daily, if after 2–4 weeks of initial dose, serum uric acid greater than 6 mg/100ml, then increase dose; increased if necessary to 120 mg once daily.

Prophylaxis and treatment of acute hyperuricaemia with initial chemotherapy for haematologic malignancies: 120 mg once daily, to be started 2 days before start of cytotoxic therapy and continued for 7–9 days, according to chemotherapy duration.

Children: NOT recommended for use in children.

Side effects: Diarrhoea, gout aggravated, headache, hepatic disorders nausea, oedema, skin reactions, altered smell and sensation, abnormal appetite, arrhythmias, arthritis, bundle branch block, chest discomfort, cholelithiasis, constipation, cough, diabetes mellitus, dizziness, drowsiness, dry mouth, dyspnoea fatigue, gastrointestinal discomfort, gastrointestinal disorders, haemorrhage, hemiparesis, hyperlipidaemia, hypertension, increased risk of infection, insomnia, joint disorders, muscle complaints, muscle weakness, musculoskeletal pain, nephrolithiasis, palpitations, proteinuria, renal failure,sexual dysfunction, altered taste, urinary disorders, vasodilation, vomiting, alopecia.

Contraindications: Not a treatment for acute gout but continue if attack develops when

already receiving febuxostat and treat attack separately. Previous history of hypersensitivity to Febuxostat.

Cautions: There have been rare but serious reports of hypersensitivity reactions, including Stevens-Johnson syndrome and acute anaphylactic shock with febuxostat. Febuxostat must be stopped immediately if these occur. Major cardiovascular disease, thyroid disease and transplant recipients.

15.2.4 Uricosuric Agents

PROBENECID

Presentation: Tablet containing 500mg probenecid.

Indications: Gout prophylaxis (correction of hyperuricaemia).

Administration: *Uricosuric therapy;* 250mg twice daily after food initially, increased after one week to 500mg twice daily which can further be increased to up to 2g daily in 2 – 4 divided doses according to plasma uric acid concentration and then reduced for maintenance.

Side effects: Occasionally nausea and vomiting, urinary infrequency, headache, flushing, dizziness, rashes. Rarely hypersensitivity, nephrotic syndrome, hepatic necrosis, aplastic anaemia.

Contraindications: History of blood disorders, porphyria, acute gout attacks, avoid aspirin and salicylates.

Caution: Ensure adequate fluid intake (at least 2 litres per day), during initial gout treatment give prophylactic colchicine or a NSAIDs (not aspirin nor any salicylates), peptic ulceration, renal impairment (avoid if severe), G6PD deficiency.

SULFINPYRAZONE

Presentation: Tablet containing 100mg, 200mg Sulfinpyrazone.

Indications: Prophylaxis of gout, hyperuricaemia.

Administration: 100 – 200mg initially, daily taken with food or milk. Increasing over 2 – 3 weeks to 600mg daily (rarely 800mg). Therapy should be continued until the serum uric acid concentration has reached normal, after which the dose can be reduced to the maintenance dose which can be as low as 200mg daily.

Side effects: Gastrointestinal disturbances, salt and water retention, gastrointestinal ulceration and bleeding, acute renal failure, jaundice, hepatitis, occasionally allergic skin reactions, rare blood disorders.

Contraindications: avoid NSAIDs hypersensitivity and cardiac diseases.

Caution: See under probenecid. Regular blood counts advisable

15.3 Neuromuscular disorders

15.3.1 Neuromuscular transmission Enhancers

15.3.1.1 Anticholinesteases

Myasthenia gravis is treated using anticholinesterases as first-line treatment and corticosteroids as a concomitant treatment when anticholinesterases treatment is failing.

Anticholinesterases enhance neuromuscular transmission in voluntary and involuntary muscles in myasthenia gravis. They prolong the action of acetylcholine by inhibiting the action of the enzyme acetylcholinesterase.

The two most commonly used Medicines are neostigmine and pyridostigmine.

Neostigmine has pronounced muscarinic action and may cause colic, excessive salivation or diarrhoea which need to be treated with an antimuscarinic drug such as atropine or propantheline. Pyridostigmine has less pronounced muscarinic effects, is less powerful and slower in action than neostigmine, but is of longer duration. It is preferred to neostigmine because of its smoother action and less frequent dosage.

Because of its brief duration of action, edrophonium is used mainly in the diagnosis of myasthenia gravis and to determine whether the patient already on treatment is receiving inadequate or excess doses of cholinergic Medicines. A single test dose gives a marked improvement in muscle power for about 5 minutes in patients who have the disease. If treatment is excessive, an injection of edrophonium will either not affect or will intensify the symptoms. Transient improvement will be seen in patients receiving inadequate treatment. The above procedure should be performed only in conjunction with someone skilled at intubation if there is respiratory impairment in the patient.

NEOSTIGMINE

Presentation: Tablet containing Neostigmine bromide 15mg; Injection containing Neostigmine methylsulphate 0.5/2.5mg/ml.

Indications: Myasthenia gravis

Administration: **Adult;**

Orally, 15 – 30mg at suitable intervals throughout the day, total daily dose 75 – 300mg.

By subcutaneous or intramuscular injection: 1 – 2.5mg at suitable intervals throughout the day (usual total daily dose 5 – 20mg).

Children:

Oral

Neonate: 1 –5mg every 4 hours, half an hour before foods. *Child* up to 6 years: initially 7.5mg;

6 –12 years: initially 15mg, usual total daily dose 150mg.

By subcutaneous or intramuscular injection;

Neonate; 50 – 250mcg every 4 hours half an hour before feeds

Child: 200 – 500mcg as required.

Side effects: Nausea, vomiting, increased salivation, diarrhoea, abdominal cramps especially at higher doses.

Contraindications: Intestinal and urinary obstruction.

Caution: Asthma, bradycardia, recent myocardial infarction, epilepsy, hypotension, parkinsonism, vagotonia, peptic ulcers, pregnancy, breastfeeding.

PYRIDOSTIGMINE BROMIDE

Presentation: Tablet containing Pyridostigmine bromide 60mg.

Indications: Myasthenia gravis.

Administration: ***Adult;*** *Orally*, 30 – 120mg at suitable intervals throughout the day, total daily dose 0.3 – 1.2g but it is inadvisable to exceed a daily dose of 720mg

Children:

Neonate; 5 – 10mg every 4 hours, ½ to 1 hour before feeds, *Up to 6 years;* initially 30mg, 6 – 12 years; initially 60mg. Usual total daily dose 30 – 60mg.

Side effects: See under neostigmine. Has weaker muscular effects.

Contraindications: See under neostigmine.

Caution: See under neostigmine.

EDROPHONIUM CHLORIDE

Presentation: Injection containing 10mg/ml Edrophonium chloride

Indications: Diagnosis of myasthenia gravis, detection of under or overdose of cholinergic medicines.

Administration: *Diagnosis;* by intravenous injection, 2mg followed after 30 seconds if no adverse reaction occurs by 8mg. In adults without suitable veins, 10mg is given intramuscularly.

Detection of under or overdose of cholinergic Medicines; by intravenous injection 2mg (best given before the next dose of anticholinesterases)

Children:
By intravenous injection 20mcg/kg body weight followed after 30 seconds (if no adverse reaction occurs) by 80mcg/kg body weight.

Side effects: See under neostigmine

Contraindications: See under neostigmine.

Caution: See under neostigmine, resuscitation facilities should be at hand; extreme caution in respiratory distress and asthma.

15.3.1.2 Corticosteroids

Corticosteroids are useful in the treatment of myasthenia gravis where thymectomy is inappropriate or to reduce the risk of surgery. The initial dose may be high (100mg prednisolone) but it is advised to start with a smaller dosage (20mg prednisolone) and increase the dose gradually. Myasthenia gravis may be exacerbated during the initial stages of treatment with corticosteroids, it is therefore advised to conduct the treatment under supervision (inpatient).

PREDNISOLONE

Presentation: Tablet containing prednisolone 5mg.

Indications: Myasthenia gravis concomitant to anticholinesterases.

Administration: Initially up to 100mg daily. Best to start with a smaller dose (20mg daily) and gradually increase. Maintenance dose; 10 – 40mg daily or every other day.

Side effects: See 15.1.2 under rheumatic disorders.

Contraindications: See under rheumatic disorders. **Caution:** See under rheumatic disorders

15.3.2 Skeletal muscle relaxants

Medicines used for relief of chronic muscle spasm or spasticity include baclofen and benzodiazepines such as diazepam. They act on the CNS and differ from muscle relaxants used in anaesthesia which block transmission at the neuromuscular junction. The underlying cause of spasticity should be identified and treated.

BACLOFEN

Presentation: Tablet containing baclofen 10mg, sugar-free liquid containing 5mg/5ml Baclofen.

Indications: Chronic severe spasticity of voluntary muscle.

Administration: 5mg 3 times daily, after food, gradually increased to maximum 100mg daily;

Children:
Initially: 0.75 – 2mg/kg daily (maximum 2.5mg/kg daily) or 2.5 mg 4 times daily increased gradually.
Maintenance:
1 – 2 years; 10 – 20 mg daily.
2 – 6 years; 20 – 30mg daily.
6 – 10 years; 30 – 60mg daily.

Side effects: Frequently sedation, drowsiness, nausea, hypotonia. Other adverse events are rare.

Contraindications: Peptic ulceration.

Caution: Psychiatric illness, cerebrovascular disease, elderly patients, diabetes mellitus, hepatic and renal impairment, history of peptic ulcer, avoid abrupt withdrawal as it may cause autonomic dysreflexia, porphyria, enhances effects of alcohol, drowsiness may cause impairment performance of skilled tasks such as driving.

DIAZEPAM

Presentation: Tablet containing Diazepam 2mg, 5mg; an oral solution containing Diazepam 2mg/5ml, 5mg/5ml; an injection containing solution Diazepam 5mg/ml; emulsion containing 5mg/ml.

Indications: Muscle spasms.

Administration: *Orally;* 2 – 15mg daily in divided doses increased to 60mg daily if necessary and according to response in spastic conditions.

In acute muscle spasm; 10mg repeated if necessary after 4 hours.

Children:

Cerebral spasticity in selected cases, oral:

1–11 months: Initially 250 mcg/kg twice daily

1–4 years: Initially 2.5 mg twice daily

5–11 years: Initially 5 mg twice daily

12–17 years: Initially 10 mg twice daily, maximum 40 mg per day.2 - 4mg daily in divided doses by intramuscular or slow intravenous injection (into a large vein at a rate of not more than 5mg/min).

Side effects: Sedation, drowsiness and lightheadedness next day, extensor hypotonus, confusion and ataxia, amnesia, dependence.

Contraindications: Respiratory depression, acute pulmonary insufficiency, chronic psychosis.

Caution: Respiratory disease, muscle weakness, history of drug abuse, marked personality disorder, pregnancy and breastfeeding, reduce dose in elderly, in hepatic and renal impairment, when given IV, facilities for reversing respiratory depression with mechanical ventilation must be at hand, risk of venous thrombophlebitis when given intravenously-this risk can be reduced by using an emulsion.

CHLORZOXAZONE

Presentation: Tablets containing 250mg, 375mg, 500mg and 750mg. Commonly occurs in combination with Ibuprofen and Paracetamol, and Diclofenac and Paracetamol, respectively.

Indications: Muscle spasms, musculoskeletal pain.

Administration: ***Adult:*** 250-750 mg PO 6-8 hourly.

Children:

20mg/kg/day PO in divided doses 8-hourly or 600 mg/m²/day PO in divided doses 8-hourly.

Side effects: Light-headedness, dizziness, drowsiness

excitement, paradoxical somnolence, malaise, rash, angioneurotic edema, gastrointestinal haemorrhage, hepatotoxicity, anaphylaxis.

Contraindications: Previous hypersensitivity.

Cautions: May cause CNS depression and impair physical and mental alertness; avoid performing tasks that require mental alertness, serious hepatotoxicity has been reported on rare occasions. Stop use at the earliest sign of toxicity.

16 Immunological Products and Vaccines

16.1 Active immunity

Vaccines may consist of:

- A live attenuated form of a virus (e.g. rubella or measles vaccine) or bacteria (e.g. BCG vaccine).
- Inactivated preparations of the virus (e.g. influenza vaccine) or bacteria, or
- Extracts of or detoxified exotoxins produced by a micro-organism (e.g. tetanus vaccine).

They stimulate the production of antibodies and other components of the immune mechanism.

For **live attenuated** vaccines, immunisation is generally achieved with a single dose (but 3 doses are required with oral poliomyelitis and oral typhoid vaccines). Live attenuated vaccines usually produce a durable immunity but not always as long as that of the natural infection. When two live virus vaccines are required (and are not available as a combined preparation) they should be given either simultaneously at different sites or with an interval of at least 3 weeks.

Inactivated vaccines may require a primary series of injections of vaccine to produce adequate antibody response and in most cases, booster (reinforcing) injections are required: the duration of immunity varies from months to many years.

Extracts of or **detoxified exotoxins** are more immunogenic if absorbed onto an adjuvant (such as aluminium hydroxide). They require a primary series of injections followed by booster doses.

Side effects: Some vaccines (e.g. poliomyelitis) produce very few reactions, while others (e.g. measles and rubella) may produce a very mild form of the disease. Some vaccines may produce discomfort at the site of injection and mild fever and malaise.

Anaphylactic reactions (see the section for management) are very rare but can be fatal.

Occasionally, there are more serious adverse effects/reactions following immunisation and those should always be reported to the pharmacovigilance centre. For full details of side effects, the product literature should always be consulted.

Contraindications: Most vaccines have some basic contra-indication to their use, and the product literature should always be consulted. In general, vaccination should be postponed if the subject is suffering from an acute illness. Minor infections without fever or systemic upset are not contra-indications. A definite severe reaction to a preceding dose is a contraindication to further doses.

Some **viral vaccines** contain small quantities of antibiotics such as neomycin or polymyxin (or both). Such vaccines may need to be withheld from individuals who are sensitive to the antibiotic. Hypersensitivity to egg contra-indicates influenza vaccine (residual egg protein present) and, if evidence of previous anaphylactic reaction, also a yellow fever vaccine.

Live vaccines should not be routinely administered to pregnant women because of possible harm to the foetus but where there is a significant risk of exposure (e.g. to poliomyelitis or yellow fever), the need for vaccination outweighs any possible risk to the

foetus. Live vaccines should not be given to individuals with impaired immune response, whether caused by disease (for special reference to AIDS, see below) or as a result of radiotherapy or treatment with high doses of corticosteroids or other immunosuppressive Medicines (see points 3,4 below). They should not be given to those suffering from malignant conditions such as leukaemia and tumours of the reticuloendothelial system.

The intramuscular route should not be used in patients with bleeding disorders such as haemophilia or thrombocytopenia.

- Poliomyelitis virus may be excreted for longer periods in HIV subjects than in normal subjects after vaccination: contacts should be warned of this and the need for washing hands after changing a vaccinated infant's nappies: HIVpositive contacts are at greater risks than normal contacts. For HIV positive symptomatic subjects, inactivated poliomyelitis vaccine may be used at the discretion of the clinician.
- For those with impaired immune response including those who have received corticosteroids within the last 3 months and chemotherapy within the last 6 months, consideration should be given to use of normal immunoglobulin after exposure to measles and varicella-zoster immunoglobulin after exposure to chickenpox or herpes zoster.
- Live vaccines should be postponed until at least 3 months later after stopping corticosteroids and 6 months after stopping the chemotherapy.
- BCG, yellow fever and oral typhoid vaccines should be avoided in HIV positive subjects because of insufficient evidence of safety.

Immunisation schedule (See schedule in appendix 1)

During the first year of life

Adsorbed Diphtheria, Tetanus and Pertussis Vaccine (triple vaccine)

3 doses at intervals of 4 weeks: first dose at 2 months of age.

If the pertussis component omitted from earlier immunisations 3 doses of Pertussis Vaccine can be given at monthly intervals to provide protection. If basic course against diphtheria and tetanus incomplete, triple vaccine (DPTer/Vac/Ads) may be used to begin or to complete course against pertussis to avoid more injections than necessary.

plus

Haemophilus Influenza type b Vaccine (Hib) 3 doses at intervals of 4 weeks: first dose at 2 months of age

also

Poliomyelitis Vaccine, Live (Oral) 3 doses at intervals of 4 weeks: first dose at 2 months of age.

Also

BCG Vaccine See section 15.4, BCG Vaccines.

Also

Measles vaccine

* Single dose at 9 months. See 15.4.11 Measles vaccine

During the second year of life

****Measles, Mumps and Rubella Vaccine, Live**

(MMR)

single dose at 12-15 months of age.

* In developing countries (including Zambia) as part of the WHO Expanded Programme on Immunisation, measles vaccine is given to infants at 9 months of age.

** In most developed countries MMR is administered to children at 12 – 15 months of age.

Haemophilus Influenzae type b vaccine (Hib) (if not previously immunised)

Single-dose at 13 months-4 years of age (over 4 years, see section 15.4 Haemophilus influenzae type b Vaccine).

Before nursery school or school entry

Adsorbed Diphtheria and Tetanus Vaccine Single booster dose

Preferably allow an interval of at least 3 years after completing the basic course; give at the same session as MMR Vaccine but use separate syringe and needle, and give after MMR (MMR less painful) in a different limb.

also

Poliomyelitis Vaccine, Live (Oral)

Singler booster dose

Preferably allow an interval of at least 3 years after completing the basic course.

also

***Measles vaccine or **Measles, Mumps and Rubella Vaccine, Live (MMR)**

Single booster dose

Give at the same session as Adsorbed Diphtheria and Tetanus Vaccine but use separate syringe and needle; give MMR first (less painful) and use different limb - alternatively, the second appointment can be made.

Between 10 - 14 years of age

BCG Vaccine (for tuberculin - negative children)

Single- dose.

May be given simultaneously with another live vaccine: otherwise, an interval of at least 3 weeks should be allowed between the two.

Before leaving school or before

Employment or further education

Adsorbed Diphtheria and Tetanus Vaccine used at school entry should **not** be used for children aged over 10 years and adults. Instead, a special low dose version combined in a single injection with tetanus vaccine should be used.

also

Poliomyelitis Vaccine, Live (Oral) Single booster dose.

During adult life

Poliomyelitis Vaccine, Live (Oral) (if not previously immunised)

3 doses at intervals of 4 weeks

No adult should remain unimmunised; health care workers in possible contact with poliomyelitis require booster dose if they have not received immunisation within last 10 years.

Rubella Vaccine, Live (for susceptible women of child-bearing age).

Single- dose

Women of childbearing age should be tested for rubella antibodies and offered rubella immunisation if seronegative - exclude pregnancy before immunisation, but see also section 15.4, Rubella Vaccine.

Adsorbed Tetanus Vaccine (if not previously immunised)

3 doses at intervals of 4 weeks.

Booster dose 10 years after the primary course and again 10 years later maintains a satisfactory level of protection if diphtheria cover also needed to give Adsorbed Diphtheria and tetanus Vaccine for adults and Adolescents.

Adsorbed Diphtheria Vaccine for Adults and Adolescents (if not previously immunised) 3 doses at intervals of 4 weeks.

Booster dose 10 years after the primary course. If tetanus cover is also needed, give Adsorbed Diphtheria and Tetanus Vaccine for Adult and adolescents.

High-risk groups

For information on high-risk groups, see section 16.4 under individual vaccines.

Hepatitis A Vaccine

Hepatitis B Vaccine

Influenza Vaccine

Pneumococcal Vaccine

Post-Immunisation pyrexia

The doctor should advise the parent that if pyrexia develops after immunisation with the triple vaccine the child can be given a dose of paracetamol followed, if necessary, by a second dose

4 to 6 hours later. The dose of paracetamol for post-immunisation pyrexia in an infant aged 2 - 3 months is 60mg; an oral syringe can be obtained from a pharmacy to give the small dose-volume required. The doctor should warn the parent that if the pyrexia persists after the second dose medical advice should be sought.

16.2 Passive Immunity

Immunity with immediate protection against certain infective organisms can be obtained by injecting preparations made from the plasma of immune individuals with adequate levels of antibody to the disease for which protection is sought. This passive immunity lasts only a few weeks; where necessary passive immunisation can be repeated.

Antibodies of human origin are usually termed *Immunoglobulins.* The term anti-serum is applied to the material prepared in animals. Because of serum sickness and other allergic-type reactions that may follow injections of antiserum, this therapy has been replaced wherever possible by the use of immunoglobulins. Reactions are theoretically possible after injection of human immunoglobulins but reports of such reactions are very rare.

16.3 Storage and Use

Care must be taken to store all vaccines and other immunological products under the conditions recommended in the product literature, otherwise, the preparation may become denatured and ineffective.

Refrigerated storage is usually necessary; many vaccines need to be stored at 2-8 degrees Celsius and not allowed to freeze. Vaccines should be protected from light. The unused vaccine in multidose vials without preservative (most live virus vaccines) should be discarded within 1 hour of first use; those containing a preservative (including oral poliomyelitis vaccine) should be discarded within 3 hours or at the end of a session. Unused vaccines should be disposed of by incineration at a registered disposal contractor.

