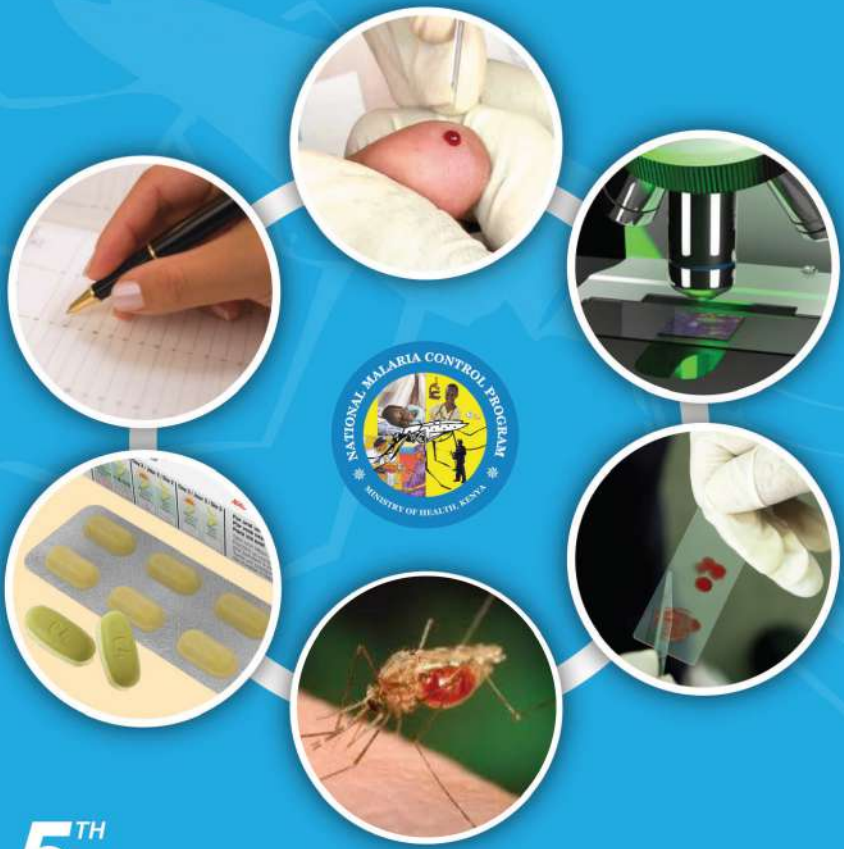
REPUBLIC OF KENYA

MINISTRY OF HEALTH

GUIDELINES FOR THE DIAGNOSIS, TREATMENT AND PREVENTION OF MALARIA IN KENYA



5TH EDITION

Revised 2018

GUIDELINES FOR THE DIAGNOSIS, TREATMENT AND PREVENTION OF MALARIA IN KENYA

Fifth Edition

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Ministry of Health

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Revised 2018

National Guidelines for the diagnosis, treatment and prevention of malaria in Kenya

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Preface

The ultimate goal of malaria control is to reduce morbidity and prevent mortality due to malaria thereby mitigating the socio-economic burden of the disease on Kenya. One of the key strategic interventions therefore is to provide early parasitological diagnosis and prompt treatment of malaria using effective medicines.

The Ministry of Health have developed these guidelines for malaria diagnosis, treatment and prevention with an aim of improving malaria case management by all health workers and having a harmonized approach in efforts aimed at the reduction of morbidity and mortality due to malaria.

It is recommended that diagnosis of malaria be confirmed by testing. Management should be based on testing outcomes. The fifth edition of the guidelines contains new information in line with the revised WHO guidelines (3rd edition)[1].

The guideline document is intended to serve as a guide to all health professionals both pre- and in-service and including those in the private sector, researchers, trainers in medical training institutions and all partners involved in the implementation of malaria case management in Kenya.

These guidelines will continue to be updated periodically taking into consideration continuous monitoring and evaluation and emerging research findings and lessons learned. We have carefully considered the cost effectiveness of recommended interventions. We expect users to continually give feedback regarding the use of relevant sections of the guidelines.

Dr. Kioko Jackson K., OGW
Acting Director Of Medical Services

[1] http://www.who.int/malaria/publications/atoz/9789241549127/en/

Acknowledgement

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We are grateful to the Malaria Interagency Coordinating Committee, members of the Case Management Technical Working Group and staff of the National Malaria Control Program for their contributions to the development of this document. We are grateful for the financial support from the United States President's Malaria Initiative (PMI) through Management Sciences for Health/Health Commodities and Services Management (MSH/HCSM) programme as well as support from the United Kingdom's Department for International Development. Technical support was received from the World Health Organization's Kenya Country Office, Inter-country Support Team and Global Malaria Program.

It is our sincere hope that the guidelines will be useful in improving prevention and case management of malaria in Kenya. By implementing the recommendations in the guidelines, there is no doubt that we shall reduce malaria related illnesses and deaths and put Kenya on the path towards a malaria free future.

Abbreviations

ACSM	Advocacy communication and social mobilization
ACT	Artemisinin based combination treatment
ADR	Adverse drug reaction
AIDS	Acquired immune-deficiency syndrome
AL	Artemether-lumefantrine
ANC	Antenatal care or clinic
BW	Birth weight
CHMT	County Health Management Teams
CQ	Chloroquine
CSF	Cerebro-spinal fluid
DHA-PPQ	Dihydroartemisinin-piperaquine
DHIS	District Health Information System
DOMC	Division of Malaria Control
DOT	Directly observed treatment
DNA	Deoxyribonucleic acid
EPR	Epidemic preparedness and response
FIND	Foundation for Innovative New Diagnostics
GCS	Glasgow coma scale
GMP	Good Manufacturing Practices
G6PD	Glucose 6-phosphate dehydrogenase
Hb	Haemoglobin
HIV	Human immune-deficiency virus
HRP2	Histidine-Rich Protein 2
IM	Intramuscular
IMCI	Integrated management of childhood illnesses
IPTp	Intermittent preventive treatment of malaria in pregnancy
IV	Intravenous
KEMSA	Kenya Medical Supplies Authority
kg	kilogram
KMIS	Kenya Malaria Indicator Survey
KNH	Kenyatta National Hospital

LFT	Liver function tests
LLIN	Long lasting insecticidal nets
M&E	Monitoring and Evaluation
mg	milligram
ml	millilitre
MSH/HCSM	Management Sciences for Health / Health Commodities and Services Management programme
NSAID	Non-steroidal anti-inflammatory drug
PCR	Polymerase chain reaction
PCV	packed cell volume
pLDH	Parasite lactate dehydrogenase
PMI	President's Malaria Initiative
PPB	Pharmacy and poisons board
QA	Quality Assurance
RDT	Rapid diagnostic test
SOP	Standard operating procedure
SP	Sulphadoxine or Sulphalene/pyrimethamine
TSS	Tropical splenomegaly syndrome
WBC	White blood cell
WHO/GMP	World Health Organization Global Malaria Program

Glossary of Terms

Afebrile: Without fever.

Anaemia: A reduction in the quantity of the oxygen-carrying pigment haemoglobin in the blood.

Anti-pyretic: A drug such as paracetamol that relieves fever without affecting the causative agent (in this case the parasite).

Artemisinin-based combination therapy (ACT): A combination of artemisinin or one of its derivatives with an antimalarial or antimalarials of a different class.

Asexual cycle: The life cycle of the malaria parasite in the host from merozoite invasion of red blood cells to schizont rupture (merozoite → ring stage → trophozoite → schizont → merozoites). Duration approximately 48hr in *plasmodium falciparum*, *p. ovale* and *p. vivax*; 72 hr in *p. malariae*.

Asexual parasitaemia: The presence in host red blood cells of asexual parasites. The level of asexual parasitaemia can be expressed in several different ways: the percentage of infected red blood cells, the number of infected cells per unit volume of blood, the number of parasites seen in one microscopic field in a high-power examination of a thick blood film, or the number of parasites seen per 200–1000 white blood cells in a high- power examination of a thick blood film.

Base: The main active part of a drug (see also salt).

Cerebral malaria: Severe *p. falciparum* malaria with cerebral manifestations, usually including coma (Glasgow coma scale <11, Blantyre coma scale <3). Malaria with coma persisting for >30min after a seizure is considered to be cerebral malaria.