Particular attention must be paid to instructions on the use of diluents. Vaccines which are liquid suspensions or are reconstituted before use should be adequately shaken to ensure uniformity of the material to be injected.

Note: The *use of jet guns* for vaccination is not advised owing to the risk of transmitting bloodborne infections, such as HIV.

16.4 Vaccines and Antisera

ANTHRAX VACCINE

Anthrax immunisation is indicated for individuals who handle infected animals, for those exposed to imported infected animal products, and for laboratory staff who work with *Bacillus anthracis.* The vaccine is the alum precipitate of an antigen from Bacillus anthracis and, following the primary course of injections, booster doses should be given at about yearly intervals. In the event of possible contract with B-anthracis, post-exposure immunisation may be indicated in addition to antimicrobial prophylaxis (obtain from Public Health Centre)

Administration: *Initial course:* 3 doses of 0.5ml. by IM injection at intervals of 3 weeks followed by a 4th dose after 6 months. *Booster doses:* 0.5 ml annually.

BCG VACCINE

Presentation: Powder for injection (live attenuated) (+diluent), 1-ml vial (multidose), containing 50mg BCG for reconstitution 50mg (Tice BCG); or containing 81mg BCG for reconstitution 81mg (TheraCys)

Indication: Adults- TB active immunization, Paeds - TB immunization, Immunotherapy for Bladder Cancer

Administration: ***Adults:***

TB exposed health care workers in high risk settings: 0.2-0.3 ml percutaneous; Conduct tuberculin test 2-3 months after percutaneous administration; if test is negative repeat vaccination.

Bladder Cancer: 81mg - Initiate treatment 7-14 days after biopsy, instill one dose into bladder; retain for 2 hours; repeat dose once weekly for 6 weeks followed by 1 treatment at 3, 6, 12, 18, and 24 months after initial treatment; 50mg - Instill one dose into bladder; retain for 2 hours; repeat dose once weekly for 6 weeks (may repeat cycle once) followed by once monthly for 6-12 months.

Children:

Neonate or infant: 0.05 ml

Child: 0.1 ml

Conduct tuberculin test 2-3 months after percutaneous administration; if test is negative, repeat vaccination after 1 year.

Side effects: Malaise, Fever, Chills, Nausea/ vomiting, local ulceration, disseminated BCG infection in immunodefcient individuals, and osteitis. Ulcer at injection site (2–6 weeks after vaccination), enlargement of regional lymph nodes, pain, redness, itching, swelling or burning at injection site, fainting.

Contraindication: Hypersensitivity, immunosuppression (corticosteroids), acquired immune deficiencies, Active tuberculosis, HIV infected patients.

Bladder- Febrile illness, Urinary tract infection, Gross hematuria, Biopsy, Transurethral resection, Traumatic catherization.

Caution: BCG strain of Mycobacterium bovis, do Mantoux skin test prior to vaccine administration, Immunity not permanent; duration unpredictable, Treat anaphylactoid reactions immediately.

BOTULISM ANTITOXIN

A trivalent botulism antitoxin is available for the post-exposure prophylaxis of botulism and for the treatment of persons thought to be suffering from botulism. It specifically neutralises the toxins produced by *Clostridium botulism* types A, B, and E.

It is not effective against infantile botulism as the toxin (type A) is seldom, if ever, found in the blood in this type of infection.

Hypersensitivity reactions are a problem. It is essential to read the contra-indications, warnings, and details of sensitivity tests on the package insert. Before treatment, checks should be made regarding previous administration of any antitoxin and history of any allergic conditions, e.g. asthma, hay fever, etc. All patients should be tested for sensitivity (diluting the antitoxin if the history of allergy).

Presentation: **Botulism Antitoxin** is a preparation containing the specific antitoxic globulins that have the power of neutralising the toxins formed by types A, B, and E of *Clostridium botulism*.

Note: The BP title Botulism Antitoxin is not used because the preparation currently available has a higher phenol content (0.45% against 0.25%).

Indications: Post-exposure prophylaxis of botulism and for the treatment of persons thought to be suffering from botulism.

Administration: *Prophylaxis:* 20ml by intramuscular injection as soon as possible after exposure.

Treatment: 20ml. (diluted to 100ml: with sodium chloride 0.9%) by slow intravenous infusion followed by 10ml 2-4 hours later if necessary, and further doses at intervals of 12-24 hours.

CHOLERA VACCINE

Presentation: Oral suspension containing 1.5-ml vial (single-dose vial) inactivated (WC/ rBS) cholera virus.

Indications: Adult - Active immunization against cholera. Primary immunization against V. cholerae. Immunization against cholera, oral Immunisation against cholera (for travelers to endemic or epidemic areas on the basis of current recommendations).

Children- active immunization against cholera.

Administration: ***Adult*** - 1 dose every 1–6 weeks for 2 doses, if more than 6 weeks have elapsed between doses, the primary course should be restarted, immunisation should be completed at least one week before potential exposure. *Booster* - A single booster dose can be given within 2 years after primary course, if more than 2 years have elapsed since the last vaccination, the primary course should be repeated.

Children:

2–5 years: three doses given more than 7 days apart (but < 6 weeks apart).

6–12 years: two doses given > 7 days apart (but < 6 weeks apart).

Note: if the interval between the primary immunization doses is delayed for > 6 weeks, primary immunization should be restarted.

Continued risk of V. cholerae infection:

2–5 years: one booster dose every 6 months.

If the interval between the primary immunization series and the booster immunization is more than 6 months, primary immunization must be repeated.

6–12 years: one booster dose after 2 years. If the interval between the primary immunization series and booster immunization is more than 2 years, primary immunization must be repeated.

Side effects: Abdominal discomfort, diarrhea, headache, mild transient GI disturbances. Rarely, allergic reactions such as anaphylaxis.

Contraindications: Anaphylaxis to the vaccine or any component of the vaccine.

ROTAVIRUS VACCINE

Presentation: Oral suspension, 5-dose vial

Indications: Immunization against gastroenteritis-caused by rotavirus.

Administration:

Children:

1 ml given as three doses - 1st dose at6 weeks of life or at first contact with unvaccinated child under 1 year; 2nd dose at 10 weeks or 4 weeks after Rota 1.

Side effects: Abdominal cramps, abdominal pain, diarrhea, nausea, vomiting.

Contraindications: History or predisposition to intussusception, severe combined immunosuppression.

Caution: Diarrhea (postpone vaccination), vomiting, immunosuppression (but not in severe combined immunodeficiency).

Diphtheria Vaccines

Protection against diphtheria is essentially due to antitoxin, the production of which is stimulated by vaccines prepared from the toxin of *corynebacterium diphtheria.* Adsorbed diphtheria vaccines are recommended for the routine immunisation of babies and are usually given in the form of a triple vaccine, **adsorbed diphtheria, tetanus, and pertussis vaccine** (see Appendix 1). Adsorbed diphtheria and tetanus vaccine are used in place of the triple vaccine when immunisation against pertussis is contra-indicated.

A booster dose of **adsorbed diphtheria and tetanus vaccine** is recommended before school entry (4-5 years of age). This should preferably be given after at least 3 years from the last dose of the basic course. A further booster dose is now recommended before school leaving: for this purpose, **adsorbed diphtheria and tetanus vaccine for adult and adolescents** (a special low-dose version combined in a single injection with tetanus vaccine) is available. For details on booster doses of the diphtheria vaccine in a child over 13 years who requires treatment of a tetanus-prone wound, see under Tetanus Vaccine. If there is documented history of fifth dose of tetanus vaccine having been given when the school leaving booster dose of adsorbed diphtheria and tetanus vaccine for adults and adolescents is due, then a booster dose of single-antigen adsorbed diphtheria vaccine for adults and adolescents should be given instead.

Other booster doses of adsorbed diphtheria vaccine are not recommended as a routine except for staff in contact with diphtheria patients or handling clinical specimens which may be pathogenic or working directly with *Corynebacterium diphtheriae:* they should be considered for a booster or primary immunisation following a risk assessment. A low dose vaccine, **adsorbed diphtheria vaccine for adults and adolescents,** is available for this purpose: immunity should be checked by antibody testing at least 3 months after completion of immunisation.

Unimmunised contacts of a diphtheria case require a primary course of 3 doses of adsorbed diphtheria vaccine at monthly intervals.

TETANUS + DIPHTHERIA (TD) VACCINE

Presentation: Injection, 10-ml vial (20 doses).

Indications: *Adult* - prophylaxis against tetanus in wound management, active immunity against diphtheria and tetanus when pertussis vaccine is contraindicated.

Children - Infants and Child younger than 6 years: Primary immunization

Administration: ***Adult***

Previously not immunized - 2 primary doses of 0.5 ml each, given at an interval of 4–6 weeks, third (reinforcing) doses of 0.5 ml 6–12 months later.

Children:

6 weeks to 1 year: three 0.5 ml doses at least 4 weeks apart, administer reinforcing doses 6–12 months after the third injection.

1–6 years: two 0.5 ml doses at least 4 weeks apart, reinforcing dose 6–12 months after second injection.

Booster immunization:

4–6 years: 0.5 ml, not necessary if the fourth dose was given after fourth birthday, routinely administer booster doses at 10-year intervals.

Older than 7 years: 0.5 ml every 10 years, to be given to children 11–12 years of age if at least 5 years have elapsed since last dose of toxoid containing vaccine.

Side effects: Dizziness, seizure, rash, nausea, vomiting, local reactions, myalgia, arthralgia.

Contraindications: Hypersensitivity to diphtheria, tetanus toxoid.

Cautions: Bleeding disorders or anticoagulant therapy.

DIPTHERIA, PERTUSSIS, TETANUS (DPT)

Presentation: Suspension containing 5-ml vial (10 doses) Diphtheria Toxoid for Injection. Each dose is 0.5 ml.

Indications: Paediatric - Immunization against Diphtheria, Pertussis, Tetanus, Haemophilus Influenza type B and Hepatitis B.

Administration:

Children:

Infants: 0.5 ml at 6, 10, and 14 weeks of birth.

Side effects: Injection site reactions (such as pain, erythema, and inflammation), fever, and malaise (within 1–2 days of immunization), usually mild. Rarely, serious hypersensitivity reactions.

Contraindication: Known severe hypersensitivity to any component of the vaccine.

Caution: Do not give subsequent doses if a serious adverse event occurs (e.g. severe allergy/anaphylaxis). Egg sensitivity to some patients for vaccines prepared using hens' eggs.

- *Immunised* contacts require a single booster dose (important: adults and children *over 10 years* must be given a low dose vaccine); those also requiring tetanus cover can be given the appropriate strength of adsorbed diphtheria vaccine combined with tetanus vaccine.
- *Previously immunised* travellers to countries where diphtheria is endemic or epidemic require a booster dose if their primary immunisation was more than 10 years ago.
- *Unimmunised travellers* require a full course of 3 doses at monthly intervals (**important:** adults and children *over 10 years* requiring either a primary course or a booster should be given a **low-dose** vaccine - those also requiring tetanus cover can be given the special low-dose version combined with tetanus vaccine).

See section 16.1 for general contra-indications.

Diphtheria vaccines for children

IMPORTANT: Not recommended for persons *aged 10 years or over* (use diphtheria vaccines for adults and adolescents instead).

ADSORBED DIPHTHERIA, TETANUS, AND PERTUSSIS VACCINE

DTPer/Vac/Ads. Prepared from diphtheria formol toxoid, tetanus formol toxoid, and pertussis vaccine adsorbed on a mineral carrier.

Administration: *Primary immunisation of children*: 0.5ml by intramuscular or deep subcutaneous injection at 2 months followed by the second dose after 4 weeks and third dose after another 4 weeks (see schedule).

Note: Adsorbed diphtheria, tetanus and pertussis vaccine is available in combination with Haemophilus influenzae type b vaccine, see under Haemophilus Influenzae type b Vaccine.

ADSORBED DIPHTHERIA AND TETANUS VACCINE

DT/Vac/Ads *(Child)* Prepared from diphtheria formol toxoid and tetanus formol toxoid adsorbed on a mineral carrier.

Administration: *Primary immunisation of children omitting pertussis component:* 0.5 ml by intramuscular or deep subcutaneous injection at 2 months followed by the second dose after 4 weeks and third dose after another 4 weeks (see the schedule, section 16.1).

Booster at school entry: 0.5 ml, (see schedule).

ADSORBED DIPHTHERIA VACCINE

Dip/Vac/Ads *(Child)*. Prepared from diphtheria formol toxoid adsorbed on a mineral carrier.

Indications: Used only for contacts of a diphtheria case or carrier

Administration:

Adults and children over 10 years: give adsorbed diphtheria vaccine for adults and adolescents (see below).

Children:

Immunised children under 10 years: one dose of 0.5 ml by intramuscular or by deep subcutaneous injection.

Unimmunised children under 10 year: three doses of 0.5ml with an interval of 4 weeks between first and second doses and another 4 weeks between the second and third doses.

Diphtheria antitoxin

Diphtheria Antitoxin is used for passive immunisation: it is prepared in horses therefore reactions are common after administration.

It is now only used in suspected cases of diphtheria (without waiting for bacteriological confirmation); tests for hypersensitivity should be first carried out.

It is no longer used for prophylaxis because of the risk of hypersensitivity. Unimmunised contacts should be promptly investigated and given erythromycin prophylaxis and vaccine (see notes above).

DIPHTHERIA ANTITOXIN DIP/SER.

Administration: *Prophylactic*: 500 to 2000 units by intramuscular injection (but **not** used, see notes above).

Therapeutic: 10 000 to 30 000 units, increased to 40 000 to 100 000 units in severe cases; doses of up to 30 000 units should be given intramuscularly but for those over 40 000 units. A portion is given intramuscularly followed by the bulk of the dose intravenously after 30 minutes-2 hours.

Note: Children require the same dose as adults, depending on the severity of the case.

Haemophilus influenza Type B vaccine

Children under the age of 13 months are at high risk of *Haemophilus influenzae* Type B infection. **Haemophilus influenzae**

type b (Hib) vaccine is a component of the primary section (16.1). The course consists of 3 doses of Haemophilus influenzae type b vaccine with an interval of 1 month between each dose. If primary immunisations against diphtheria, tetanus, pertussis and poliomyelitis have already been commenced or completed, children under the age of 13 months should still receive 3 doses of Haemophilus influenzae type b vaccine at monthly intervals. Children over the age of 13 months are at a lower risk of infection and, if not previously immunised, need receive only 1 dose of the vaccine. The risk of infection falls sharply after the age of 4 years therefore the vaccine is not normally required for children over 4 years. However, it may be given to those over 4 years who are considered to be at increased risk of invasive *Haemophilus influenzae* Type B disease (such as those with sickle cell disease and those receiving treatment for malignancy). Also, asplenic children and adults, irrespective of age or the interval from splenectomy, should receive a single dose of Haemophilus influenzae type b vaccine; those under one year should be given three doses. For elective splenectomy, the vaccine should ideally be given at least 2 weeks before the operation. Side effects reported include fever, headache, malaise, irritability, prolonged crying, loss of appetite, vomiting, diarrhoea and rash (including urticaria); convulsions, erythema multiform, and transient cyanosis of the lower limbs have been reported.

See section 15.1 for general contra-indications.

- **Single component**

Every single component may be used to complete a course started with any other single component product listed below.

HIB TITER (by Wyeth)

Presentation: Capsular polysaccharide of *Haemophilus influenzae* type b (conjugated to a protein carrier).

Administration: *For primary immunisations:* By intramuscular injection; 0.5 ml; 3 doses are required at intervals of 1 month (see the schedule of section 16.1).

Note: If required, Haemophilus influenzae type b vaccine is available in combination with adsorbed diphtheria, tetanus and pertussis vaccine (see below); alternatively, *Hib TITER* may be combined with *Trivax-AD* brand of adsorbed diphtheria, tetanus and pertussis vaccine in the same syringe (final combined volume = 1 ml). Available, as part of the childhood immunisation schedule.

ACT-HIB (by Pasteur Merieux)

Presentation: Injection powder for reconstitution, capsular polysaccharide of *Haemophilus influenzae* type b (conjugated to a protein carrier).

Administration: *For primary immunisation:* By IM or deep subcutaneous injection, 0.5 ml; 3 doses are required at intervals of 1 month (see the schedule, section 16.1).

Note: If required, Haemophilus influenzae type b vaccine is available in combination with adsorbed diphtheria, tetanus and pertussis vaccine (see below); alternatively, ACT-HIB may be reconstituted with 0.5 ml of Pasteur Merieux brand of adsorbed diphtheria, tetanus, and pertussis vaccine.

Available as part of the childhood immunisation schedule.

- **With diphtheria, tetanus and pertussis vaccines**

Each combined product may be used to complete a course started with any other combined product listed below; important see also under Adsorbed Diphtheria, Tetanus and Pertussis Vaccine.

ACT-HIB DTP DC (by Pasteur) Merieux)

Presentation: *Injection,* powder for reconstitution, capsular polysaccharide of *Haemophilus influenzae* type B (conjugated to a protein carrier) with diluent containing diphtheria toxoid, tetanus and *Bordetella pertussis* cells.

Administration:

Children: *for primary immunisation*
Under 4 years: by intramuscular or deep subcutaneous injection, 0.5 ml; 3 doses are required at intervals of 1 month (see the schedule, section 16.1).

Available, as part of the childhood immunisation schedule.

TRIVAX-HIB (by Glaxo-Smith) Kline) Merieux)

Presentation: *Injection,* powder for reconstitution, capsular polysaccharide of *Haemophilus influenzae* type b (conjugated to a protein carrier) with diluent containing diphtheria toxoid, tetanus toxoid and *Bordetella pertussis* cells.

Administration:

Children: *for primary immunisation*
Under 10 year: by intramuscular injection; 0.5ml; 3 doses are required at intervals of 1 month (see the schedule, section 16.1)

Available, as part of the childhood immunisation schedule.

Hepatitis A Vaccine

Hepatitis A vaccine is prepared from formaldehyde-inactivated hepatitis A virus grown in human diploid cells.

Immunisation is recommended for:

- Staff and residents of homes for those with severe learning difficulties.
- Prevention of secondary cases in closed contacts of confirmed cases of hepatitis A, with seven days of onset of disease in the primary case.
- Laboratory staff who work directly with the virus.
- Haemophiliacs treated with Factor VIII or Factor IX concentrate or who have liver disease or who have been infected with hepatitis B or hepatitis C:
- Travellers to high-risk areas, individuals who are at risk due to their sexual behaviour. Immunisation should be considered for: patients with chronic liver disease:
- Workers at risk of exposure to untreated sewage.

Haemophiliacs and patients with chronic liver disease should be checked for previous exposure before immunisation.
Normal immunoglobulin (section 16.5.1) provides short-term protection against hepatitis A, but antibody titres after 3 primary courses of hepatitis A vaccine are well more than those found after the administration of normal immunoglobulin.

Side effects: Usually mild: transient soreness, diarrhoea, erythema, and induration at the injection site. Less common effects: fever, malaise, fatigue, headache, nausea, and loss of appetite; generalised rashes are occasionally reported.

See section 16.1 for general contraindications.

- Single component

AVAXIM (by Pasteur) Merieux)

Presentation: Injection suspension of formaldehyde-inactivated hepatitis A virus (GBM grown in human diploid cells) 320 antigen units/ml adsorbed onto aluminium hydroxide.

Administration: By intramuscular injection (see note below), 0.5 ml as a single dose; booster dose 0.5 ml 6-12 months following the initial dose; further booster doses, 0.5 ml every 10 years.

Children:
under 16 years, not recommended.

Note: The deltoid region is the preferred site of injection. The subcutaneous route may be used for patients with haemophilia.

HAVRIX MONODOSE (by Glaxo-Smith Kline)

Presentation: Injection suspension of formaldehyde-inactivated hepatitis A virus (HM 175 grown in human diploid cells) 1440 ELISA units/ml adsorbed onto aluminium hydroxide.

Administration: By intramuscular injection (see note below), 1 ml as a single dose; booster dose, 1 ml 6-12 months following the initial dose.

Children:

1-15 years; 0.5ml, booster dose for child, 0.5ml 6-12 months after the initial dose. If a booster dose is not given after the recommended interval, it may be delayed by up to 3 years after the primary dose.

Note. The deltoid region is the preferred site of injection adults. The subcutaneous route may be used for patients with haemophilia.

VAQTA PAEDIATRIC AND ADOLESCENT (by Pasteur/ Merieux)

Presentation: Injection of suspension of formaldehyde inactivated hepatitis A virus (grown in human diploid cells) 50 antigen units/ml adsorbed onto aluminium hydroxide.

Administration: By intramuscular injection (see note below)

Children:

2-17 years: 0.5 ml as a single dose; booster dose 0.5 ml 6-18 months following the initial dose; under 2 years of age, not recommended.

Note: The deltoid region is the preferred site of injection.

- **With hepatitis B vaccine Twinrix, See Hepatitis B Vaccine**

HEPATITIS B VACCINE

Presentation: Suspension containing single-dose vial and multidose vials for injection.

Indications: ***Adult*** - Active immunization against hepatitis B, post-exposure prophylaxis. ***Children:*** Primary immunization against Hepatitis B, Hepatitis B prophylaxis for infants born to hepatitis B surface antigen-positive mother; Percutaneous, ocular, mucous membrane exposure; sexual exposure.

Administration: 3 doses of 1 ml, with an interval of 1 month between the frst and second dose and 5–11 months between the second and third doses.

Children:

Primary immunization against Hepatitis B, IM

Neonate, infant, or child from birth: One monovalent dose at birth, then two or three subsequent doses of monovalent or combined hepatitis B vaccine administered according to schedules of national routine immunization programmes.

Generally, subsequent doses after birth dose are given at 2, 4, and 6 or 12 months of age, depending on the vaccine used.

Three doses: the second coming after one month and the third given 5 months after the second dose (or at a minimum at least 2 months after the second dose).

Hepatitis B prophylaxis for infants born to hepatitis B surface antigen-positive mother, IM

Neonate: One dose of vaccine with hepatitis B immunoglobulin (in the opposite thigh) within 12 hours of birth (yet preferably immediately after birth), then three subsequent doses as per primary immunization (as above).

Percutaneous/ocular/mucous membrane exposure, IM

Child all ages: Administer frst dose of vaccine within 7 days and hepatitis B immunoglobulin within 72 hours

Sexual exposure, IM

Child all ages: Administer frst dose of vaccine and hepatitis B immunoglobulin within 14 days.

Adverse effects: Common: Transient injection site reactions (pain, redness, itching, swelling or burning, small hard lump which may persist for some weeks), transient fever, fainting. Rarely: Malaise, myalgia.

Contraindications: History of anaphylaxis to any component of the vaccine.

Cautions: In case of acute febrile illness, halt all vaccinations until patient recovers from febrile illness. Where the patient immunodefcient (advanced HIV infection, diabetes, chronic liver disease or chronic renal failure), there may be reduced immunogenicity of the vaccine.

ENGERIX B (by Glaxo-Smith Kline)

Presentation: Injection of suspension of hepatitis B surface antigen (by, prepared from yeast cells by recombinant DNA technique) 20 mcg/ml adsorbed onto aluminium hydroxide.

Administration: By intramuscular injection (see note below), 3 doses of 1ml (20 mcg), the second 1 month and the third 6 months after the first dose; more rapid (e.g. for travellers), third dose 2 months after the first dose with a booster at 12 months.

Children:

Birth to 12 years; 3 doses of 0.5 ml (10 mcg).

Infants born to HBsAg-positive mother (see also above); 3 doses of 0.5ml (10 mcg), first dose at birth with hepatitis B immunoglobulin injection (separate site).

Note: Deltoid muscle is the preferred site of injection in adults; anterolateral thigh is preferred site in infants and children; not to be injected into the buttock (vaccine efficacy reduced); subcutaneous route used for patients with haemophilia.

B-VAX II (By Pasteur Merieux)

Presentation: Injection of suspension of hepatitis B surface antigen (prepared from yeast cells by recombinant DNA technique) 10 mcg/ml adsorbed onto aluminium hydroxide.

Administration: By intramuscular injection (see note below) 3 doses of 1ml (10 mcg), the second 1 month and the third 6 months after the first dose; more rapid (e.g. for travellers), third dose 2 months after the first dose with a booster at 12 months.

Children:

Birth to 15 years; 3 doses of 0.5 ml (5 mcg).

Infants born to HBsAg-positive mothers (see also above): 3 doses of 0.5ml (5 mcg), first dose at birth with hepatitis B immunoglobulin injection (separate site).

Note: Deltoid muscle is preferred site of injection in adults; anterolateral thigh is preferred site in infants and children; not to be injected into the buttock (vaccine efficacy reduced); subcutaneous route used for patients with haemophilia.

Single component for dialysis and predialysis patients.

HB-VAX II 40 (By Pasteur Merieux)

Presentation: A suspension of hepatitis B surface antigen (prepared from yeast cells by recombinant DNA technique) 40 mcg/ml adsorbed onto aluminium hydroxide.

Administration: By intramuscular injection (see note below) 3 doses of 1ml (40 mcg), the second one month and the third 6 months after the first dose; booster doses may be required in those with low antibody concentration.

Note: Deltoid muscle is the preferred site of injection in adults; subcutaneous route used for patients with haemophilia.

- With hepatitis A vaccine

TWINRIX (by Glaxo-Smith Kline)

Presentation: Inactivated hepatitis A virus 720 ELISA units and recombinant (DNA) hepatitis B surface antigen 20 mcg/ml adsorbed onto aluminium hydroxide and aluminium phosphate.

Administration: By intramuscular injection onto deltoid muscle (see note below); primary

course of 3 doses of 1ml, the second 1 month and the third 6 months after the first dose; 1ml booster dose 5 years after the start of primary course for those at continued risk

Children:
1-15 years: 0.5ml.

Note: Primary course should be completed with Twinrix (single component vaccines given at appropriate intervals may be used for booster dose); not to be injected into the buttock (vaccine efficacy reduced); subcutaneous route used for patients with haemophilia (but the immune response may be reduced).

Important: Twinrix is **not** recommended for post-exposure prophylaxis following percutaneous (needle-stick), ocular or mucous membrane exposure to hepatitis B virus.

HPV (QUADRIVALENT)

Presentation: Injection, Solution containing singe or multidose vial for HPV types 6, 11, 16, and 18.

Indications: Prevention of cervical cancer, genital warts, and other pre-cancerous lesions caused by human papilloma virus (HPV) types 6, 11, 16, and 18, especially if given before sexual activity begins.

Administration:

Children:
1st dose for females at 10 to 14 years of age, the second and third doses are given 6 months after the first dose, all 3 doses should be given within a 12-month period.

Side effects: Though not known to be harmful, vaccination should be postponed until completion of pregnancy.

Contraindications: Pregnancy - not known to be harmful, but vaccination should be postponed till after pregnancy.

Caution: Do not switch to bivalent vaccine, use one vaccine product for the entire course.

Influenza vaccine

While most viruses are antigenically stable, the influenza viruses A and B (especially A) are constantly altering their antigenic structure as indicated by changes in the haemagglutinins (H) and neuraminidases (N) on the surface of the viruses. Influenza vaccines in use must contain the H and N components of the prevalent strain or strains. Every year the World Health Organization recommends which strains should be included.

The recommended strains are grown in the allantoic cavity of chick embryos (therefore contraindicated in those hypersensitive to eggs).

Interactions: See appendix (Influenza Vaccine)

Since **influenza vaccines** will not control epidemics, they are recommended *only for persons at high risk*. Annual immunisation is strongly recommended for those of all ages, especially the elderly, with any of the following conditions: chronic respiratory disease, including asthma, chronic heart disease, chronic renal failure, diabetes mellitus, immunosuppression due to disease or treatment, including asplenia or splenic dysfunction. Influenza immunisation is also recommended for residents of nursing homes, residential homes for the elderly, and other long-stay facilities.

INACTIVATED INFLUENZA VACCINE (SPLIT VIRION) (By Pasteur Merieux)

Inactivated influenza vaccine (split virion) Flu/Vac/Split.

Administration: 0.5ml by deep subcutaneous or by intramuscular injection.

Children:
6 months – 3 years: 0.25 ml repeated once after 4-6 weeks.
4-12 years: 0.5ml repeated once after 4-6 weeks; single doses are appropriate for children who have already been immunised.

BEGRIVAC (By Wyeth)

Inactivated influenza vaccine (split virion) Flu/ Vac/Spli.

Administration: 0.5ml by deep subcutaneous or by intramuscular injection.

Children:

6-36 months; 0.25ml or 0.5ml repeated once after 4-6 weeks.

3-12 years; 0.5ml repeated once after 4-6 weeks;

Single doses are appropriate for children who have already been immunised.

FLUARIX (by Glaxo-Smith Kline)

Inactivated influenza vaccine (split virion) Flu/ Vac/split.

Administration: 0.5ml by deep subcutaneous or by intramuscular injection.

Children:

6 months to 35 months: 0.25-0.5ml

3-12 years 0.5ml repeated once after 4-6 weeks.

Single doses are appropriate for children who have already been immunised.

FLUVIRIN (By MEDEVA)

Inactivated influenza vaccine (surface antigen) flu/ Vac/SA.

Administration: 0.5ml by deep subcutaneous or by intramuscular injection.

Children:

6 months to 35 months: 0.25-0.5ml

3-12 years: 0.5ml repeated once after 4-6 weeks.

Single doses are appropriate for children who have already been immunised.

FLUZONE (By Pateur Merieux)

Inactivated influenza (split virion) Flu/Vac/ split.

Administration: 0.5ml by deep subcutaneous or by intramuscular injection.

Children:

6-36 months; 0.5ml repeated once after 4-6 weeks

4-12 years: 0.5ml repeated once after 4-6 weeks; single doses are appropriate for children who have already been immunised.

INFLUVAC SUB-UNIT (By Solvay)

Inactivated influenza vaccine (surface antigen) Flu/Vac/SA.

Administration: 0.5ml by deep subcutaneous or by intramuscular injection.

Children:

6 months-4 years: 0.25ml repeated once after 4-6 weeks.

4-13 years: 0.5ml repeated once after 4-6 weeks.

*S*ingle doses are appropriate for children who have already been immunised.

Measles Vaccine

Measles vaccine is used for active immunisation against measles. In most developed countries, children are immunised against measles using a combined Measles, Mumps and Rubella (MMR) vaccine during the second year of life. In developing countries including Zambia, a measles vaccine is administered at 9 months (can be given in certain circumstances from 7 months) and forms part of WHO Expanded Programme on Immunisation (EPI). In both instances, a second dose is often given later on in childhood.

Administration of a measles-containing vaccine to children may be associated with mild measles-like syndrome with a measles-like rash and pyrexia about a week after injection. Much less commonly, convulsions and, very rarely, encephalitis have been reported. Convulsions in infants are much less frequently associated with measles vaccines than with other conditions leading to febrile episodes.

Both the Measles and MMR vaccines may be used in the control of outbreaks of measles (see under MMR Vaccine).

- Single antigen vaccine

Measles vaccine: routine vaccination against measles is recommended for all children in the country at 9 months or at least during the first year of life from 9 months of age. A second dose is given at 18 months and the third dose at school entry (see the schedule in 16.1.)

The measles vaccine is generally not recommended in children less than 9 months in whom maternal antibodies may prevent a response. However, it has been administered in infants at 7 months in certain circumstances e.g. during a measles outbreak.

Measles vaccine can be given as prophylaxis after exposure to measles such as during an outbreak as long as it is given within 72 hours of exposure.

MEASLES VACCINE

Measles vaccine live (meas/Vac/live) is a preparation of suitable live attenuated strain of measles virus grown in cultures of chick embryo cells or human diploid cells

Administration: 0.5ml administered by deep subcutaneous injection into the upper arm.

Combined vaccine, see under MMR vaccine

MMR vaccine

A combined **measles/mumps/rubella vaccine** (MMR vaccine) has been introduced to eliminate rubella (and congenital rubella syndrome), measles, and mumps. Every child should receive two doses of MMR vaccine by entry to primary school unless there is a valid contraindication (see below) or parental refusal.

The first dose of MMR vaccine is given to children aged 12-15 months. A second (booster) dose has been given before starting school at 3-5 years of age (see the schedule, section 15.1), Children presenting for their pre-school booster who have not received their first dose of MMR vaccine should be given a dose of MMR vaccine followed 3 months later by a second dose. At school-leaving age or entry into further education. Individuals of both sexes who have not received either MR or MMR vaccines should be offered MMR immunisation.

MMR vaccine may also be used in the control of outbreaks of measles and should be offered to susceptible children within 3 days of exposure to infection (**important:** MMR vaccine is not suitable for prophylaxis following exposure to mumps or rubella since the antibody response to the mumps and rubella components is too slow for effective prophylaxis).

Children with partially or impaired immune responsiveness should not receive live vaccines (for advice on AIDS see section 16.1). If they have been exposed to measles infection they should be given normal immunoglobulin (section 16.5.1).

Malaise fever or a rash may occur following the first dose of MMR vaccine, most commonly about a week after immunisation and lasting about 2 to 3 days. Parotid swelling occasionally occurs, usually in the third week. After the second dose of MMR vaccine, adverse reactions are considerably less common than after the first dose. Post-vaccination meningoencephalitis was reported (rarely and with complete recovery) following immunisation with MMR vaccine containing Urabe mumps vaccine, which has been discontinued; no cases have been confirmed in association with the currently-used Jeryl Lynn mumps vaccine. Children with post-vaccination symptoms are not infectious.

Contraindications: Children with an untreated malignant disease or altered immunity (for advice on vaccines and AIDS see section 16.1), and those receiving immunosuppressive Medicines or radiotherapy, or high-dose corticosteroids, children who have received another live vaccine by injection within 3 weeks, children with allergies to neomycin, kanamycin and Gelatin children with acute febrile illness (vaccination should be deferred).

Adverse reactions: Include idiopathy, thrombocytopenic purpura within six weeks,

"leaflets are available to provide parents with advice for reducing fever" (including the use of Paracetamol).

If given to women, pregnancy should be avoided for 1 month (as for rubella vaccine); should not be given within 3 months of an immunoglobulin injection.

It should be noted that; children with a personal or close family history of convulsions should be given MMR vaccine, provided the parents understand that there may be a febrile response: immunoglobulin must not be given with MMR vaccine since the immune response to rubella and mumps may be inhibited; doctors should seek specialist paediatric advice rather than withhold vaccination;

There is increasing evidence that MMR vaccine can be given safely even when the child has had an anaphylactic reaction to food containing egg (dislike of egg or refusal to eat is not a contraindication).

MMR VACCINE

Live measles, mumps, and rubella vaccine.

Administration: 0.5ml deep subcutaneous or by intramuscular injection. Available as MMR II (Pasteur Merieux) or Priorix (SmithKline Beecham).

MEASLES/RUBELLA

Presentation: Powder for injection + diluent, containing 5-ml vial for 10 doses.

Indications: Immunisation against measles and rubella.

Administration:

Children:
0.5 ml administered subcutaneously into the right upper arm (deltoid muscle) 1st dose: at 9 months or at first contact after 9 months for children under 5 years; 2nd dose: at 18 months or first contact after 18 months.

Side effects: Sleep disturbances, unusual crying in infants, swelling of the Parotid (usually in the third week). Rarely, arthropathy, idiopathic thrombocytopenic purpura, optic neuritis, peripheral neuritis.

Contraindication: Reduced antibody response to measles component after immunoglobulin administration or blood transfusion. It is advisable to leave an interval of at least 3 months before MMR immunization.

Cautions: MMR vaccine should not be administered on the same day as yellow fever vaccine, there should be a 4-week minimum interval between the vaccines. Hepatic impairment: Dose adjustment not necessary. Renal impairment: Dose adjustment not necessary.

Meningococcal Polysaccharide Vaccine

Meningococcal Polysaccharide Vaccine is indicated for visits of longer than 1 month to areas of the world where there is a risk of acquiring meningococcal infection particularly for travellers proposing to travel 'rough'. Travellers with asplenia (or severe dysfunction of the spleen) also particularly require protection.

These areas include Delhi, Nepal, Burma, Pakistan, Mecca (see below), and the meningitis belt of Africa, which encompasses southern sub-Saharan parts of Senegal, Mali, Niger, Chad and Sudan; all of Gambia, Guinea, Togo and Benin; South-west Ethiopia; the northern part of Sierra Leone, Liberia, Ivory Coast, Nigeria, Cameroon, Central African Republic, Uganda and Kenya.

Saudi Arabia requires vaccination of pilgrims to Mecca during the Haj annual pilgrimage; this may apply to others visiting Saudi Arabia in the months leading up to August.

The need for immunisation of laboratory staff who work directly with Neisseria meningitidis should be determined by assessing the risk. See section 15.1 for general contra-indications.

AC VAX (by Glaxo-Smith Kline)

Meningococcal polysaccharide vaccine, Neiman/ Vac. Prepared from *Neisseria meningitidis* (meningococcus) groups A and C.

Administration: ***Adult*** **and** ***child*** aged 2 months and over, 0.5ml by deep subcutaneous or intramuscular injection.

MENGIVAC (A + C) (By Pasteur Merieux)

Meningococcal polysaccharide vaccine, Neiman/ Vac. Prepared from *Neisseria meningitidis* (meningococcus) group A and C.

Administration: ***Adult and child*** aged over 18 months: 0.5ml by deep subcutaneous or intramuscular injection.

Note: The lower age range for AC Vax and Mengivac (A+C) differ; in the case of Mengivac (A+C) the product literature states that young children and infants respond less well to the vaccine than older children and adults with little response to the Group C polysaccharide under 18 months of age and a poor response to Group A polysaccharide under 3 months of age. Additionally, protection in infants under 18 months of age is of shorter duration.

Mumps Vaccine

Mumps vaccine consists of a live attenuated strain of virus grown in chick embryo tissue culture. See under MMR vaccine and section 16.1 for contraindications.

MUMPSVAX (By Pasteur Merieux)

Mumps vaccine (Jeryl Lynn strain).

Administration: **A*dult*** **and** ***child*** over 1 year; 0.5ml by subcutaneous injection.

- Combined vaccines with measles and rubella see MMR Vaccine.

Pertussis vaccine (Whooping cough vaccine)

Pertussis vaccine is usually given combined with diphtheria and tetanus vaccine (in a triple vaccine) starting at 2 months of age (see section 16.1).

Convulsions and encephalopathy have been reported as rare complications, but such conditions may arise from other causes and be falsely attributed to the vaccine. Neurological complications after whooping cough itself are considerably more common than after the vaccine.

As with any other elective immunisation procedure, it is advisable to postpone vaccination if the child is suffering from an acute illness until fully recovered. Minor infections, without fever, or systemic upset are not reasons to delay immunisation. Immunisation should not be carried out in children who have a history of the severe general reaction to a preceding dose. In these children, immunisation should be completed with adsorbed diphtheria and tetanus vaccine. Where there has been a severe local reaction or pyrexia, a cellular pertussis vaccine may be used.

The following reactions should be regarded as severe:

Local - an extensive area of redness and swelling which becomes indurated and involves most of the anterolateral surface of the thigh or a major part of the circumference of the upper arm.

General - a temperature of 39.5 degrees C or more within 48 hours of vaccine, anaphylaxis, bronchospasm, laryngeal oedema, generalised collapse, prolonged unresponsiveness, prolonged inconsolable screaming, and convulsions occurring within 72 hours.

A personal or family history of allergy is **not** a contraindication to immunisation against whooping cough; nor are stable neurological conditions such as cerebral palsy or spina bifida.

Children with problem histories. When there is a personal or family history of febrile convulsions, there is an increased risk of these occurring after pertussis immunisation. In such children, immunisation is recommended but advice on the prevention of fever should be given at the time of immunisation.

In a British study, children with a family history of epilepsy were immunised with pertussis vaccine without any significant adverse events.

These children's developmental progress has been normal. In children with a close family history (first-degree relatives) of *idiopathic epilepsy*, there may be a risk of developing a similar condition, irrespective of vaccine Immunisation is recommended for these children.

Where there is a still-evolving neurological problem, immunisation should be deferred until the condition is stable. Children whose epilepsy is well controlled may receive a pertussis vaccine. When there has been a documented history of cerebral damage in the neonatal period, immunisation should be carried out unless there is evidence of an evolving neurological abnormality. If immunisation is to be deferred, this should be stated on the neonatal discharge summary. Where there is doubt, appropriate advice should be sought from a consultant paediatrician, district immunisation coordinator or consultant in communicable disease control *rather than withholding vaccine.*

Older children: there is no contraindication to the administration of pertussis vaccine to unimmunised older children to protect the individuals and siblings under the age of immunisation; there is no upper age limit. However, no suitable vaccine is available for children over 7 years.

Guidance for immunisation against pertussis in the absence of single-antigen pertussis vaccine is available at ww.doh.gov.uk.

Pneumococcal Vaccine

PNEUMOCOCCAL VACCINE (10 VALENT ADSORBED CONJUGATE)

Presentation: Injection (suspension), 2-ml vial (4 doses).

Indications: *Paediatric* - active and primary immunization against Streptococcus pneumoniae.

Administration:

Children:

Infant - 3 doses of 0.5 ml, IM, minimum interval between doses: 4 weeks, first dose at 6 weeks of life or at first contact with unvaccinated child under 5 years. Second dose at 10 weeks or 4 weeks after PCV1. Third dose at 14 weeks or 4 weeks after PCV2.

Side effects: Myalgia, transient injection site reactions (pain, redness, itching, swelling or burning, small hard lump which may persist for some weeks), transient fever, fainting. Rarely, allergic reactions, cellulitis, seizures, angioedema.