Cinchonism: Poisoning caused by an overdose of cinchona or the alkaloids quinine, quinidine, or cinchonine derived from it.

Combination treatment: A combination of two or more different classes of antimalarial medicines with unrelated mechanisms of action.

Cure: Elimination of the symptoms and asexual blood stages of the malaria parasite that caused the patient or caregiver to seek treatment.

Drug resistance: The World Health Organization (WHO) defines resistance to antimalarials as the ability of a parasite strain to survive and/or to multiply despite the administration and absorption of a medicine given in doses equal to or higher than those usually recommended but within the tolerance of the subject, provided drug exposure at the site of action is adequate. Resistance to antimalarials arises because of the selection of parasites with genetic mutations or gene amplifications that confer reduced susceptibility.

Endemic: Occurring frequently in a particular region or population.

Essential medicines: Are those drugs that satisfy the health care needs of the majority of

the population; they should therefore be available at all times in adequate amounts and in appropriate dosage forms, at a price the community can afford.

Febrile: With an increase in temperature compared with the normal.

Fever: An increase in body temperature above the normal temperature i.e. above a normal temperature of 37.5°C.

Febrile convulsions: Convulsions occurring in children aged 6 months - 6yrs due to fever caused by infection outside the central nervous system.

Gametocytes: Sexual stages of malaria parasites present in the host red blood cells.

Hyperpyrexia: Temperature over 39.5°C.

Hypersensitivity: An abnormal response to the presence of a particular antigen, which may cause a variety of tissue reactions ranging from serum sickness to an allergy.

Hypnozoites: Persistent liver stages of *p. vivax* and *p. ovale* malaria that remain dormant in host hepatocytes for an interval (most often 3–45 weeks) before maturing to hepatic schizonts. These then burst and release merozoites, which infect red blood cells. Hypnozoites are the source of relapses.

Immunity: All those natural processes which prevent infection, re-infection, or super-infection, or which assist in destroying parasites or limiting their multiplication, or which reduce the clinical effects of infection.

Isotonic solution: Refers to two solutions having the same osmotic pressure across a semipermeable membrane.

Lumbar puncture: The insertion of a needle into the fluid-filled space of the spinal cord in the lumbar region and the removal of a sample of that fluid for examination.

Monotherapy: Antimalarial treatment with a single medicine (either a single active compound or a synergistic combination of two compounds with related mechanism of action).

Non-immune: Having no immunity at all to a particular organism or disease.

Parenteral: The provision of medication into the body by any means other than through the alimentary canal (oral route or rectal), such as by subcutaneous, intramuscular or intravenous injection.

Plasmodium: A genus of protozoan vertebrate blood parasites that includes the causal agents of malaria. *Plasmodium falciparum, p. malariae, p. ovale* and *p. vivax* cause malaria in humans. Human infections with the monkey malaria parasite, *p. knowlesi* have also been reported from forested regions of South-East Asia.

Pre-erythrocytic development: The life-cycle of the malaria parasite when it first enters the host. Following inoculation into a human by the female anopheles mosquito, sporozoites invade parenchyma cells in the host liver and multiply within the hepatocytes for 5–12 days, forming hepatic schizonts. These then burst liberating merozoites into the bloodstream, which subsequently invade red blood cells.

Proficiency assessment: It is a process of exposing practicing microscopists to slides of

known results with a view of assessing their ability to correctly read slides.

Pruritus: Itching caused by local irritation of the skin or at times nervous disorders.

Radical cure: In *p. vivax* and *p. ovale* infections only, this comprises a cure as defined above plus prevention of relapses by killing hypnozoites.

Rapid diagnostic test (RDT): Is an immunochromatographic test for malaria presented in form of a dipstick, cassette or card in which the coloured line indicates that plasmodial antigens have been detected.

Recrudescence: The recurrence of asexual parasitaemia after treatment of the infection with the same infection that caused the original illness. This results from incomplete clearance of parasitaemia due to inadequate or ineffective treatment. It is, therefore, different to a relapse in *p. vivax* and *p. ovale* infections, and it differs from a new infection or re-infection (as identified by molecular genotyping in endemic areas).

Recurrence: The recurrence of asexual parasitaemia following treatment. This can be caused by a recrudescence, a relapse (in *p. vivax* and *p. ovale* infections only) or a new infection.