Contraindications: History of anaphylaxis to any component of the vaccine.

Cautions: Acute febrile illness - postpone all vaccinations until patient is well. 23-valent (unconjugated) polysaccharide vaccine is not recommended for children under 2 years.

PNEUMOCOCCAL VACCINE (13 VALENT OR HIGHER ADSORBED CONJUGATE)

Presentation: Injection, single or multidose vial

Indications: *Adult 19 to 65 years of age with specified underlying medical conditions* - active immunization against Streptococcus pneumoniae.

Paediatric - Primary immunization against Streptococcus pneumoniae.

Administration: ***Adult*** **-** 0.5 ml as a single dose, IM.

Children:

IM injection using pneumococcal polysaccharide conjugated vaccine (13vPCV)

Infant: three doses of 0.5 ml, a minimum of 4 weeks apart, booster can be given at 12 months of age.

Infant presenting late for vaccination: two doses of 0.5 ml at least 4 weeks apart followed by a third dose at 13 months.

1–5 years, previously not vaccinated or not completed primary course: 0.5 ml as a single dose or 0.5 ml separated by 2 months in the immunocompromised or those with asplenia or splenic dysfunction.

Revaccination of children who are at increased risk of pneumococcal disease and its complications due to underlying health conditions, SC or IM injection using 23-valent pneumococcal polysaccharide vaccine (23vPPV).

Over 2 years: 0.5 ml as a single dose and subsequently every 5 years.

Side effects: Myalgia, transient injection site reactions (pain, redness, itching, swelling or burning, small hard lump which may persist for some weeks), transient fever, fainting. Rarely, allergic reactions, cellulitis, seizures, angioedema.

Contraindications: history of anaphylaxis to any component of the vaccine.

Cautions: Acute febrile illness - postpone all vaccinations until patient is well.

PNEUMOVAX II (By Pasteur Merieux)

Polysaccharide from each of 23 capsular types of pneumococcus.

Administration: 0.5ml by subcutaneous or intramuscular injection.

Children:

Under 2 years, not recommended (suboptimal response and also safety and efficacy not established).

PNU-IMUNE (By Wyeth)

Polysaccharide from each of 23 capsular types of pneumococcus.

Administration: 0.5ml subcutaneous or intramuscular injection.

Children:

Under 2 years not recommended.

See Appendix 1.

PREVENAR

The polysaccharide of each of 7 capsular types of pneumococcus adsorbed into aluminium phosphate.

Administration: Intramuscular injection

Children:

2-6 months: 3 doses each of 0.5ml separated by intervals of 1 month and a further dose in the second year of life

7-11 months: 2 doses each of 0.5ml separated by an interval of 1 month and a further dose in the second year of life;

1-2 years: 2 doses each of 0.5ml separated by an interval of 2 months.

Note: Reltoid muscle is the preferred site of injection in young children anterolateral thigh is preferred site in infants.

POLIO VACCINE (IPV) (INACTIVATED)

Poliomyelitis Vaccines

Presentation: Injection, multidose vial, Injection inactivated poliomyelitis virus, types 1, 2, and 3.

Indications: Adult - active immunization against poliomyelitis in unimmunized or incompletely immunized adults exposed to wild poliovirus (routine immunization in adults is not recommended)

Paediatric - primary immunization of children against poliomyelitis.

Administration: ***Adult*** - 0.5ml two doses 1 – 2 months apart with third dose 6 – 12 months later.

Children:

0.5 ml by IM injection at 14 weeks or at first contact with an unvaccinated child below 1 year.

Side effects: Pain, redness, itching, swelling or burning, small hard lump (which may persist for some weeks) on injection site, transient fever,

fainting. Rarely: malaise, myalgia, arthralgia, lymphadenopathy, peripheral neuropathy, delayed hypersensitivity reactions, allergic reactions (including anaphylaxis).

Contraindications: History of anaphylaxis to any component of the vaccine.

Cautions: Acute febrile illness (postpone all vaccinations until patient is well).

POLIO VACCINE LIVE

Presentation: Injection, multidose vial, Injection inactivated poliomyelitis virus, types 1, 2, and 3.

Indications: ***Adult*** - active immunization against poliomyelitis in unimmunized or incompletely immunized adults exposed to wild poliovirus (routine immunization in adults is not recommended)

Paediatric - primary immunization of children against poliomyelitis.

Administration: ***Adult*** - 0.5ml two doses 1 – 2 months apart with third dose 6 – 12 months later.

Children:
0.5 ml by IM injection at 14 weeks or at first contact with an unvaccinated child below 1 year.

Side effects: Pain, redness, itching, swelling or burning, small hard lump (which may persist for some weeks) on injection site, transient fever, fainting. Rarely: malaise, myalgia, arthralgia, lymphadenopathy, peripheral neuropathy, delayed hypersensitivity reactions, allergic reactions (including anaphylaxis).

Contraindications: History of anaphylaxis to any component of the vaccine.

Cautions: Acute febrile illness (postpone all vaccinations until patient is well).

Rabies Vaccine

Pre-exposure, prophylactic immunisation with human diploid cell rabies vaccine should be offered to those at high risk - laboratory staff who handle the rabies virus, those working in quarantine stations, animal handlers, veterinary surgeons and field workers who are likely to be exposed to bites of possibly infected wild animals, certain port officials, and health workers who are likely to come into close contact with patients with rabies. Pre-exposure immunisation is also recommended for those living or travelling to enzootic areas who may be exposed to unusual risk.

For *prophylactic use,* the vaccine produces a good antibody response when given in a 3-dose schedule on days 0,7, and 28, with a booster dose every 2-3 years to those at continued risk. For travellers to enzootic areas who are not animal handlers, 2 doses given 4 weeks apart may be acceptable *provided that post-exposure treatment is readily available;* for those who remain at continued risk, a booster dose should be given 6-12 months later followed by a booster every 2-3 years.

Post-exposure treatment depends on the level of risk in the country concerned and the individual's immune status. For the *post-exposure treatment of fully immunised patients:* countries with no risk, generally no treatment required; countries with low risk and high risk, two booster doses are needed (one on day 0 and one on day 3-7). For the *post-exposure treatment of previously immunised patients* (or those whose prophylaxis is possibly inadequate): countries with no risk, generally no treatment required; countries with low risk a course of injections should be started as soon as possible after exposure (days 0, 3, 7, 14 and 30); countries with high risk, as for countries with low risk, **plus** rabies immunoglobulin on day 0 (section 16.1). The course may be discontinued if it is proved that the patient was not at risk.

Staff in attendance on a patient who is highly suspected of, or known to be suffering from, rabies should be offered immunisation. Four intradermal doses of 0.1ml of human diploid cell vaccine (Pateur Merieux) given on the same day at different sites (ensuring correct intradermal technique) has been suggested for this purpose (unlicensed route).

There are no specific contra-indications to this diploid cell vaccine and its use should be considered whenever a patient has been attacked by an animal even if there is no direct evidence of rabies in the attacking animal.

RABIES VACCINE BP PASTEUR MERIEUX (by Pasteur Merieux)

Presentation: Freeze-dried inactivated Wistar rabies virus strain PM/WI 38 1503-3M cultivated in human diploid cells. Single-dose vial with a syringe containing diluent.

Indications: Pre-exposure, prophylactic immunisation and post-exposure treatment.

Administration: ***Prophylactic:*** 1ml by deep subcutaneous or intramuscular injection in the deltoid region, on days 0, 7, and 28; also, booster doses every 2-3 years to those at continued risk; see above for 2 dose schedule.

Post-exposure: 1ml by deep subcutaneous or intramuscular injection in the deltoid region, see notes above. Staff in attendance, see notes above.

Cautions: Studies have shown that when this vaccine is injected into the gluteal region there is a poor response. Concomitant administration of chloroquine may also affect the antibody response. Because of the potential consequences of inadequately treated rabies exposure and because there is no indication that foetal abnormalities have been associated with rabies vaccination, pregnancy is **not** considered a contraindication to postexposure prophylaxis. If there is a substantial risk of exposure to rabies, pre-exposure prophylaxis may also be indicated during pregnancy.

Rubella Vaccine

The selective practice of protecting women of childbearing age from the risk of rubella (German measles) in pregnancy has been replaced by practice of eliminating rubella in children. The single-antigen rubella immunisation programme for 10-14-year-old girls has been discontinued. All children should be immunised with rubella containing vaccine (measles, mumps and rubella) at 12-15 months and 3-5 years (see MMR vaccine).

Rubella vaccine may conveniently be offered to previously *immunised and seronegative post-partum women.* Immunising susceptible post-partum women a few days after delivery is important as far as the overall reduction of congenital abnormalities is concerned, for about 60% of these abnormalities occur in the babies of multiparous women.

PREGNANCY. Rubella immunisation should be avoided in early pregnancy, and women of childbearing age should be advised not to become pregnant within 1 month of immunisation.

However, despite active surveillance in the UK, the USA, and Germany, no case of congenital rubella syndrome has been reported following inadvertent immunisation shortly before or during pregnancy. There is thus no evidence that the vaccine is teratogenic, and routine termination of pregnancy following inadvertent immunisation should **not** be recommended; potential parents should be given this information before deciding on termination.

See section 15.1 for general contra-indications.

RUBELLA VACCINE, LIVE RUB/ VAC (LIVE)

Presentation: Prepared from Wistar RA 22/3 strain propagated in human diploid cells.

Administration: 0.5ml by deep subcutaneous or by intramuscular injection (see the schedule, section 16.1 and notes above).

- For Combined vaccines, see under MMR vaccine.

Smallpox Vaccine

Smallpox immunisation is no longer required routinely because global eradication has been achieved.

Anti-snake venom sera

- **Polyvalent**

Anti-snake venom sera is a lyophilised powder. It is effective against venoms of the following corresponding poisonous snakes:

- Black Mamba (Dendroaspis Polylepis)
- Gaboon Viper (Bitis Gabonica Rhinoceros)
- Russel's Viper (Vipera Russelli)
- Saw-Scaled Viper (Echis Carinatus)

Snakebite should be treated immediately. The following first aid measures are of great value in snake bite management.

Institute measures to combat shock which has a major physiological element in it.

A ligature should be bound at some moderate distance above the bitten part to prevent the venom from spreading to the upper part of the limb.

The bite wound should be cleaned in the usual surgical way. The bitten part should be immobilised as in fracture cases.

To derive the greatest benefit out of the anti-snake venom serum treatment, the serum should be injected as soon as possible after the snake bite.

It is advisable to check the manufacturer's instructions before administering the serum.

ANTI-SNAKE VENOM SERUM POLYVALENT

Presentation: A white or pale-yellow lyophilised powder in 10ml vials.

Indications: Antitoxic therapy in bites from the above-mentioned snakes. It can also be used in cases where specific antiserum is not available or when the species is not known.

Administration: As a first dose 20ml of the reconstituted serum should be injected intravenously very slowly (1ml per minute). The second dose should be given after 1 hour if symptoms persist. If symptoms persist, (these vary depending on the venom) further doses can be given every 6 hours until symptoms disappear completely. In viper cases, some serum should be injected around the site of the bite to prevent gangrene which results due to the destructive effect of the localised viper venom on the tissue.

Side effects: Serum sickness, thermal reactions and acute anaphylaxis.

Caution: Before administration of the anti-snake serum it is necessary to find out from the patient of any allergies and if possible test for sensitivity by injecting the patient 0.1ml of the serum diluted 1:10 in normal saline or saline/glucose. The patient should then be observed for 30 minutes for local or general reaction. If the test dose produces a reaction, this should be countered immediately with 1:100 adrenaline and if necessary corticosteroids. But if the symptoms of snakebite are severe it may not be advisable to wait for 30 minutes to observe reactions to the test dose. In such cases, it may be better to inject 1ml of adrenaline 1:1000 intramuscularly at the same time as the serum to minimise the risk of anaphylaxis.

Tetanus Vaccines (Tetanus Toxoids)

Tetanus vaccines stimulate the production of the protective antitoxin. In general, adsorption on aluminium hydroxide, aluminium phosphate, or calcium hydroxide, aluminium phosphate, or calcium phosphate improves antigenicity.

Adsorbed tetanus vaccine is offered routinely to babies in combination with adsorbed diphtheria vaccine (DT/Vac/Ads (Child), and more usually also combined with killed *Bordetella pertussis* organisms as a triple vaccine, adsorbed diphtheria, tetanus, and pertussis vaccine (DTPer/Vac/Ads). See schedule, section 16.1).

In children, the triple vaccine not only gives protection against tetanus in childhood but also gives the basic immunity for subsequent booster doses of adsorbed tetanus vaccine at school entry and at school leaving (combined with low-dose adsorbed diphtheria vaccine) and also when a potential tetanus- the contaminated injury has been received. Normally, booster doses of adsorbed tetanus vaccine should not be given unless more than 10 years have elapsed since the last booster dose because of the possibility that hypersensitivity reactions may develop. If a child over the age of 13 years requires a tetanus booster for a tetanus-prone wound then, provided more than 10 years have elapsed since the school-entry booster, adsorbed tetanus vaccine combined

with low-dose adsorbed diphtheria vaccine can be given; the routine booster at school leaving age is omitted.

Active immunisation is important for persons in older age groups who may never have had a routine or complete course of immunisation when younger. In these persons, a course of adsorbed tetanus vaccine may be given. Very rarely, tetanus has developed after abdominal surgery; patients awaiting elective surgery should be asked about tetanus immunisation and immunised if necessary. All laboratory staff should be offered a primary course if unimmunised.

Any adult who has received 5 doses is likely to have life-long immunity; booster doses on injury should only be required if more than 10 years have elapsed since the last dose.

Wounds are considered to be tetanus-prone if they are sustained *either* more than 6 hours before surgical treatment *or* at any interval after injury and are puncture-type or show much-devitalised tissue or are septic or are contaminated with soil or manure. All wounds should receive thorough surgical toilet. For *clean wounds*, a booster dose of adsorbed tetanus vaccine is given if the primary course (or booster dose) was given more than 10 years previously; non-immunised individuals (or whose immunisation status is not known) should be given a full course of the vaccine. For *tetanus prone wounds,* treatment is as for clean wounds with the addition of a dose of tetanus immunoglobulin (section 16.5); in an immunised individual who has received a dose of adsorbed tetanus vaccine within the previous 10 years the immunoglobulin may only be needed if the risk of infection is considered to be especially high (e.g. contamination with manure). Antibiotic treatment (with benzylpenicillin or amoxicillin + clavulanic acid) may also be required for tetanus-prone wounds. See section 16.1 for general contraindications.

Single antigen vaccines

The BP directs that when Tetanus Vaccine is prescribed or demanded and the form is not stated, adsorbed Tetanus Vaccine may be dispensed or supplied.

ADSORBED TETANUS VACCINE

Presentation: Prepared from tetanus formol toxoid with a mineral carrier (aluminium hydroxide).

Administration: 0.5ml or as stated on the label, by intramuscular or deep subcutaneous injection, followed after 4 weeks by a second dose and after a further 4 weeks by a third.

For Combined vaccine, see Diphtheria Vaccines above.

Typhoid Vaccines

Typhoid immunisation is advised for travellers to countries where sanitation standards may be poor, although it is not a substitute for scrupulous personal hygiene (see section 15.6). Immunisation is also advised for laboratory workers handling specimens from suspected cases.

Capsular **polysaccharide typhoid vaccine** is given by *intramuscular or deep subcutaneous injection* with a booster dose every 3 years on continued exposure. Local reactions, including pain, swelling or erythema may appear 48-72 hours after administration.

An **oral typhoid vaccine** is also available. It is a **live attenuated** vaccine contained in an enteric-coated capsule. It is taken *by mouth* as three doses of one capsule on alternate days, providing protection 7-10 days after the last dose. Protection may persist for up to 3 years in those constantly (or repeatedly) exposed to *Salmonella typhi,* but occasional travellers require a repeat course at intervals of 1 year.

Contraindications: Immunosuppressed Individuals (whether due to disease or its treatment) and is inactivated by concomitant administration of antibiotics or sulphonamides. Oral typhoid vaccine and oral poliomyelitis vaccine should be given at least 3 weeks apart on theoretical grounds. Administration of a dose of oral typhoid vaccine should be coordinated so that mefloquine is not taken for at least 12 hours before or after a dose (vaccination with oral typhoid vaccine should preferably be completed at least 3 days before the first dose of mefloquine).

Side effects: Abdominal cramps, diarrhoea, headache, fever and hypersensitivity reactions including rarely anaphylaxis.

For general contraindications to vaccines, see section 16.1.

- Polysaccharide vaccine for injection

TYPHIM VI (By Pasteur Merieux)

Presentation: Vicapsular Polysaccharide typhoid vaccine, 50 mcg/ml virulence polysaccharide antigen of *salmonella Typhi.*

Administration: 0.5ml by deep subcutaneous or intramuscular injection. Children under 18 months, may show suboptimal response.

VIVOTI (By MEDEVA)

Presentation: Capsules, enteric-coated, live attenuated salmonella Typhi.

Administration: ***Adult*** **and** ***children*** over 6 years; 1 capsule on days 1, 3 and 5.

Under 6 years, not recommended.

COUNSELLING: Swallow as soon as possible after placing in the mouth with a cold or lukewarm drink: it is important to store in the refrigerator.

Yellow fever vaccine

Yellow fever vaccine consists of a live attenuated yellow fever virus (17D strain) grown in developing chick embryos. Immunisation is indicated for those travelling or living in areas where the infection is endemic and for laboratory staff who handle the virus or who handle clinical material from suspected cases. Infants under 9 months of age should only be vaccinated if the risk of yellow fever is unavoidable since there is a small risk of encephalitis. The vaccine should not be given to those with impaired immune responsiveness, or who have had an anaphylactic reaction to the egg; it should not be given during pregnancy (but where there is a significant risk of exposure the need for immunisation outweighs any risk to the foetus). See section 16.1 for further contraindications.

Reactions are few. The immunity which probably lasts for life is officially accepted for 10 years starting from 10 days after primary immunisation and for a further 10 years immediately after revaccination.

YELLOW FEVER VACCINE

Presentation: Live Yel/Vac A suspension for chick embryo proteins containing attenuated 17D strain virus.

Administration: 0.5ml by subcutaneous injection.

16.5 Immunoglobulins

Human immunoglobulins have replaced immunoglobulins of animal origin (antisera) which were frequently associated with hypersensitivity. Injection of immunoglobulins produces immediate protection lasting for several weeks.

The two types of human immunoglobulin preparation are **normal immunoglobulin** and **specific immunoglobulins.**

16.5.1 Normal immunoglobulin (Gamma Globulin)

Human normal immunoglobulin ('hnIg') is prepared from pools of at least 1000 donations of human plasma; it contains immunoglobulin G, antibody to measles, mumps, varicella, hepatitis A, rubella and other viruses that are currently prevalent in the general population.

Caution and side effects. Side effects of immunoglobulins include malaise, chills, fever, and rarely anaphylaxis.

Contraindications: Patients with a known class-specific antibody to immunoglobulin A (IgA).

Normal immunoglobulin may **interfere with immune response to live viruses' vaccines** which should therefore only be given **at least**

3 weeks before or 3 months after an injection of normal immunoglobulin (this does not apply to yellow fever vaccine since normal immunoglobulin does not contain antibody to this virus). For travellers, if there is insufficient time, the recommended interval may have to be ignored.

INTRAMUSCULAR

Normal immunoglobulin is administered by intramuscular injection for the protection of susceptible contacts against hepatitis A virus (infectious hepatitis), measles and, to a lesser extent, rubella.

HEPATITIS A: Control of hepatitis A depends on good hygiene and many studies have also shown the value of normal immunoglobulin in the prevention and control of outbreaks of this disease.

It is recommended for controlling infection in contacts in closed institutions and also, under certain conditions, in school and home contacts, and for occasional or short-term travellers going to areas where the disease is highly endemic (all countries excluding Northern and Western Europe, North America, Australia, and New Zealand). Hepatitis A vaccine is preferred for those visiting such countries frequently or who stay for longer than 3 months.

MEASLES: Normal immunoglobulin may be given for prophylaxis in children with compromised immunity (and in adults with compromised immunity who have no measles antibodies); it should be given as soon as possible after contact with measles. It should also be given to children under 12 months with recent severe illness for whom measles should be avoided; MMR vaccine should then be given (after at least 3 months) at around the usual age.

RUBELLA: Immunoglobulin after exposure does not prevent infection in non-immune contacts and is not recommended for the protection of pregnant women exposed to rubella. It may, however, reduce the likelihood of a clinical attack which may possibly reduce the risk to the fetus. It should only be used when termination of pregnancy would be unacceptable when it should be given as soon as possible after exposure. Serological follow-up of recipients is essential. For routine prophylaxis, see Rubella Vaccine.

REPLACEMENT THERAPY: Normal immunoglobulin` may also be given by IM for replacement therapy, but IV formulations (see below under intravenous) are normally preferred.

NORMAL IMMUNOGLOBULIN

Presentation: Solution for Injection or infusion containing 16%, 1g, 2.5g, 3g, 5g, 6g, 10g, and 12g Normal immunoglobulin.

Indication: Post-exposure prophylaxis against hepatitis A infection, Prevention of clinical attack of Rubella in pregnancy, Replacement therapy in primary and secondary immunodeficiency disorders; Immune-mediated disorders; Kawasaki disease.

Administration: ***Adult:***

Post-exposure prophylaxis against hepatitis A infection: 1 dose of 1000mg by deep IM injection

Prevention of Clinical attack of Rubella in pregnancy: 1 dose of 750mg by deep IM injection to females of childbearing potential.

By intramuscular injection (expressed in terms of volume of 16%)

Hepatitis A prophylaxis: 0.02 – 0.04ml/kg body weight. Greater exposure risk: 0.06 – 0.12 ml/kg body weight. *Measles prophylaxis;* 0.2ml/kg body weight. To allow attenuated attack, 0.04ml/kg body weight.

Rubella in pregnancy, prevention of clinical attack: 750ml.

Antibody deficiency syndromes, consult product literature.

Children:

Post-exposure prophylaxis against hepatitis A infection

Neonate-9 years: 1 dose of 500mg by deep IM injection;

10-17 years: 1 dose of 1000mg by deep IM injection.

Kawasaki disease

1 dose of 2g/kg daily by IV infusion (with concomitant aspirin) given within 10 days of onset of symptoms (may also be used in children with a delayed diagnosis).

By intramuscular injection (expressed in terms of volume of 16%)

Hepatitis A prophylaxis

0.02 – 0.04ml/kg body weight. Greater exposure risk: 0.06 – 0.12 ml/kg body weight.

Measles prophylaxis

0.2ml/kg body weight. To allow attenuated attack, 0.04ml/kg body weight.

Other Indications stated above: Consult product literature

Cautions and Contraindications: see notes above.

Note: Special formulations for intravenous administration are available for replacement therapy for patients with congenital agammaglobulinaemia and hypogammaglobulinaemia, for the treatment of idiopathic thrombocytopenic purpura and Kawasaki syndrome, and the prophylaxis of infection following bone marrow transplantation.

16.5.2 Specific Immunoglobulins

Specific immunoglobulins are prepared by pooling the plasma of selected donors with high levels of the specific antibody required.

Although a hepatitis B vaccine is now available for those at high risk of infection, specific hepatitis B immunoglobulin ('HBIg') is available for use in association with the vaccine for the prevention of infection in the laboratory and other personnel who have been accidentally inoculated with hepatitis B virus, and in infants born to mothers who have become infected with this virus in pregnancy or who are high-risk carriers.

Following exposure of an unimmunised individual to an animal in or from a high-risk country, specific rabies immunoglobulin of human origin should be injected at the site of the bite should be washed with soap water and also given intramuscularly. Rabies vaccine should also be given (for details see Rabies Vaccine).

For tetanus-prone wounds, tetanus immunoglobulin of human origin ('HTIG') should be used in addition to wound toilet, antibiotic treatment and, where appropriate, adsorbed tetanus vaccine (for details see Adsorbed tetanus).

Varicella-zoster immunoglobulin **(VZIG)** is recommended for individuals who are at risk of severe varicella and who have no antibodies to varicella-zoster virus and who have significant exposure to chickenpox or herpes zoster. Those at increased risk include neonates of women who develop chickenpox 7 days before or 28 days after delivery, women exposed at any stage of pregnancy, and the immunosuppressed including those who have received corticosteroids in the previous 3 months at the following dose equivalents of prednisolone: *children* 2mg/kg daily for at least 1 week or 1mg/kg daily for 1 month; *adults* about 40 mg daily for more than 1 week

Varicella vaccine is available on a named patient basis from SmithKline Beecham or Pasteur Merrieux.

CYTOMEGALOVIRUS IMMUNOGLOBULIN

Presentation: Suspension for infusion containing 100 units/ml

Indications: Prophylaxis of cytomegalovirus infection in patients taking immunosuppressants (transplant recipients).

Administration: *Adult and Children:* by intravenous infusion (consult product literature)

Side effects: Haemolysis, cutaneous lupus erythematosus, embolism and thrombosis, haemolytic anaemia, hypotension, infusion related reactions, aseptic meningitis, myocardial infarction, renal impairment, transfusion-related acute lung injury

Contraindications: Selective IgA deficiency with IgA antibodies

Caution: Interference with live virus vaccines.

HEPATITIS B IMMUNOGLOBULIN

Presentation: Solution for injection containing 500 Units per ml

Indications: Prophylaxis against Hepatitis B infection; Prevention of hepatitis B re-infection more than 6 months after liver transplantation in stable HBV-DNA negative patients; Prevention of transmitted infection at birth; Other Indications: Prophylaxis against hepatitis B infection after exposure to hepatitis B virus-contaminated material; Prevention of hepatitis B in haemodialysed patients; Prophylaxis against re-infection of transplanted liver.

Administration: **Adult:**

Prophylaxis against hepatitis B infection (IM): 500 units administered as soon as possible after exposure (within 24–48 hours, but no later than 7 days after exposure);

Prevention of hepatitis B re-infection more than 6 months after liver transplantation in stable HBV-DNA negative patients (SC):

BW up to 75 kg: 500 units once weekly;

BW above 75kg: 1000 units once weekly; to be started 2–3 weeks after last dose of intravenous hepatitis B immunoglobulin.

Other Indications: Consult product literature.

Children:

Prophylaxis against hepatitis B infection (IM)

Neonate-4 years: 250 units;

5-9 years: 300 units;

10-17 years: 500 units; to be administered as soon as possible after exposure (within 24–48 hours, but no later than 7 days after exposure).

Prevention of transmitted infection at birth (IM):

Neonate: 250 units as soon as possible after birth (<12 hours)

Side effects: Upper abdominal pain**,** headache, hypertension, hypotension.

Contraindications: Not indicated in partially or previously immunised individuals (unless immunocompromised); If more than 7 days have passed since the first dose of rabies vaccine or more than 1 day since the second dose of rabies vaccine; if the rabies exposure was more than 12 months prior.

Caution: IgA deficiency, Interference with live virus vaccines

RABIES IMMUNOGLOBULIN

Presentation: Solution for injection containing 500 Units, >2.5IU

Indications: Post exposure treatment against rabies infection

Administration: ***Adult and Children:*** 20units/kg, administered by infiltration in and around the cleansed wound. If the wound is not visible or is healed or infiltration of whole volume is not possible, give remainder by IM injection in anterolateral site (remote from vaccination site).

Side effects: Arthralgia, headache, hypersensitivity, hypotension, influenza like illness, tachycardia

Contraindications: Not indicated in partially or previously immunised individuals (unless immunocompromised); If more than 7 days have passed since the first dose of rabies vaccine or more than 1 day since the second dose of rabies vaccine; if the rabies exposure was more than 12 months prior.

Caution: IgA deficiency, Interference with live virus vaccines

TETANUS IMMUNOGLOBULIN

Presentation: Suspension for injection containing 250 Units

Indications: Post exposure prophylaxis

Administration: ***Adult and Children:***

Prophylactic: 250 units or 500 units by IM injection (use higher dose if more than 24 hours have elapsed since injury, or there is risk of heavy contamination, or following burns or if patient weighs more than 90kg). A second dose

of 250 units given after 3-4 weeks if patient is immunosuppressed or if active immunisation with tetanus vaccine is contraindicated.

Therapeutic: 30-300 units/kg (5000-10,000 units) *Tetanus immunoglobulin for intravenous use* (used for proven or suspected clinical tetanus)

Side effects: Hypotension and anaphylactic reaction.

Caution: IgA deficiency, Interference with live virus vaccines

VARICELLA-ZOSTER

Presentation: Suspension for injection containing 250mg varicella- zoster Ig.

Indications: Prophylaxis against varicella infection

Administration: *Adult:* 1 g, to be administered as soon as possible and not later than 10 days after exposure; second dose to be given if further exposure occurs more than 3 weeks after first dose

Children:
Neonate-5 years: 250mg;
6-10 years: 500mg
11-14 years: 750mg to be administered as soon as possible; second dose to be given if further exposure occurs more than 3 weeks after first dose.

Side effects: Hypotension, tachycardia, hypersensitivity, skin reactions

Caution: Pregnancy (See notes above), IgA deficiency, Interference with live virus vaccines

Note. No evidence that it is effective in the treatment of severe disease. An *intravenous preparation* of normal immunoglobulin (see Intravenous Therapy,) may be used to provide an immediate source of antibody.

ANTI-D (RHo) IMMUNOGLOBULIN TET/VAC/ ADS

Anti-D (Rh_o) immunoglobulin is available to prevent a rhesus-negative mother from forming antibodies to foetal rhesus-positive cells which may pass into the maternal circulation. The objective is to protect any subsequent child from the hazard of haemolytic disease of the newborn. Anti-D immunoglobulin should be administered following any sensitising episode (e.g. abortion, miscarriage and birth); it should be injected within 72 hours of the episode but even if a longer period has elapsed it may still give protection and should be administered. The dose of anti-D immunoglobulin is determined according to the level of exposure to rhesus-positive blood.

Note. Rubella vaccine may be administered in the postpartum period simultaneously with anti-D (Rho) immunoglobulin injection providing separate syringes are used and the products are administered into contralateral limbs If blood is transfused, the antibody response to the vaccine may be inhibited and test for antibodies should be formed after 8 weeks and the subject revaccinated if necessary.

MMR vaccine should not be given within 3 months of an injection of anti-D (Rho) immunoglobulin injection.

Indications: See notes above and under Administration.

Administration: ***Prevention of Rh_0(D) sensitization to a rhesus-negative woman (with a negative coombs test);***

Following abortion or birth of the rhesus-positive infant: 500 units immediately or within 72 hours by deep IM injection;

For transplacental bleeding of over 4-5ml foetal red cells: extra 100-125 units per ml foetal red cells.

Following any potentially sensitising episode (e.g. stillbirth, amniocentesis) up to 20 weeks' gestation: 250 units per episode (after 20 weeks, 500 units) immediately or within 72 hours.

Following RH_0(D) incompatible blood transfusion: 125 units per ml of transfused rhesus-positive red cells

Antenatal prophylaxis: 500 units may be given at weeks 28 and 34 of pregnancy, a further dose is still needed immediately or within 72 hours of delivery **OR** 1500 IU may be given at 28 weeks and an additional 1500 IU immediately after delivery or within 72 hours post-partum.

Side effects: Chills, fever, headache, malaise, skin reactions.

Contraindications: Rhesus-negative woman with a positive coombs test.

Cautions: Immunoglobulin A deficiency, possible interference with live virus vaccines

INTERFERON GAMMA-1B (Immune interferon)

Indications: An adjunct to antibiotics to reduce the frequency of serious infection in patients with chronic granulomatous disease.

Administration: By subcutaneous injection, 50 mcg/m^2, 3 times a week;

Patients with body surface area of 0.5m^2 or less, 1.5 mcg/kg 3 times a week

Side effects: Fever, headache, chills, myalgia, fatigue; nausea, vomiting, arthralgia, rashes and injection-site reactions reported.

Contraindications: Children under 6 months.

Caution: Severe hepatic or renal impairment; seizure disorders or compromised central nervous system function; pre-existing cardiac disease (including ischaemia, congestive heart failure, and arrhythmias); monitor before and during treatment: haematological tests (including full blood count, differential white cell count, and platelet count), blood chemistry tests (including renal and liver function tests) and urinalysis

DRIVING: May impair the ability to drive or operate machinery; effects may be enhanced by alcohol.

16.6 International Travel

No particular immunisation is required for travellers to the United States, Europe, Australia, or New Zealand although all travellers should have immunity to tetanus and poliomyelitis (and childhood immunisations should be up to date). In Non-European areas surrounding the Mediterranean, in Africa, the Middle East, Asia, and South America, certain special pre-caution are required.

Long term travellers to areas that have a high incidence of **poliomyelitis** or **tuberculosis** should be immunised with the appropriate vaccine; in the case of poliomyelitis previously immunised, adults may be given a booster dose of oral poliomyelitis vaccine. BCG immunisation is recommended for travellers proposing to stay for longer than one month (or in close contact with the local population) in Asia, Africa, or Central and South America; it should preferably be given three months or more before departure.

Yellow Fever immunisation is recommended for travel to specific African and South American countries. Many countries require an International Certificate of Vaccination from individuals arriving from, or who have been travelling through endemic areas, whilst other countries require a certificate from all entering travellers.

Immunisation against **meningococcal meningitis** is recommended for several areas of the world. (for details see 16.4).

Protection against **hepatitis A** is recommended for travellers to high-risk areas. Hepatitis A vaccine (see 16.4.) is preferred particularly for frequent travellers or for stays longer than 3 months. Normal immunoglobulin can be used in as an alternative for short or infrequent travel. Those who require immunisation less than 10 days before departure may be given the single-dose vaccine plus normal immunoglobulin at a different injection site. Administration of normal immunoglobulin at the same time as the vaccine, at different injection sites, does not affect the rate of seroconversion but the level of antibody may be reduced (see also 16.5.1.)

Hepatitis B vaccine is recommended for those travelling to areas of high prevalence who intend to seek employment as health care workers or who plan to remain there for lengthy periods and who may therefore be at increased risk of acquiring infection as a result of medical or dental procedures carried out in

those countries. Short term tourists or business travellers are not generally at increased risk of infection but may place themselves at risk by their sexual behaviour when abroad.

Prophylactic immunisation against **rabies** is recommended for travellers to enzootic areas on long journeys to remote areas out of reach of immediate medical attention.

Typhoid vaccine is indicated for travellers to those countries where typhoid is endemic but the vaccine is no substitute for personal precaution. Food should be freshly prepared and hot, and uncooked vegetables (including green salads) should be avoided. Only fruits which can be peeled should be eaten. Only suitable bottled water or tap water that has been boiled or treated with sterilising tablets should be used for drinking. This advice applies to cholera and other diarrhoeal diseases (including traveller's diarrhoeal).

Cholera vaccine has little value in preventing infections and should not be given for international travel.

17 General Treatment of Poisoning

Some commonest poisons in Zambia are organophosphates, drug injection (e.g. co-trimoxazole, paracetamol, etc.), alcohol, carbon monoxide. All cases of poisoning or suspected poisoning must be admitted to a Health facility. Most cases of poisoning do not require specific antidotes or active removal of the poison. Most patients must be treated symptomatically.

Only a few poisons like opioids, paracetamol and iron require specific antidotes.

Corrosive Substances

Do not induce vomiting in case of ingestion of corrosive substances (like acid, petroleum products or gastric lavage).

17.1 Specific Antidotes

NALOXONE

Presentation: Injection containing 400mcg/ml naloxone hydrochloride

Indications: Overdose with opioids

Administration: *IV injection*: 0.8 – 2mg repeated at intervals of 2 – 3 minutes to a maximum of 10mg if the respiratory function does not improve (then question diagnosis).

Subcutaneous or i.m injection; as for IV injection. Use only: if IV route is not feasible (onset of action slower)

Continuous IV infusion: 2mg diluted in 500ml IV infusion i.e. normal saline and/or 5% dextrose solution at a rate adjusted according to the response.

Children:
10mcg/kg, subsequent dose of 100 mcg/kg if no response.

PRALIDOXIME

Presentation: Injection containing 200mg/ml Pralidoxime Mesylate

Indications: Organophosphate poisoning.

Administration: *Intramuscular injection;* 1g initially followed by 1 – 2 further doses if necessary. In very severe poisoning the initial dose can be doubled, usual maximum 12g in 24 hours.

Slow intravenous injection (diluted to 10 – 15 ml with water for injection and given over 5 – 10 minutes). In very severe poisoning initial dose can be doubled. Maximum 12g in 24 hours.

Children:
20 – 60 mg/kg as required depending on the severity of poisoning and response.
Only effective if given within 24 hours.

ATROPINE

Presentation: Injection containing 1 mg (as sulphate) in 1-ml ampoule

Indications: Treatment of cholinergic effects associated with organophosphate or carbamate poisoning

Administration*: Adult*

By IM or IV injection *(depending on severity of poisoning):*

Initial dose of 1–2 mg for mild poisoning, and up to 6 mg for severe poisoning, every 5–10 minutes until the secretions are minimal, ventilation is adequate, skin becomes flushed and dry, pupils dilate, and tachycardia develops.

Treatment should be repeated if muscarinic symptoms reappear.

In moderate to severely poisoned adults, atropine is given for at least 2 days. In severe cases, atropine therapy should be withdrawn gradually to avoid abrupt recurrence of symptoms (e.g., pulmonary oedema).

Children:
By IM or *IV injection*
Infant or child: 20 mcg/kg (maximum dose 2 mg) every 5–10 minutes (depending on the severity of poisoning) until the skin becomes flushed and dry, pupils dilate, and tachycardia develops; dose may be repeated every 1–4 hours for at least 24 hours to maintain atropine effect.

Side effects: Dry mouth, blurred vision, photophobia, flushing and dryness of skin, rash, difficulty in micturition, constipation, arrhythmias, tachycardia, palpitations, fever, Nausea, vomiting, confusion, closed-angle glaucoma, seizures.

Contraindications: Primary glaucoma or predisposition to narrow anterior chamber angle glaucoma, known hypersensitivity to atropine or other anticholinergic agents.

Caution: Patients with obstructive disease of the GIT, cardio spasm, paralytic ileus or intestinal atony, reflux esophagitis, severe ulcerative colitis or megacolon complicating ulcerative colitis, prostatic enlargement, unstable cardiovascular status in acute hemorrhage, toxemia of pregnancy, myasthenia gravis. Atropine should not be given to febrile patients, or when the ambient temperature is high.

ACETYLCYSTEINE

Presentation: Injection containing 200mg/ml of Acetylcysteine in ampoules of 10 ml

Indications: Paracetamol overdose.

Administration: *Intravenous infusion:* initially 150mg/kg in 200 ml over 15 minutes, followed by 50mg/kg in 500ml over 4 hours, then 100mg/kg in 1000ml over 16 hours.

Side effects: Rashes, anaphylaxis, nausea and vomiting, bronchospasms.

Caution: Asthma, in elderly patients with severe respiratory insufficiency.

METHIONINE

Presentation: Tablets containing 250mg Methionine

Indications: Paracetamol overdose.

Administration: *Adult*; 2.5g initially, followed by three further doses of 2.5g every 4 hours.

Children:
1g every 4 hours for 4 doses

Side effects: Nausea, vomiting, drowsiness and irritability

Caution: May precipitate hepatic encephalopathy in patients with established liver disease.

FOMEPIZOLE

Presentation: Injection containing 5 mg/ml (as sulphate) in 20-ml ampoule.

Indications: Methanol and Ethylene glycol poisoning.

Administration: ***Adult:*** Loading dose of 15 mg/kg followed by 10 mg/kg every 12 hours for 4 doses; the dose should then be increased to 15 mg/kg every 12 hours until serum concentrations of ethylene glycol or methyl alcohol are <20 mg per 100 ml.

All doses should be given by IV infusion over 30 minutes in at least 100 ml of sodium chloride 0.9% or glucose 5%.

In patients who also require haemodialysis, give every 4 hours during haemodialysis sessions.

Children:
Consult product literature

Adverse effects: Headache, nausea, dizziness, drowsiness, and taste disturbances, abdominal or back pain, fever, rash and other hypersensitivity reactions, GI disturbances,

hypotension, tachycardia or bradycardia, shock, anuria, multi-organ system failure, disseminated intravascular coagulation, anaemia, lymphangitis, pharyngitis, and hiccups, seizures, lightheadedness, agitation, anxiety, vertigo, fushing, nystagmus, abnormal smell, and speech or visual disturbances, injection site reactions, Transient increases in hepatic enzyme values and eosinophilia.

FLUMAZENIL

Presentation: Injection containing 100mcg/ml (5-ml amp) Flumazenil.

Indications: Reversal of sedative effects of benzodiazepines in anaesthesia, clinical procedures, intensive care;

Administration: ***Adult****:*

Reversal of sedative effects of benzodiazepines in anaesthesia and clinical procedures, by IV injection: 200 mcg, dose to be administered over 15 seconds, then 100 mcg every 1 minute if required; usual dose 300–600 mcg, maximum 1 mg per course *Reversal of sedative efects of benzodiazepines in intensive care,* by IV injection: 300 mcg, dose to be administered over 15 seconds, then 100mcg every 1 minute if required, maximum 2 mg per course.

Reversal of sedative effects of benzodiazepines in intensive care (if drowsiness recurs after injection): Initially by IV infusion, 100–400 mcg/hour, adjusted according to response; alternatively, by IV injection 300 mcg, adjusted according to response.

Children:

Reversal of sedative effects of benzodiazepines, by IV injection

Neonate: 10 mcg/kg every 1 minute, dose to be administered over 15 seconds

Child: 10 mcg/kg every 1 minute (max. per dose 200 mcg); dose to be administered over 15 seconds, maximum 1 mg per course, maximum 50mcg/kg per course.