Relapse: The recurrence of asexual parasitaemia in *p. vivax* and *p. ovale* malaria deriving from persisting liver stages. Relapse occurs when the blood stage infection has been eliminated but hypnozoites persist in the liver and mature to form hepatic schizonts. After variable intervals of weeks to months, the hepatic schizonts burst and liberate merozoites into the bloodstream.

Resistance: See drug resistance.

Salt: Any compound of a base and an acid, e.g. quinine dichloride or quinine sulphate.

Schizonts: Mature malaria parasites in host liver cells (hepatic schizonts) or red blood cells (erythrocytic schizonts) that are undergoing nuclear division. This process is called schizogony.

Sensitive: Possessing the ability to respond to a stimulus.

Severe anaemia: Haemoglobin concentration of <5g/100 ml (haematocrit <15%). Severe falciparum malaria. Acute falciparum malaria with signs of severity and/or evidence of vital organ dysfunction.

Slide rechecking: It is a verification process where slides are reexamined by a second reader and a third reader where there is disagreement.

Sporozoites: Motile malaria parasites that are infective to humans, inoculated by a feeding female anopheles mosquito. The sporozoites invade hepatocytes.

Treatment failure: A failure to achieve the desired therapeutic response after the initiation of therapy. Treatment failure is not synonymous with drug resistance.

Trophozoites: A stage of development of the malaria parasites within host red blood cells. Mature trophozoites contain visible malaria pigment.

Uncomplicated malaria: Symptomatic infection with malaria parasitaemia without signs of severity and/or evidence of vital organ dysfunction.

Malaria Treatment Snapshot

Diagnosis of Malaria

All people with suspected malaria should have a parasitological test to confirm the diagnosis.

A rapid diagnostic test (RDT) *or* microscopy can be used to confirm the diagnosis. If needed, only microscopy can be used to monitor response to treatment.

Treatment of uncomplicated *p. falciparum* malaria

Treat adults and children (excluding pregnant women in their first trimester) with uncomplicated *p. falciparum* malaria with an artemisinin-based combination therapy (ACT)

The current recommended first line ACT isartemether plus lumefantrine, (AL).

The second line ACT is dihydroartemisinin plus piperaquine, (DHA/PPQ)

All ACTs should contain *at least three days* treatment with an artemisinin-derivative.

Treatment of uncomplicated *p. falciparum* malaria in special risk groups

Treat pregnant women with uncomplicated *p. falciparum* malaria in the first trimester with seven days of quinine plus clindamycin (if unavailable use an ACT).

Treat infants weighing less than 5 kg with uncomplicated *p. falciparum* malaria with an ACT dosed at the same mg/kg target as for children weighing 5 kg.

People with *p. falciparum* hyperparasitemia are at increased risk of death and require close monitoring in addition to an ACT.

Treatment of uncomplicated *p. vivax, p. ovale and p. malariae* malaria

Treat all adults (excluding pregnant women in the first trimester) and children with uncomplicated *non-falciparum* malaria using the first line ACT similar to treatment of *p. falciparum.*

Preventing relapse in *p. vivax* or *p. ovale* malaria

Treat all adults and children (excluding pregnant or breastfeeding women, infants, and people with G6PD deficiency) with *P.vivax*or *P.ovale* in all transmission setting with a 14-day course of 0.25 -0.5mg/kg per day of primaquine in addition to ACT to prevent future relapse.

Pre-referral treatment of severe malaria pending transfer to higher level facilities

At health care levels where treatment of severe malaria is not possible, but injections are available, give a single dose of intramuscular artesunate 2.4mg/kg for adults and 3.0mg/kg for children <20 kg and refer to an appropriate facility for further care. Use artemether3.2mg /kg or quinine 20mg/kg if artesunate is not available.

In settings where intramuscular injections are unavailable or not possible, treat children below the age of six years with a single dose of rectal artesunate10mg/kg and refer immediately to an appropriate facility for further care.

Treatment of severe malaria

Severe malaria is a medical emergency and all patients should be treated as in-patients and provided the highest level of care including intensive supportive care available

Treat all adults including pregnant women in all trimesters and children with severe malaria with intravenous or intramuscular artesunate for a minimum of 3 doses/ or 24hrs.