Reversal of sedative effects of benzodiazepines (ifdrowsiness recurs after injection), by IV infusion

Neonate: 2–10 mcg/kg/hour, adjusted according to response.

Child: 2–10 mcg/kg/hour (max. per dose 400 mcg/hour), adjusted according to response

Reversal of sedative efects of benzodiazepines in intensive care, by IV injection

Child: 10 mcg/kg every 1 minute (max. per dose 200 mcg), dose to be administered over 15 seconds, maximum 2 mg per course, maximum 50mcg/kg per course

Side effects: Anxiety, diplopia, dry mouth, eye disorders, fushing, headache, hiccups, hyperhidrosis, hyperventilation, hypotension, insomnia, nausea, palpitations, paraesthesia, speech disorder, tremor, vertigo, vomiting, abnormal hearing, arrhythmias, chest pain, chills, cough, dyspnoea, nasal congestion, seizure (more common in patients with epilepsy), withdrawal syndrome. **Note:** For continuous IV infusion, dilute with glucose 5% or sodium chloride 0.9%

Caution:

- Flumazenil should only be administered by, or under the direct supervision of, personnel experienced in its use.
- Avoid rapid injection following major surgery and in high-risk or anxious patients.
- Benzodiazepine dependence may precipitate withdrawal symptoms.
- Children - ensure neuromuscular blockade cleared before giving.
- Head injury - rapid reversal of benzodiazepine sedation may cause convulsions.
- History of panic disorders - risk of recurrence.
- Prolonged benzodiazepine therapy for epilepsy - risk of convulsions.
- Short-acting - repeat doses may be necessary.

Benzodiazepine effects may persist for at least 24hrs

DEFERASIROX

Presentation: Tablets containing 100mg and 400mg of Deferasirox.

Indication: Chronic iron overload caused by blood transfusion and/or iron prepartions.

Administration: *Oral:*

Transfusion-related chronic iron overload when desferrioxamine is contraindicated or inadequate in patients with beta thalassaemia major who receive infrequent blood transfusions:

Initially 7–21 mg/kg once daily, dose adjusted according to serum-ferritin concentration and amount of transfused blood, then adjusted in steps of 3.5–7 mg/kg every 3–6 months; maintenance dose adjusted according to serum-ferritin concentration, maximum 28 mg/kg per day, usual maximum 21 mg/kg.

Transfusion-related chronic iron overload when desferrioxamine is contraindicated or inadequate in patients with other anaemias:

Initially 7–21 mg/kg once daily, dose adjusted according to serum-ferritin concentration and amount of transfused blood, then adjusted in steps of 3.5–7 mg/kg every 3–6 months, maintenance dose adjusted according to serum-ferritin concentration, maximum 28 mg/kg per day, usual maximum 21mg/kg.

Chronic iron overload when desferrioxamine is contraindicated or inadequate in non-transfusion dependent thalassaemia syndromes:

Initially 7mg/kg once daily, then adjusted in steps of 3.5–7 mg/kg every 3–6 months, maintenance dose adjusted according to serum-ferritin concentration and liver-iron concentration; maximum 14 mg/kg per day.

Children: ***oral:***

Transfusion-related chronic iron overload when desferrioxamine is contraindicated or inadequate inpatients with beta thalassaemia major who receive frequent blood transfusions (7 ml/kg/month or more of packed red blood cells)

2–5 years: Initially 7–21 mg/kg once daily, dose adjusted according to serum-ferritin concentration and amount of transfused blood, then adjusted in steps of 3.5–7 mg/kg every 3–6 months; maintenance dose adjusted according to serum-ferritin concentration; maximum 28 mg/kg per day, usual maximum 21 mg/kg.

Transfusion-related chronic iron overload in patients with beta thalassaemia major who receive frequent blood transfusions (7 ml/kg/month or more of packed red blood cells)

6–17 years: Initially 7–21 mg/kg once daily, dose adjusted according to serum-ferritin concentration and amount of transfused blood, then adjusted in steps of 3.5–7 mg/kg every 3–6 months; maintenance dose adjusted according to serum-ferritin concentration; maximum 28 mg/kg per day, usual maximum 21 mg/kg.

Transfusion-related chronic iron overload when desferrioxamine is contraindicated or inadequate in patients with other anaemias

2–17 years: Initially 7–21 mg/kg once daily, dose adjusted according to serum-ferritin concentration and amount of transfused blood, then adjusted in steps of 3.5–7 mg/kg every 3–6 months, maintenance dose adjusted according to serum-ferritin concentration, maximum 28 mg/kg per day, usual maximum 21 mg/kg.

Chronic iron overload when desferrioxamine is contraindicated or inadequate in non-transfusion dependent thalassaemia syndromes

10–17 years: Initially 7 mg/kg once daily, maintenance dose adjusted according to serumferritin concentration and liver-iron concentration; maximum 7 mg/kg per day.

Side effects: Constipation, diarrhoea, GI discomfort,headache, nausea, skin reactions, urine abnormalities, vomiting, anxiety, cataract, cholelithiasis, dizziness, fatigue, fever, GI haemorrhage (including fatal cases), hearing impairment, hepatic disorders,laryngeal pain, maculopathy, oedema, renal tubular disorders, sleep disorder, optic neuritis, SCARs, acute

kidney injury, alopecia, anaemia aggravated, hyper-ammonaemic encephalopathy, hypersensitivity vasculitis, lens opacity, leucopenia, metabolic acidosis, nephrolithiasis, neutropenia, pancreatitis acute, pancytopenia, thrombocytopenia.

Contraindications: None

Cautions: Avoid in pregnancy and breastfeeding

DEFEROXAMINE (DESFERRIOXAMINE)

Presentation: Powder for injection containing 500 mg (as mesilate) in a vial.

Indications: Acute iron poisoning, Chronic iron overload, Aluminium overload in end-stage renal failure, and Diagnosis of aluminium and iron overload.

Administration: ***Adult***

Acute iron poisoning**,** by slow IV infusion:

Initially 15 mg/kg/hour, reduced after 4–6 hours so that total dose does not exceed 80 mg/kg in 24 hours.

Chronic iron overload**,** by SC or IV infusion:

Lowest efective dose (usually within range of 20–60 mg/kg/day) 4–7 days a week.

Aluminium overload in end-stage renal failure, by IV infusion: 5 mg/kg, once a week during last hour of dialysis;

Diagnosis of iron overload, by IM injection: 500 mg

Diagnosis of aluminium overload, by IV infusion:

5 mg/kg during last hour of dialysis.

Children:

The preferred route of administration is IV.***Acute iron poisoning***, slow IV infusion

Neonate, infant, or child: Initially 15 mg/kg/hour, reduced after 4–6 hours so that total dose does not exceed 80 mg/kg in 24 hours; maximum dose 6 g/day. By IM: 50 mg/kg/dose every 6 hours; maximum dose 6 g/day.

Note: More than 24 hours of therapy are required for acute iron overdose. Therapeutic endpoints to cease infusion are poorly defned but may be indicated by clinically stable patient and serum iron< 60 micromol/L.

Chronic iron overload, SC or IV infusion:

Infant or child: Initially up to 30 mg/kg over 8–12 hours, on 3–7 days per week; for established iron overload, the dose is usually between 20 and 50 mg/kg daily; the dose should reflect the degree of iron overload; use the lowest efective dose.

Diagnosis of iron overload, by IM: 500 mg

Side effects: Injection site reactions including redness, pain, swelling, rashes and itch, hypotension (especially when given too rapidly by IV injection), fever, arthralgia, myalgia, rash, anaphylactoid reactions, Renal failure, non-cardiogenic pulmonary oedema, disturbances of hearing and vision (including lens opacity and retinopathy), Anaphylaxis, acute respiratory distress syndrome, neurological disturbances Chronic use - Growth retardation, bone deformities (both with high doses), Neurosensory deafness, Bone marrow depression, ocular toxicity, mucormycosis and other unusual infections.

Cautions: Renal impairment, eye and ear examinations before and at 3-month intervals during treatment are necessary to assess toxicity, aluminium encephalopathy (may exacerbate neurological dysfunction), for all children monitor body weight and height at 3-month intervals (risk of growth restriction with excessive doses). Hepatic impairment: No dosage adjustment necessary. Renal impairment: Metal complexes excreted by kidneys (in severe renal impairment dialysis increases rate of elimination).

ETHANOL

Presentation: Injection containing 100% Ethanol in 10-ml amp; Oral liquid (medicinal) containing 95–98% Ethanol in 1 ml, 5 ml.

Indications: Toxicity due to ingestion of Methanol or ethylene glycol.

Administration: ***Adult***

IV: Initial 600 to 700 mg/kg (7.6–8.9 ml/kg) using a 10% solution; goal is to maintain serum ethanol levels above 100 mg/dL

Oral: Initial 600 to 700 mg/kg (7.6–8.9 ml/kg) using a 98% solution.

Notes for oral: Dilute solution to ≤20% to reduce risk of gastritis; must be administered precisely at 60-minute intervals.

Dose adjustment for hemodialysis

» IV: 169 mg/kg/hour equivalent to 2.13 ml/kg/hour using a 10% solution

» Oral: 169 mg/kg/hour equivalent to 0.22 ml/kg/hour using a 98% solution.

Children:
Reduce ethanol loading dose if methanol or ethylene-glycol ingested with alcohol; may need to increase ethanol maintenance dose in patients with chronic alcohol consumption
Loading dose: (oral) 95% EtOH: 0.8–1 ml/kg
40% EtOH (80 proof undiluted liquor): 2 ml/kg
43% EtOH (86 proof undiluted liquor): 1.8 ml/kg
Maintenance dose (oral):
43% EtOH: 0.1 ml/kg/hour
95% EtOH: 0.1 ml/kg/hour
IV dose (10% EtOH)
10% EtOH = 7.9 g/dL
Loading: 8–10 ml/kg IV, not to exceed 200 ml
Maintenance: 0.83 ml/kg/hour IV
10% EtOH = 7.9 g/dL
40% EtOH (80 proof undiluted liquor) = 31.6 g/dL
43% EtOH (86% proof undiluted liquor) = 34 g/dL
95% EtOH (absolute alcohol) = 75 g/dL
Continue maintenance dose until methanol or ethylene glycol levels are below 10 mg/dL.

Side effects: Adverse efects: Intoxication, low blood pressure (hypotension) with fushing, agitation, low blood sugar (hypoglycemia), nausea, vomiting, excessive urination.

Contraindications: Hypersensitivity, seizure disorder, diabetic coma, subarachnoid injection of dehydrated alcohol in patients receiving anticoagulants. **Cautions:** Caution in diabetes mellitus, gout patients, hepatic impairment, shock pregnancy and breastfeeding.

LIPID EMULSION

IV lipid emulsion therapy (also known as lipid resuscitation therapy) is the current recommended treatment for local anesthetic systemic toxicity It is also recommended as an adjunct to advanced cardiac life support measures in suspected LAST induced cardiac arrest. It may be used for many other acute toxicities and poisonings. Drug classes that have been investigated include; tricyclic antidepressants, CCBs, beta-blockers, antipsychotics, insecticides, and organophosphates. Specifc drugs also studied include bupropion, lamotrigine, cocaine, and diphenhydramine.

Presentations: Injection containing 20% in 200 ml to 500 ml measure.

Indications: Treatment for local anesthetic systemic toxicity, an adjunct to advanced cardiac life support measures in suspected LAST induced cardiac arrest, other acute toxicities and poisonings.

Administration: ***Adult:***

Patients under 70 kg: Rapid 1.5 ml/kg (of lean body weight) bolus of 20% lipid emulsion followed by a 0.25 ml/kg/min infusion.

Note: The same bolus dose is repeatable, along with doubling the infusion rate if cardiovascular instability continues. The recommended dosing limit is approximately 12 ml/kg.

Children:
Consult product literature

Side effects: Cholestasis, increase in blood bilirubin, cytolytic hepatitis, cholecystitis, abnormalities in liver function tests, increase in pancreatic enzymes

Contraindications: Severe disorders of fat metabolism such as in severe liver damage and acute shock.

Cautions: Fat overload syndrome may occur, usually reversible upon discontinuation.

PHYTOMENADIONE (VITAMIN K1, PHYTONADIONE)

Presentations: Injection containing 10 mg/ml in 1ml amp; and tablet containing 10mg Vitamin K.

Indications: Antagonist to warfarin, warfarin-induced hypoprothrombinaemia, Moderate and severe haemorrhage.

Administration: ***Adult***

Antagonist to warfarin, warfarin-induced hypoprothrombinaemia, no bleeding or minor bleeding, by slow IV injection: 500 mcg; oral, up to 5 mg.

Moderate haemorrhage, oral or by IM injection: 10–20 mg.

Severe haemorrhage, by slow IV injection: 5–10 mg.

Children:
Reversal of coumarin anticoagulation when continued anticoagulation required or if no significant bleeding: by IV injection

15–30 mcg/kg (max. per dose 1 mg) for 1 dose, repeat as necessary

Reversal of coumarin anticoagulation when anticoagulation not required or if significant bleeding by IV injection

250–300 mcg/kg (max. per dose 10 mg) for 1 dose

Side effects: Hypersensitivity reactions including fushing, dyspnoea, bronchospasm, dizziness, hypotension and respiratory or circulatory collapse which may be due to polyethoxylated castor oil surfactant in some injection formulations, rather than due to phytomenadione.

Cautions: IV injections should be given very slowly (risk of vascular collapse). Hepatic impairment: Higher doses may be required for adequate response. Renal impairment: Dose reduction not necessary.

PROTAMINE

Presentations: Injection containing 10 mg/ml (as a sulphate) in 5-ml amp.

Indications: Heparin overdose

Administration: ***Adult***

Heparin overdose, by IV injection over approximately 10 minutes: 1 mg neutralizes 80–100 IU heparin sodium when given within 15 minutes; if more time has elapsed, less protamine is needed as heparin is rapidly excreted.

Children:
Heparin overdose *by IV injection or IV infusion*

1 month–12 years: 1 mg of protamine neutralizes approximately 100 units of heparin if <30 minutes has elapsed since overdose, 500–750 mcg if 30–60 minutes has elapsed, 375–500 mcg if 60–120 minutes has elapsed, 250–375 mcg if over 120 minutes has elapsed; maximum dose 50 mg; do not exceed a rate of 5 mg/min.

By SC injection

1 month–12 years: 1 mg neutralizes approximately 100 units of heparin; give 50–100%
of the total dose by IV injection (rate not exceeding
5 mg/min), then give any remainder of the dose by IV infusion over 8–16 hours; maximum total dose 50 mg

Side effects: Nausea, vomiting, lassitude, fushing, hypotension/hypertension, Bradycardia, dyspnoea, allergic reactions (including angioedema, anaphylaxis), cardiovascular collapse, pulmonary vasoconstriction/hypertension.

Cautions: If used in excess, protamine has an anticoagulant efect, allergic reactions increased in persons at risk including previous

treatment with protamine or protamine insulin, fish allergies, rapid administration or high dose. Hepatic and renal impairment: Dose reduction not necessary.

Notes:

- 1 mg neutralizes approximately 100 units of unfractionated heparin when given within 15 minutes, if longer time, less protamine is needed as heparin is rapidly excreted.
- Activated partial thromboplastin time (APTT) or other appropriate blood clotting parameters should be monitored.
- Not to be administered at a rate exceeding 5 mg/min.
- May be diluted, if necessary, with sodium chloride 0.9

SODIUM NITRITE

Presentation: Injection containing 30 mg/ml in 10-ml amp.

Indications: Poisoning with cyanides (used in conjunction with sodium thiosulphate below).

Administration: ***Adult***

Poisoning with cyanides (used in conjunction with sodium thiosulphate, see below): The usual dosage regimen is 300 mg of sodium nitrite (10 ml of a 3% solution) given intravenously over 2 to 20 minutes followed by 12.5 g of sodium thiosulphate (50 ml of a 25% solution or 25 ml of a 50% solution) given intravenously over 10 minutes. The methaemoglobin concentration should not be allowed to exceed 30 to 40%.

Children:

Poisoning with cyanides (used in conjunction with sodium thiosulphate)

1 month to 18 years: 4 to 10 mg/kg to a maximum of 300 mg (0.13 to 0.33 ml/kg of a 3% solution; maximum 10 ml) by IV injection over 5 to 20 minutes, followed by sodium thiosulphate 400 mg/kg to a maximum of 12.5 g (as a 25 or 50% solution) by IV injection over 10 minutes.

Side effects: Sodium nitrite may cause nausea and vomiting, abdominal pain, dizziness, headache, cyanosis, tachypnoea, and dyspnoea. Blurred vision, confusion, anxiety, diaphoresis, fatigue, and generalised numbness or tingling have also been reported. Vasodilatation has resulted in syncope, hypotension, and tachycardia, arrhythmias, cardiovascular collapse, coma, convulsions, and death have occurred in overdose. treatment of hydrogen sulfde poisoning.

Contraindication: Hypotension, kidney impairment.

Cautions: Blood pressure monitoring (can cause hypotension), Carcinogenicity (it is a precursor for the formation of N-nitroso compounds such as nitrosamines); severe methaemoglobinaemia has been reported; excreted by the kidneys and care is needed.

SODIUM THIOSULPHATE

Presentation: Injection containing 250 mg/ml in a 50-ml amp.

Indications: Cyanide poisoning

Administration*:* ***Adult:*** 300 mg of sodium nitrite (10 ml of a 3% solution, see above) given intravenously over 2 to 20 minutes followed by 12.5 g of sodium thiosulphate (50ml of a 25% solution or 25 ml of a 50% solution) given intravenously over 10 minutes; if symptoms of cyanide toxicity recur, it has been suggested that the injections of nitrite and thiosulphate may be repeated after 30 minutes at half the initial doses.

Children:

1 month to 18 years: Sodium nitrite 4 to 10 mg/kg to a maximum of 300 mg (0.13 to 0.33 ml/kg of a 3% solution, maximum 10 ml, as stated above) by IV injection over 5 to 20 minutes, followed by sodium thiosulphate 400 mg/kg to a maximum of 12.5 g (as a 25 or 50% solution) by IV injection over 10 minutes.

Side effects: The toxicity of sodium thiosulphate is low. Hypematraemia, hypotension, nausea and vomiting, diarrhoea,

diuresis, and metabolic acidosis have been reported and are thought to be due to both the intrinsic osmotic properties of sodium thiosulphate, and from thiocyanate which is formed when sodium thiosulphate is used to treat cyanide poisoning. A salty taste in the mouth and a warm sensation over the body have also been reported.

Contraindication: Hypertension, oedema, congestive heart failure, hepatic and renal impairments.

Caution: An increased clotting time has occurred l to 3 days after use of sodium thiosulphate. Sodium thiosulphate may exacerbate hypertension or oedema and should be used with caution in patients who may have these symptoms such as those with congestive heart failure, liver cirrhosis, renal impairment, and toxaemia of pregnancy.

17.2 Non-Specific Antidotes

ACTIVATED CHARCOAL

Presentation: Powder for oral liquid containing 50g Actavated Charcoal.

Indications: Poisoning: Adsorbs a variety of drugs and chemicals (e.g., physical binding of a molecule to the surface of charcoal particles); desorption of bound particles may occur unless the ratio of charcoal to toxin is extremely high.

Administration: ***Adult****:* Oral 50 to 100 g as a single dose, as soon as possible after ingestion of poison, but it may still be effective up to 1 hour after ingestion of the poison or longer in the case of modifed release (m/r) preparations or drugs with antimuscarinic (anticholinergic) properties; repeated doses are given after overdosage with carbamazepine, dapsone, phenobarbital, quinine, theophylline.

Children:
Neonate, infant, or child: 1g/kg (maximum 50 g) as a single dose as soon as possible after ingestion of poison

Active elimination of poisons, oral

Neonate, infant, or child: 1 g/kg (maximum 50 g) every 4 hours.

Side effects: Black stools, colicky abdominal pain, nausea, vomiting, constipation or diarrhoea, Bowel obstruction, aspiration, pneumonitis.

Contraindications: Poisoning by hydrocarbons with high potential for harm if aspirated, poisoning by corrosive substances (may prevent visualization of lesions caused by poison), alcohols, malathion, cyanides, metal salts including iron and lithium salts. unprotected airway, GI tract (GIT) not intact, bowel obstruction.

Cautions: Drowsy or unconscious child (risk of aspiration (intubate before administration via nasogastric or gastric tube), not efective for poisoning with alcohols, clofenotane (dicophane, dichlorodiphenyltrichloroethane [DDT]), cyanides, malathion, and metal salts including iron and lithium. No dose adjustment necessary in renal and hepatic impairments.

Interactions with other medicines: Acetylcysteine, acetylcysteine (antidote), citalopram, digoxin, methotrexate, theophylline, acarbose, lefunomide, miglitol.

TABLE 1: INFANT/CHILD IMMUNISATION TABLE

<table>
<tr><td colspan="10">Age</td><td>Vaccines Birth</td></tr>
<tr><td>1
mo</td><td>2
mos.</td><td>4
mos.</td><td>6
mos.</td><td>12
mos.</td><td>15
mos.</td><td>18
mos.</td><td>4-6
year</td><td>11-12
year</td><td>14-16
year</td><td rowspan="6">Hepatitis B+
Diphtheria , Tetanus toxoids & Pertussis vaccine 1
Haemophilus influenzae type b **
Poliovirus ++
Measles, mumps, rubella $$
Measles alone
Varicella zoster virus</td></tr>
<tr><td colspan="4">Hep B-1 (EPI)</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td colspan="4">Hep B-2</td><td colspan="3">Hep B-3</td><td colspan="2">Hep B S</td><td></td></tr>
<tr><td></td><td>DTP
Hib
OPV</td><td>DTP
(EPI)
Hib
OPV
(EP I)</td><td>DTP
Hib
OPV</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td colspan="5">DTP (DtaP at >/ = mos</td><td colspan="3">Td</td></tr>
<tr><td colspan="5">OPV
MMR
Measles at 9 mos!
(EPI)
Varicell!a!</td><td></td><td>DTP or
DtaP
OPV
MM R</td><td>Or
MMR!
Varicel-la***</td><td></td></tr>
</table>

Key to table 1

+ If mother HBsAg neg.' recommended 1st dose is 2.5ug of Recombivax HB (Smith Kline Beecham).

If mother HBsAg pos.' give infant 0.5ml HBIG within 12 hours of birth and either 5ug of Recombivax HB or 10ug Engerix-B at a separate site.

1 Acellular pertussis vaccine licensed for 4th and 5th dose for children aged >15 months.

** 3 licensed H. influenza protein conjugate vaccines. A 4th, available in 1997, combines Haemophilus B with Hepatitis B.

++ Inactivated polio vaccine acceptable alternative for patients with congenital or acquired immunodeficiency.

$$ Second dose anytime > 1 month after 1st dose.

11 Anytime after age 12 months. If no reliable history of chickenpox, vaccinate at age 1112 years.

Table 2

ADULT IMMUNISATION TABLE							
AGE GROUP	**(Years)**	**VACCINE/TOXOID**					
	Td 2	Measles	Mumps	Rubella	Influenza	Pneumococcal	Hepatitis B 4
– 24		x	x	x			Individuals at high risk regardless of age.
– 64	x	x3	x				See table for post-exposure
>/=65	x				x	x	Prophylaxis

Key to table 2

- From Guide for Adult Immunization, 3rd ED., Am Coll Physicians, 1994 See AnIM 12:35, 1996, and IDCP 5:490, 1996.
- Td = tetanus + diphtheria toxoids, adsorbed for adult use (contains 5fl units tetanus +
- 2fl units diphtheria vs childhood vaccine, which contains 5fl units tetanus + 12.5 Fl u diphtheria).
- Indicated for persons born in 1957 or later. Serotest and immunize especially during outbreaks.
- Screen all pregnant women for HBsAg (give HBIG and vaccine to infants born to
- HBsAg –positive mothers). Those at h exposure, other sexually transmitted diseases, household and sexual contacts or HBV carriers, health care and public safety workers with exposure to blood, residents and staff or institutions for retarded, haemodialysis patients, recipients of Factor VII or IX concentrates, morticians.

ADMINISTRATION SCHEDULE FOR ABOVE PLUS, OTHER SELECTED VACCINES ($)

Hepatitis A (Havrix, Vagta): 1.0ml IM and repeat in 6 – 12 months. Antibodies detectable after 15 days; use immune serum globulin. 0.02ml/kg IM for immediate protection. Indication: for travellers to endemic areas.

(*Med. Letter 37:51, 1995; IDCP 5:122, 1996)*

Hepatitis B (Engerix B, Recombivax HB): 3 doses; initial, 1 month later, 6 months after 1st. Give IM in the deltoid (not in buttocks), use 1 ½ inch needle; give SC only in patients at risk of bleeding (haemophiliacs). (Seroprotection associated with titers – 10mIU/ml.)

Influenza (killed virus): One dose (0.5ml) IM. Annual reimmunization with current vaccine recommended.

Measles (Attenuvax) (live virus vaccine): Unless contraindicated. $ one dose (0.5ml) sc preferably in outer aspect upper arm. Booster not required.

Measles + Rubella + Mumps (MMR) (live virus): Unless contraindicated $ (do not give to pregnant women), one dose (0.5ml) sc as with measles. Booster not required.

Pneumococcal (Pneumovax 23, Pnu-Immune 23) (pure antigens, 23): One dose (0.5ml) sc. Booster not required except possible individuals at high risk (nephrotic syndromes, renal failure, transplant recipients, splenectomy patients, HIV positive who received vaccine > 6 years before).

Td (toxoids, not live): Primary: Two doses IM at least 4 weeks apart, 3rd dose 6 – 12 months after 2nd. Booster: every 10 years.

Typhoid (Typhim Vi): A single IM dose of 25mcg yields 95% seroconversation.

Minimal side effects.

For travellers and lab. Workers.

Varicella (Varivax): 0.5ml sc. Repeat 4 – 8 weeks later. For susceptible adolescents/ adults who are:

(1) health care workers

(2) susceptible household contact immunocompromised persons,

(3) work in schools/day care centres,

(4) College students/military,

(5) non-pregnant women of child bearing age.

$ Review package insert for specific product being administered.

ANTI-TETANUS PROPHYLAXIS, WOUND CLASSIFICATION, IMMUNISATION

Table 3

<table>
<tr><th colspan="3">WOUND CLASSIFICATION</th><th colspan="4">IMMUNISATION SCHEDULES</th></tr>
<tr><th>Non-Tetanus Prone</th><th>History of Tetanus Immunisation</th><th colspan="2">Tetanus –Prone Wound</th><th colspan="2">Non-Tetanus Prone Wound</th><th>Clinical Features</th><th>Tetanus Prone</th></tr>
<tr><td></td><td></td><td>TD1 2</td><td>TIG</td><td>Td</td><td>TIG</td><td rowspan="2">Age of would
Configuration
Depth
Mechanisms of injury</td><td rowspan="2">6 hours
Stellate, avulsion> 1cm
Missile, crush burn,</td></tr>
<tr><td rowspan="2">/= 6 hours
Linear

/= 1cm
Sharp surface (glass, knife)</td><td>Unknown or
< 3 doses or more doses</td><td>Yes
No 3</td><td>Yes
No</td><td>Yes
No 4</td><td>No
No</td></tr>
<tr><td colspan="6">1. Td = Tetanus & Diphtheria toxoids absorbed (adult)
TIG = Tetanus immunoglobulin (human)
2. Yes if wound > 24 hours old.
For children < 7 years, DPT (DT if pertussis vaccine contraindicated;
For persons >/= 7 years, TD preferred to tetanus toxoids alone.!
3. Yes if > 5 years since last booster
4. Yes if > 10 years since last booster.
from MMWR 39:37, 1999 (Jan.

from ACS Bull, 69:22, 23, 1984, No.</td></tr>
</table>

RABIES POST-EXPOSURE PROPHYLAXIS (1)

All Wounds should be cleaned immediately and thoroughly with soap and water.

Table 4

Evaluation and disposition of Animal	Recommendations for Prophylaxis!
Health and available for 10 day observation. Rabid or suspected rabid! Unknown (escaped)	Do not start unless animal develops symptoms, then immediately begin HRIG + HDCV or RVA. Immediate vaccination. Consult public health officials.
Regard as rabid	Immediate vaccination.
	Almost never require anti-rabies treatment.
Post-Exposure Immunisation Schedule (Unvaccinated Persons)	
Regimen	
IU/kg, if feasible infiltrate of dose around the wound(s), the rest IM in gluteal area. Not in same syringe as vaccine.(3) 1.0 ml IM in deltoid area (only acceptable site in adults and older children; younger children, outer aspect of thigh) (never in gluteal area). Days 0, 3, 7, 14, 28.	

Key to Table 4

Animal Type
Dogs, cats
Skunks, hyenas, bats, foxes, most carnivores
Livestock; rabbits, hares, hamsters, guinea pigs, rats, mice, monkeys
Immunizing Product
HRIG2! Vaccine: HDCV or RVA2!
1 From Morb Mort Weekly Report 40:RR-3, 1991 (March 22)! 2 HRIG = Human rabies immunoglobulin! (Hyperab, Imogan Rabies); HDCV = Human diploid cell vaccine, rabies (inactivated) Imovax Rabies); RVA = Rabies vaccine absorbed (inactivated), liquid (should not be used intradermally) 3 In reported post-exposure treatment failure, only identified deficiency was failure to infiltrate wound(s) with HRIG

HEPATITIS B POST-EXPOSURE PROPHYLAXIS FOR ADULTS (Percutaneous, Permucosal, Sexual)

Table 5

EXPOSURE SOURCE	
HBsAg	Status Unknown!
HB vaccine!	Do HBsAg test on source of ! exposure!
No treatment!	mlU/ml give 1 dose HB ! vaccine, if >/= 10 no treatment.! <10
* Value of HBIG > 7 days post-exposure (MMWR 40:12, 1991).	

EXPOSED PERSON	
	HBsAg+
Unvaccinated	HBIG 5.0ml IM*+ HB vaccine
Vaccinated (antibody response unknown)	Test exposed for anti-HBs, if /= 10 mlU/ml no treatment, if 10mlU/ml: HBIG + 1 dose HB vaccine

APPENDIX 2

DRUG INTERACTIONS

Interactions can occur either between one drug and another drug or between a drug and food or drink. When two Medicines have similar side effects, they can also interact. The interaction may be potentiation or antagonism of one drug by another or occasionally some other effect. Drug interaction may be pharmacodynamic or pharmacokinetic.

Pharmacodynamic interactions

These are interactions between Medicines that have similar or antagonistic pharmacological effects or side effects. This may be due to competition at receptor sites or occurs between Medicines acting on the same physiological system.

Pharmacokinetic interactions

These interactions occur when one drug alters the absorption, distribution, metabolism or excretion of another, thus increasing or decreasing the amount of drug available to produce its pharmacological effects. Pharmacokinetic interactions occurring with one drug in a related group cannot be assumed to occur with related Medicines unless their pharmacokinetic properties are known to be similar. Pharmacokinetic interactions are of several types:

Affecting absorption: The rate of absorption or the total amount of drug absorbed can both be altered by drug interactions. Reductions in the total amount absorbed, however, may result in ineffective therapy. Delayed absorption, however, is rarely of clinical importance unless high peak plasma concentrations are required.

Due to changes in protein binding: Most Medicines are loosely bound to plasma protein. Protein binding sites are non-specific and one drug can displace another thereby increasing its proportion free to diffuse from plasma to its site of action. Displacement rarely produces more than transient potentiation because this increased concentration of free drug results in an increased rate of elimination. Displacement from protein binding plays a part in the potentiation of warfarin by phenylbutazone, sulphonamides and tolbutamide, but the importance of these interactions is due mainly to the fact that warfarin metabolism is also inhibited.

Affecting metabolism: Many Medicines are metabolized in the liver. Induction of the hepatic microsomal enzyme system by one drug can gradually increase the rate of metabolism of another, resulting in lower plasma concentrations and a reduced effect. On withdrawal of the inducer, plasma concentrations increase and toxicity may occur. Barbiturates, griseofulvin, most antiepileptics and rifampicin are the most important enzyme inducers in man. Medicines affected include warfarin and oral contraceptives.

Affecting renal excretion: Medicines eliminated through the kidney by both glomerular filtration and active tubular secretion. Competition occurs between those that share active transport mechanisms in the proximal tubule. Thus probenecid delays the excretion of any Medicines including penicillins and some cephalosporins, indomethacin and dapsone. Aspirin may increase the toxicity of methotrexate by a similar mechanism.

Many drug interactions are harmless, and the severity of interaction varies from one patient to another. Medicines with a small therapeutic ratio (e.g. phenytoin) and those that require careful control of dosage (e.g. anticoagulants, antihypertensives and antidiabetics) are most often involved. Patients at increased risk from drug interactions include the elderly and those with impaired renal or hepatic function.

DRUG INTERACTION TABLE

AFFECTED DRUG	INTERACTS WITH	OUTCOME
Antidiabetics	Analgesics Antibacterials Antifungals Uricosurics	NSAIDs may enhance the effects of sulphonylureas Chloramphenicol, co-trimoxazole, 4-quinolones, sulphonamides and trimethoprim enhance the effect of sulphonylureas Fluconazole and miconazole increase plasma concentrations of sulphonylureas. Sulphinpyrazone enhances the effect of sulphonylureas
ACE inhibitors	Anaesthetics Analgesics Cyclosporin Diuretics Lithium Potassium salts	Anaesthetics enhance the hypotensive effect of ACE inhibitors Antagonism of the hypotensive effect Increased risk of hypokalaemia Enhanced hypotensive effect which can be extreme. Reduced excretion of lithium Hyperkalaemia
Amantadine	Alcohol Antimuscarinics Antiparkinsonism agents	Enhanced effects of extrapyramidal side effects. Enhanced effects of antimuscarinics Enhanced effects of antiparkinsonian agents
Aminoglycosides Aminoglycosides (cont.)	Antifungals Cyclosporine Diuretics Non-polarising muscle relaxants Radiographic contrast Vancomycin	Increased risk of nephrotoxicity with amphotericin Increased risk of nephrotoxicity Increased risk of ototoxicity with loop diuretics. Effect of non-polarising muscle relaxants enhanced Increased risk of nephrotoxicity Increased risk of ototoxicity and nephrotoxicity

DRUG INTERACTION TABLE

AFFECTED DRUG	INTERACTS WITH	OUTCOME
Beta-blockers (Note: systemic absorption following topical application possible)	Anaesthetics Antiarrhythmics Antihypertensives Calcium channel blockers Sympathomimetics	Enhanced hypotensive effect. Increased risk of bupivacaine toxicity with propranolol. Increased risk of myocardial depression and bradycardia Increased risk of lignocaine toxicity with propranolol Enhanced hypotensive effect. Increased risk of withdrawal hypertension with clonidine Increased risk of bradycardia and AV block with diltiazem. Occasionally severe hypotension and heart failure with nifedipine. Asystole, severe hypotension and heart failure with verapamil Severe hypertension with adrenaline and noradrenaline. Severe hypertension also possible with sympathomimetics contained in anorectics and cough and cold remedies
Calcium channel blockers (Note: Grapefruit increases plasma concentrations of dihydropyridine calcium channel blockers except amlodipine) Calcium channel blockers (cont.)	Anaesthetics Antiarrhythmics Antihypertensives Beta-blockers Cardiac glycosides Cyclosporin Theophylline	Verapamil increases the hypotensive effect of general anaesthetics and risk of AV delay. Amiodarone-induced risk of bradycardia, AV block. Myocardial depression increased by diltiazem and verapamil. Plasma concentration of quinidine reduced by nifedipine. With verapamil raised plasma concentration of quinidine which may cause extreme hypotension. Enhanced hypotensive effect. Increased risk of the first-dose hypotensive effect of post-synaptic alpha-blockers such as prazosin Increased risk of bradycardia and AV block with diltiazem. Occasionally severe hypotension and heart failure with nifedipine. Asystole, severe hypotension and heart failure with verapamil. Plasma concentration of digoxin increased by diltiazem nicardipine, verapamil and possibly nifedipine. Increased AV block and bradycardia with verapamil. Plasma concentrations of cyclosporin increased by diltiazem, nicardipine and verapamil. Diltiazem, verapamil and possibly other calcium channel blockers enhance the effect of theophylline.

DRUG INTERACTION TABLE

AFFECTED DRUG	INTERACTS WITH	OUTCOME
Cardiac glycosides Cardiac glycosides (cont.)	Antiarrhythmics Antifungals Antimalarials Calcium channel blockers Diuretics	Plasma concentration of digoxin increased by amiodarone and quinidine (halve maintainance dose of digoxin) Increased toxicity of hypokalaemia occurs with amphotericn. Plasma concentration of digoxin increased by itraconazole. Quinine! and possibly chloroquine raises plasma concentration of digoxin (maintenance dose of digoxin should then be halved). Possible increased risk of bradycardia with mefloquine. Plasma concentration of digoxin increased by diltiazem, nicardipine,verapamil and possibly nifedipine Increased AV block and bradycardia with verapamil. Increased toxicity of hypokalaemia occurs with acetazolamide, loop diuretics and thiazides Effects of digoxin! enhanced by spironolactone.!
Cephalosporins	Oral anticoagulants Alcohol	Effects of warfarin! and nicoumalone enhanced by cephamandole and possibly others. Disulfiram like reactions (tachycardia, flushing, diarrhoea) with cefamandole!
Chloramphenicol	Phenobarbitone Rifampicin Iron salts, vitamin B	Chloramphenicol may be less effective due to lower levels in the body Response to vitamin B1reduced!
Cotrimoxazole and sulphonamides	Antcoagulants Antidiabetics Anticonvulsants Antimalarials Cyclosporin	Effect of nicoumalone and warfarin enhanced. Effect of sulphonylureas enhanced Antifolate effect and plasma concentration of phenytoin increased. Increased risk of antifolate effect with pyrimethamine Increased risk of nephrotoxicity

AFFECTED DRUG	INTERACTS WITH	OUTCOME
Erythromycin	Carbamazepine	Increased levels of carbamazepine resulting in nausea, vomiting, ataxia
	Theophyllines	Increased serum levels of theophyllines resulting in nausea, vomiting, seizures, apnea
	Corticosteroids	Enhanced effects of corticosteroids
	Clozapine	Increased serum levels of clozapine, CNS toxicity
Erythromycin (cont.)	Cyclosporine	Increased serum levels of cyclosporine
	Digoxin	Increased serum levels of digoxin
	Cisapride	Increased Q-T interval, risk of arrhythmias
	Ergot alkaloids	Peripheral ischemia
	Oral anticoagulants	May increase prothrombin time
	Valproic acid	Increased levels of valproic acid
	Astemizole	Increased cardiotoxicity
Ethambutol	Aluminium salts	Absorption of ethambutol reduced
Ganciclovir	Probenecid	Metabolism of ganciclovir probably reduced (increased plasma half-life)
	Zidovudine	Increased toxicity (myelosuppression) of ganciclovir
Halofantrine	Chloroquine, mefloquine, quinine, Antiarrhythmics, Antidepressants, Antihistamines, Antipsychotics, Betablockers, Diuretics	Halofantrine in combination with any of these Medicines is dangerous as fatal cardiac arrhythmias can occur. If the patient has taken mefloquine or chloroquine as prophylaxis, do not use halofantrine to treat an attack of malaria
Isoniazid	Antacids	Absorption of isoniazid reduced
	Antiepileptics	Metabolism of carbamazepine, ethosuximide and phenytoin inhibited resulting in enhanced effects
	Narcotic analgesics	Prolonged effect of narcotic analgesics

AFFECTED DRUG	INTERACTS WITH	OUTCOME
4-Quinolones	Anticoagulants	Enhanced effect of warfarin and nicoumalone with ciprofloxacin, nalidixic acid and norfloxacin.
4-Quinolones (cont.)	Antidiabetics	Effect of sulphonylureas enhanced
	Cyclosporin	Increased risk of nephrotoxicity
	Multivalent metallic cations (Ca, Al, Fe, Mg, Zn) including sucralfate, antacids, multivitamins	Absorption of ciprofloxacin, norfloxacin and ofloxacin reduced (50 - > 90%)
	Probenecid, loop diuretics	Excretion ciprofloxacin, nalidixic acid and norfloxacin reduced.
	Theophyllines	Increased plasma theophylline concentration.
Rifampicin	Antacids	Absorption of rifampicin reduced
	Anticoagulants	Accelerated metabolism of nicoumalone and warfarin resulting in suboptimal coagulation
	Antidiabetics	Increased metabolism of chlorpropamide, tolbutamide and possibly other sulphonylureas resulting in reduced effect
	Antiepileptics	Phenytoin metabolism increased (reduced plasma concentration)
	Antifungals	Metabolism of fluconazole, itraconazole and ketoconazole increased (reduced plasma concentrations)
	Antivirals	Increased metabolism of indinavir possibly saquinavir (reduced plasma concentrations)
	Corticosteroids	Corticosteroid metabolism increased therefore replacement doses need to be increased.
	Oral contraceptives	Contraceptives effect reduced and can result in spotting, pregnancy
Rifampicin (cont.)	Cyclosporins	Accelerated metabolism of cyclosporin resulting in reduced effect
	Theophyllines,	Metabolism of theophylline increased
	Quinidine	Metabolism of quinidine enhanced (plasma-quinidine concentration reduced)