Give children weighing less than 20 kg 3mg/kg per dose of artesunate.

Heavier children and adults should receive 2.4mg/kg per dose of artesunate.

Once the patient has received at least 24hrs of parenteral therapy, AND is able to tolerate oral therapy, complete treatment with three-days of the first line ACT, AL.

Prevention of malaria in pregnancy

In malaria endemic areas, give Intermittent Preventive Treatment (IPTp) with SP to all pregnant women at every scheduled antenatal visit commencing at the start of the second trimester. Each SP dose should be given at least one month apart.

1. Introduction

1.1 BACKGROUND

Malaria is one of the leading causes of morbidity and mortality, particularly in children under five years of age in Kenya. *Plasmodium falciparum* is the commonest cause of malaria in Kenya. Interventions to control malaria in Kenya have been integrated and include:

- Provision of prompt and effective treatment or malaria case management
- Vector control using long lasting insecticidal nets, indoor residual spraying and other integrated vector management strategies
- Prevention and treatment of malaria in pregnancy
- Epidemic preparedness and response and
- Advocacy, communication and Social mobilization

The provision of prompt and effective treatment is the cornerstone of malaria case management. The treatment policy for malaria has changed in the past due to failing therapeutic efficacy from chloroquine (CQ) to sulphadoxine-pyrimethamine (SP) in 1998 and subsequently to the currently recommended artemisinin-based combination therapies (ACTs) in 2004. ACTs are at present the best treatment for uncomplicated malaria and the efficacy of the treatments recommended in this guideline continue to be monitored regularly.

1.2 OBJECTIVE

The objective of this treatment guideline is to provide the target audience with evidence-based recommendations for the treatment of malaria. Information is shown on the treatment of uncomplicated malaria and severe malaria including disease in special risk groups for example young children and pregnant women as well as chemoprophylaxis for special groups including travellers from non-malaria endemic countries.

1.3 TARGET AUDIENCE

These guidelines are intended for: All health professionals (doctors, nurses, clinical officers, pharmacists and laboratory technologists). Public health and policy specialists working in hospitals, research institutions, medical schools, non-governmental organizations and agencies; working as partners in health or malaria control may also find this guideline useful.

1.4 FORMULATIONS

Only ACTs that are **co-formulated** (both medicines combined in the same tablet) should be used for the treatment of uncomplicated malaria in Kenya. In order for the ACT to provide its

intended benefits of effective treatment and extended useful therapeutic life of both drugs, it is strongly recommended that ACTs should include **at least 3 days of treatment with an artemisinin derivative[1].** Paediatric formulations should be used for infants and children in order to ensure the correct dosing. Where available, child friendly formulations (flavoured / liquefiable by dose) should be used. All other previously used monotherapies including oral artemisinins should not be used for treatment of malaria and will not be licensed for this purpose anymore.

1.5 DIAGNOSIS BASED TREATMENT

Diagnosis of malaria is based on detection of parasites and parasite products in the blood (parasitological or confirmatory diagnosis) following clinical suspicion. It is currently recommended to confirm diagnosis of malaria in all age-groups and in all epidemiological settings. The two methods used routinely for parasitological diagnosis of malaria are microscopy or RDTs. This is done to ensure that patients with fever arising from other causes are managed accordingly and treatment is targeted to patients with confirmed malaria infection.

Efforts are underway to ensure diagnostic tests are available at all levels of the health care system. Under no circumstances should a patient with suspected malaria be denied treatment, or provided with delayed treatment for lack of a parasitological diagnosis.

Parasitological diagnosis of malaria is recommended for all patients with suspected malaria, appropriate **treatment should NEVER be delayed or denied** due to inability to test for malaria.

[1] World Health Organization 2015. *Guidelines for the treatment of malaria 3rd edition.* WHO-GMP Geneva.

2. Malaria in Kenya

Malaria is a disease caused by parasites of the genus *plasmodium*. Nationally, *plasmodium falciparum* is the predominant species (98.2%) while *p. malariae, p. ovale* is 1.8% often occurring as mixed infections. The last three Kenya Malaria Indicator Survey (KMIS) surveys have not identified presence of *p. vivax* in the country.