APPENDIX 3

HAEMATOLOGICAL REFERENCE RANGES FOR ADULTS

TEST		NORMAL RANGE
1	**WBC (TOTAL)**	4 –11 X 10^9/L
2	**WBC (DIFFERENTIAL)** NEUTROPHILS LYMPHOCYTES MONOCYTES EOSINOPHILS BASOPHIL	 40 –75% 20 –45% 2 – 10% 1 – 6% 1%
3	RBC	MEN:- 4.5 – 6.5 x 10^{12}/L WOMEN:- 3.8 – 5.8 x 10^{12}/L
4	Hb	MEN:- 130-180g/L WOMEN:- 120-160g/L
5	Hct (PVC) (Ratio)	MEN:- 0.40-0.54 WOMEN: 0.37-0.47
6	MCV	76 – 96fL
7	MCH	27 – 32pg
8	MCHC	30 – 35g/dl
9	PLATELET COUNT	150 – 400 x 10^9/L
10	Prothrombin Time (PT)	12 – 16 seconds
11	Activated Partial Thromboplastin Time (APTT)	30 – 40 seconds
12	BLEEDING TIME (IVY'S METHOD)	2 – 7 minutes
13	CLOTTING TIME (TUBE METHOD)	2 – 8 minutes
14	RETICULOCYTE COUNT	0.5 – 2.5%
15	ESR	MEN:- Up to 10mm/hr MEN:- Over 50 years up to 12 – 14mm/hr WOMEN:- Up to 12mm/hr WOMEN:- Over 50 years up to 19 – 20mm/hr

HAEMATOLOGICAL REFERENCES RANGES DURING PREGNANCY AND OBSTETRIC DELIVERY

TEST	PREGNANCY	DELIVERY
WBC (TOTAL)	5.0 – 16.0 x 10^9/L	<40.0 x 10^9/L
WBC (DIFFERENTIAL)		
NEUTROPHILS	2.5-14.0 X 10^9/L	<36.0 X 10^9/L
LYMPHOCYTES	Slightly lower than non-pregnant	
MONOCYTES		Low
EOSINOPHILIS	<0.1 X 10^9/L	<0.02 X 10^9/L
BASOPHILIS	<1%	<1%
Platelets	120-320 x 10^9/L	Raised post-partum

CLINICAL CHEMISTRY REFERENCE RANGES IN ADULTS

Blood/Serum/Plasma

TEST	LOW LIMIT	HIGH LIMIT	UNIT
Na^+	134	144	Mmol/L
K+	3.5	5.0	“
Cl^+	95	107	“
Urea	1.70	8.3	“ µmol/L
Creatinine	63	120	mmol/L
Glucose (fasting)	3.5	5.5	mmol/L
Glucose (Random)	3.9	6.6	umol/L
Uric acid	140	450	U/L
ALT/SGPT	5	37	U/L
AST/SGOT	5	36	U/L
ALP	36	275	U/L
GGT	7	52	U/L
LDH	0.0	460	U/L
ACP	2.5	5.2	U/L
CK/CPK CKMB	0.0	170	U/L
a – Amylase	1.0	25	U/L g/L g/L mmol/L
Total protein	0.0	200	mmol/L µmol/L
Albumin	66	87	µmol/L
Calcium	36	46	mmol/L
Phosphate	2.1	2.5	Mmol/L
Bilirubin: Total	0.8	1.5	mmol/L
Direct	3.4	17	mmol/L mg/L
TEST	0.8	5.1	µmol/L g/L
Total cholesterol	**LOW**	**LIMIT**	mosmol/L g/L mg/dL
High-density lipoprotein	2.8	5.5	
Low-density lipoprotein	1.0	1.8	
Triglycerides	0.0	5.0	
C-reactive protein	0.0	2.3	
Total iron	0.0	10	
Transferrin	9.0	30	
Osmolality	2.0	4.0	
Fibrinogen	275	295	
Magnesium	1.5	4.0	
	1.7	2.19	

TEST	LOW LIMIT	HIGH LIMIT	UNIT
Total glycated haemoglobin	4.0	8.0	%
Cerebrospinal fluid			
Chloride	120	130	mmol/L
Glucose	0.6	2.5	mmol/L
Protein	0.15	0.45	g/L
Urine	2.5	8.0	mmol/day
Calcium	7100	17700	“mol/day
Creatinine: Female	5300	15900	“mol/day
:Male	300	1000	mosmol/L
Osmolality	16	48	mmol/day
Phosphate	35	90	mmol/day
K+	140	260	mmol/day
Na+			
TEST	**LOW LIMIT**	**HIGH LIMIT**	**UNIT**
Protein			
S.G	1.016	1.025	<0.1 g/day
Urea	250	600	mmol/day
Uric acid	1480	4430	“mol/day
VMA	97	137	<8 !mg/day
Creatinine clearance: Male	88	128	ml/min
Female	15	30 (3hrs urin)e	ml/min
Lithium Clearance			ml/min

ENDOCRINOLOGY REFERENCE RANGES

THYROID HORMONES REFERENCES RANGES (ADULTS)

T3 1.5 ---------- 3.7 nmol/L

T4 50.0 ---------- 129.0 nmol/L

TSH 0.8 ---------- 5.0 mU/L

REPRODUCTIVE HORMONES

		REFERENCE RANGE	
		FEMALE	MALE
Prolactin		110 – 550 mU/L	50 –500 mU/L
	Early follicular	2.6 – 6.0 iU/L	
	Luteal phase	1.6 – 5.5 iU/L	
FSH	Post menopause	128-130 iU/L	1.2-5.0 iU/L
	Early follicular	3.0-12.0 iU/L	
	Ovulation peak	25.0-65.0 iU/L	
	Luteal phase	2.5-13.0 iU/L	
LH	Post menopause	25.0-120 iU/L	2.0-9.5 iU/L
	Follicular phase	110-440 pmol/L	
	Luteal phase	367-770 pmol/L	
	Pre-ovulation peak	500-1285 pmol/L	
Estradiol	Post menopause	36-128 pmol/L	36-128pmol/L
	Follicular phase	0.6-3.2 nmol/L	
Progesterone	Luteal phase	9.5-79.5 nmol/L	0.3-3.2 nmol/L
Testosterone		0.3-3.6 nmol/L	10.4-31.2 nmol/L

APPENDIX 4

ADDITIVES TO I.V. FLUIDS

Guidelines for the direct addition of medicaments to infusion containers.

1. Medicines should only be added to infusion containers when constant plasma concentrations of the drug are required or when there is no alternative.
2. In general, only one drug should be added to any infusion container and the components should be of known compatibility (see table) Medicines must not be added to containers of blood, plasma, parenteral amino acid preparations, mannitol and sodium bicarbonate solution.
3. The giving set should not be used for more than 24 hours and strict asepsis should be maintained throughout.
4. It is good practice to examine intravenous infusion from time to time while they are running to ensure that the rate of flow is satisfactory. If any sign of contamination or any other sign of interaction is observed the infusion should be discontinued.

Problems involving Additives.

- Some Medicines including most antibiotics become unstable and deteriorate in a large volume of fluid. Most of these (i.e. antibiotics corticosteroids and parental vitamins) are better given intermittently by injection into the intravenous infusion set.
- The accidental entry and subsequent growth of micro-organisms convert the infusion fluid pathway into a vehicle for infection with microorganisms.
- Dosage may be inaccurate if the rate of infusion changes (e.g. drip blocks).

APPENDIX 5

MEDICINES INCOMPATIBILITIES IN INTRAVENOUS FLUID

DRUG	INCOMPATIBLE WITH	REASON
The Penicillins (Na + or K+ salts of Benzyl-penicillin and the Semi-synthetic Penicillins)	Tetracyclines Gentamicin	Precipitation Inactivation
	Tetracyclines	Precipitation
	Penicillin	Precipitation
	Sulphonamides (Na + salts)	Precipitation
Hydrocortisone Sodium Succinate	Hydrocortisone Sodium Succinate	Precipitation
		Tetracycline
Tetracyclines	Calcium salts	Chelate formed
Gentamicin	Sodium Bicarbonate All Penicillins	Precipitation
Ampicillin	All other antibiotics	Reduced activity of Gentamicin
	Hydrocortisone Sodium Phosphate	Loss of potency

APPENDIX 6

Drug use in pregnancy

Many medicines can disrupt the development of the foetus (especially during the first trimester) or can have effects on maturing babies and newborns through Medicines excreted in breast milk. Often the effect of the Medicines on the foetus and babies are unknown.

Generally, Medicines should be avoided in pregnancy Some Medicines are known to be safe (e.g. penicillin), others have a slight risk, which is outweighed by the benefit of the treatment (e.g. malaria is much more dangerous to pregnancy than anti-malarial Medicines).

The list below contains references to Medicines found in this formulary. It is not a comprehensive list of all Medicines.

Drug	Comment
Ace Inhibitor (1,2,3,)	Avoid, can affect foetal and neonatal blood pressure control and renal function; possible skull defects.
Alcohol (1,2,)	Regular alcoholics teratogenic, possible growth retardation.
Aminoglycosides (2,3,)	Auditory or vestibular nerve damage, greatest risk with streptomycin, less risk gentamycin but avoid unless essential.
Aminophylline	see theophylline
Amitriptyline	see antidepressants
Anaesthetics general (3)	Depress neonatal respiration
Anaesthetics local (3)	Large doses cause neonatal respiratory depression, hypotonia and bradycardia
Anticoagulants heparin (1,2,3,)	osteoporosis after prolonged use
Anticoagulants oral (1,2,3,)	congenital malformations Foetal and neonatal haemorrhage
Artemether	Insufficient information
Oral antidepressants (3)	tachycardia, irritability and muscle spasms (e.g. imipramine), avoid unless the benefit outweighs the risk
Antiepileptics	The benefit of treatment outweighs risks to the foetus, risk increases if more than 1 drug used (see also individual Medicines)
Antihistamines	No evidence of teratogenicity
Antimalarials (1,3,)	The benefit of treatment outweighs the risk to the foetus,(see also an individual drug)
Antipsychotics (3)	avoid clozapine, extrapyramidal effects in neonates occasionally observed.
Aspirin (3)	Impaired platelet function, risk of haemorrhage, delayed onset and increased duration of labour. Avoid in the last weeks of pregnancy. High doses cause the closure of the foetal ductus arteriosus in utero and possible pulmonary hypertension of the new born.
Atenolol	See beta-blockers
Beclomethasone	See corticosteroids
Bendrofluazide	See diuretics
Beta blockers	May cause intrauterine growth retardation, neonatal hypoglycaemia and bradycardia
Betamethasone	See corticosteroids
Calcium Channel blockers	May inhibit labour and maybe teratogenic

Captopril	See ACE inhibitors
Carbamazepine (1)	Possibly teratogenic
Carbimazole (2,3,)	Neonatal goitre and hypothyroidism
Cephalosporins	Not known to be harmful
Chloramphenicol (3)	Neonatal “grey syndrome”
Chlordiazepoxide	See hypnotics and anxiolytics
Chlormethiazole	See hypnotics and anxiolytics
Chloroquine	See antimalarials
Chlorpheniramine	See antihistamines
Chlorpromazine	See antipsychotics
Clomiphene	possible effects on foetal development
Clozapine	Avoid
Codeine	See opioid analgesics
Contraceptives, Oral	epidemiological evidence suggests no harmful effect
Corticosteroids (2,3,)	Only if the benefit is high e.g. asthmatic attack
Cotrimoxazole (1)	Theoretical teratogenic risk
Danazol (1,2,3,)	Weak androgenic effects
Dapsone (3)	Neonatal haemolysis and methaemoglobinaemia. Adequate folic acid supplements necessary
Dexamethasone	See corticosteroids
Diazepam	See hypnotics and anxiolytics
Digoxin	May need a dosage adjustment
Diltiazem	See calcium channel
Diuretics (3)	Should not be used to treat hypertension in pregnancy. Thiazides cause neonatal thrombocytopenia
Doxycycline	See tetracycline
Ergotamine (1,2,3,)	Oxytocic effect on the pregnant uterus
Erythromycin	Not known to be harmful
Ethinylestradiol	See contraceptives, oral
Fluconazole	avoid Antidepressants
Glibenclamide	See sulphonylureas
Griseofulvin (1,2,3,)	avoid, fetotoxicity and teratogenicity
Haloperidol	See antipsychotics
Heparin	See anticoagulants
Hydralazine (1,2)	possible toxicity
Hydrochlorothia-zide	See diuretics
Hydrocortisone	see corticosteroids
Hydroxyprogester-one	See progesterones
Hypnotics and anxiolytics	Avoid
Ibuprofen	See NSAIDs
Idoxuridine	Possible toxicity
Imipramine	Avoid, see also antidepressants
Insulin (1,2,3,)	Insulin requirements should be frequently reassessed.
Iodine (2,3,)	neonatal goitre and hypothyroidism
Kanamycin	See aminoglycosides
Ketamine	See anaesthetics: General
Ketoconazole	possibly teratogenic
Labetalol	See beta-blockers
Levodopa	Possible toxicity
Lignocaine	See anaesthetic, local
Lithium (1,)	Dose requirements increased, neonatal goitre and lithium toxicity. Rick of teratogenicity, including cardiac abnormality
Lorazepam	See hypnotics and anxiolytics
Mebendazole	Possible toxicity
Mefloquine	Possibly teratogenic
Metform in	avoid

Metoclopramide	Not known
Metronidazole	Avoid high doses
Nalidixic	See 4 quinolones
Nalaxone	Only if benefit outweighs risk
Naproxen	See NSAIDs
Neomycin	See aminoglycocides
Nifedipine	See calcium channel blockers
Nitrazepam	See hypnotics and anxiolytics
Nitrofurantoin (3)	May produce neonatal haemolysis
Nitrous oxide	See anaesthetics, general
Norethsterone	See contraceptives, oral
NSAIDs (3)	Avoid unless large benefit of treatment. Regular use causes closure of ductus arteriosus in utero and possible persistent pulmonary hypertension of the newborn
Nystatin	Unknown
Oestrogens	See contraceptives respiration
Opioid analgesics (3)	Depress neonatal respiration
Paracetamol	Not known to be harmful
Pethidine Analgesics	See opioid analgesics
Phenobarbitone (1,2,)	Congenital malformation, neonatal bleeding tendency
Phenytoin (1,3,)	Congenital malformation - see also anti epileptics
Pilocarpine	Avoid
Pindolol	See beta blockers
Podophylline (1,2,3,)	Avoid: neonatal death and teratogenic
Povidone iodine (2,3,)	Sufficient iodine may be absorbed to affect foetal thyroid
Prednisolone	See corticosteroids
Primaquine (3)	Neonatal haemolysis and methaemoglobinaemia
Progesterones (1)	High doses possibly teratogenic
Promethazine	See antihistamines
Propranolol	see betablockers
Pyrimethamine +	Possibly teratogenic
Sulphadoxine (1)	neonatal haemolysis and methaemoglobinaemia
Quinine (1) reported	No adverse effects
Quinolones (1,2,3,)	possible antropathy
Rifampicin(1)	High doses teratogenic
Spironolactone	Possible toxicity
Streptomycin	See aminoglycocides
Sulphonylureas (3)	Neonatal hypoglycaemia, avoid, substitute with insulin
Tetracyclines (1)	Effects on skeletal development
Tetracycline (2,3,)	Dental discoloration
Theophyllin (3)	Neonatal irritability and apnoea have been reported
Thiazides (3)	Neonatal thrombocytopaenia possible
Thiopentone	See anaesthetics: General
Thioridazine	See antipsychotics
Timolol	See beta-blockers
Trimethoprim (1)	Teratogenic risk
Warfarin	See anticoagulants

APPENDIX 7

DRUG USE IN BREASTFEEDING

Administration of some Medicines to nursing mothers may cause toxicity in the infant (e.g. ergotamine), whereas others may affect the neonate (e.g. digoxin). Toxicity to the infant can occur if the drug enters the milk in pharmacologically significant quantities. Milk concentrations of some Medicines might exceed those in maternal plasma so that therapeutic doses in the mother might be toxic to the infant. For many Medicines, there is insufficient evidence to provide guidance and it is therefore only advisable to administer those Medicines that are necessary to the mother during breastfeeding.

The following list contains the Medicines covered in this formulary that should be used with caution or which should be avoided in breastfeeding.

Alcohol	Large amounts may be persistent pulmonary hypertension for the newborn.
Amiloride	Avoid
Aminophylline	See theophylline
Amitriptyline	See antidepressants
Anticoagulants, oral	Risk of haemorrhage, warfarin appears to be safe
Antidepressants	Small amount of tricyclics in breast milk, manufacturers Advise to avoid
Antihistamines	A significant amount of some antihistamines although not known to be harmful
Antipsychotics	Avoid, possible effects on the development of the nervous system
Acetyl salicylic acid	Avoid
Atenolol	See beta-blockers
Artemether	Insufficient information
Barbiturates	Avoid if possible, a large dose may cause drowsiness
Beclomethasone	See corticosteroids
Bendrofluazide	See thiazides
Benzodiazepines	Avoid repeated doses, lethargy and weight loss in infant
Beta blockers	Monitor infant, possible toxicity due to beta-blockade, but amount excreted of most beta-blockers too small, atenolol has greatest risk
Betamethasone	See corticosteroids
Bromocriptine	Suppress lactation
Captopril	Avoid
Carbamazepine	Probably amount too small to be harmful
Carbimazole	Amounts in milk may be harmful
Cephalosporins	Excreted in low concentrations
Chloramphenicol	Avoid, may cause neonatal " Grey syndrome"
Chlordiazepoxide	See benzodiazepines
Chlormethiazole	An amount too small to be harmful
Chloroquine	Amount probably too small to be harmful
Chlorpromazine	Drowsiness in infant reported
Cimetidine	Monitor infant
Ciprofloxacin	Avoid, high concentration on breast milk
Codeine	An amount too small to be harmful

Contraceptives, oral	Avoid combined oral contraceptives until weaning or 6 months after birth. Adverse effects on lactation
Corticosteroids	Continuous high doses may affect infant adrenal function
Cotrimoxazole	Small risk of jaundiced infants
Danazol	Avoid, possible weak androgenic effects
Dexamethasone	See corticosteroids
Lisinopril	No information
Lithium	Monitor infant for possible intoxication
Lorazepam	See benzodiazepines
Mebendazole	No information
Mefloquine	Avoid
Metoclopramide	Avoid
Metronidazole	Avoid
Nalidixic acid	Small risk
Naloxone	No information
Naproxen	An amount too small to be harmful
Nifedipine	An amount too small to be harmful
Nitrazepam	See benzodiazepines
Nitrofurantoin	May be harmful in some individuals
Norethisterone	See contraceptives, oral
Nystatin	No information
Oestrogens	See contraceptives, oral
Opioid	Depress neonatal respiration
Paracetamol	Not known to be harmful
Penicillins	Not known to be harmful
Pethidine	See opioid analgesics
Phenobarbitone	Avoid when possible, drowsiness may occur, but the risk is small
Phenytoin	A small amount is milk
Pilocarpine	Avoid
Pindolol	See beta-blockers
Podophyllin	Avoid: neonatal death and teratogenic
Povidone Iodine	Sufficient iodine may be absorbed to affect foetal thyroid
Prednisolone	See corticosteroids
Primaquine	Neonatal haemolysis and methaemoglobinaemiaa
Diazepam	See benzodiazepines
Digoxin	An amount too small to be harmful
Diltiazem	Avoid
Disopyramide	Monitor infant for antimuscarinic effects
Doxycycline	See tetracyclines
Enalapril	An amount too small to be harmful
Ergotamine	Avoid
Erythromycin	Not known to be harmful
Ethinyloestradiol	See contraceptives, oral
Fentanyl	Avoid
Fluconazole	Avoid
Fluoxetine	Avoid
Glibenclamide	See Sulphonylureas
Haloperidol	See antipsychotics
Hydrochlorothiazide	See thiazides
Hydrocortisone	See corticosteroids
Ibuprofen	An amount too small to be harmful. The short course is safe in the usual dose
Idoxuridine	May make breast milk taste unpleasant
Imipramine	Avoid, see also antidepressants
Insulin	An amount too small to be harmful
Indomethacin	Maybe harmful
Iodine	Harmful, if required stop breastfeeding, the danger of hypothyroidism

Isoniazid	Monitor possible toxic effects, theoretical risk of convulsion and neuropathy
Progesterones	High doses suppress lactation
Promethazine	See antihistamines
Propranolol	See beta-blockers
Pyrmentamine	No adverse effect + Sulfadoxine
Quinine	High doses are teratogenic, but malaria may outweigh the risk
4 Quinolones	Possible arthropathy
Rifampicin	An amount too small to be harmful
Spironolactone	See aminoglycosides

Sulphonylureas	Neonatal hypoglycaemia, avoid, substitute with insulin
Tetracyclines	Effects on skeletal development. Avoid.
Theophylline	Neonatal irritability and apnoea have been reported
Thiazides	Possible suppression of lactation
Thiopentone	See anaesthetics: General
Thioridazine	See antipsychotics
Timolol	See beta-blockers
Trimethoprim	Short term use not known to be harmful
Warfarin	See anticoagulants

DRUG INDEX A

C

D

N

O

P

Q

Notes


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HEALTH ACCESS
INITIATIVE


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