2.1 EPIDEMIOLOGY OF MALARIA IN KENYA

Kenya has four malaria epidemiological zones, with diversity in risk determined largely by altitude, rainfall patterns and temperature. The zones are:

- ***Endemic:*** Areas of stable malaria have altitudes ranging from 0 to 1,300 metres around Lake Victoria in western Kenya and in the coastal regions. Rainfall, temperature and humidity are the determinants of the perennial transmission of malaria. The vector life cycle is usually short and survival rates are high because of the suitable climatic conditions. Transmission is intense throughout the year, with annual entomological inoculation rates between 30 and 100.

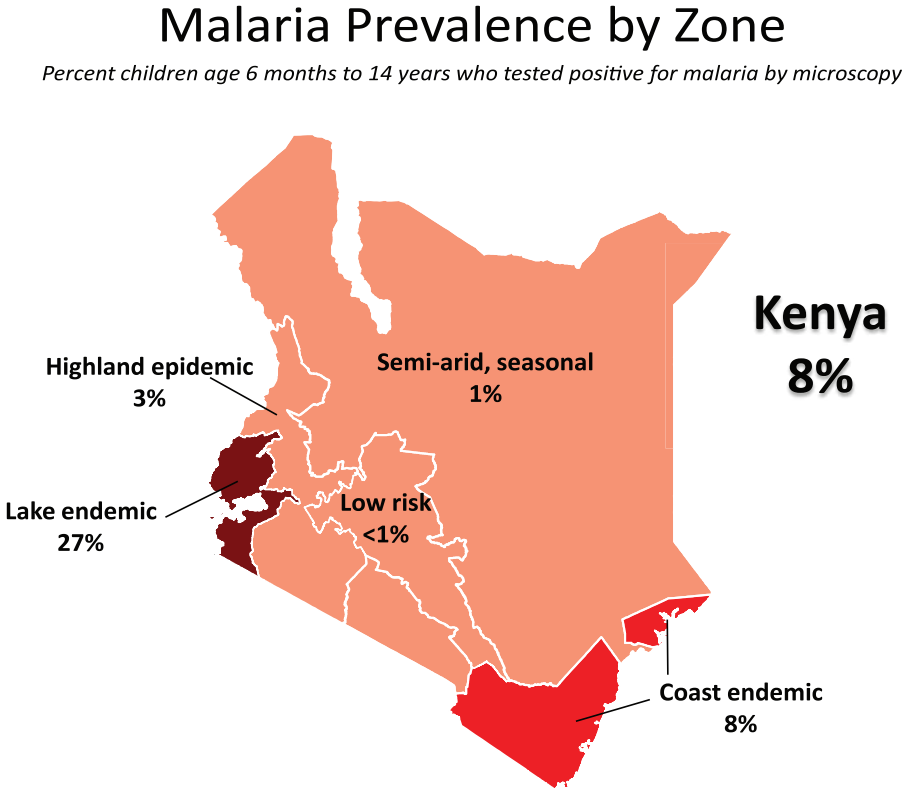
- ***Seasonal transmission:*** Arid and semi-arid areas of northern and south-eastern parts of the country experience short periods of intense malaria transmission during the rainfall seasons. Temperatures are usually high and water pools created during the rainy season provide breeding sites for the malaria vectors. Extreme climatic conditions like the *El Niño* southern oscillation lead to flooding in these areas, resulting in epidemic outbreaks with high morbidity rates owing to the low immune status of the population.

- ***Epidemic prone areas of western highlands of Kenya:*** Malaria transmission in the western highlands of Kenya is seasonal, with considerable year-to-year variation. Epidemics are experienced when climatic conditions favour sustainability of minimum temperatures around 18°C. This increase in minimum temperatures during the long rains favours and sustains vector breeding, resulting in increased intensity of malaria transmission. The whole population is vulnerable and case fatality rates during an epidemic can be up to ten times greater than those experienced in regions where malaria occurs regularly.

- ***Low risk malaria areas:*** This zone covers the central highlands of Kenya including Nairobi. The temperatures are usually too low to allow completion of the sporogonic cycle of the malaria parasite in the vector. However, the increasing temperatures and changes in the hydrological cycle associated with climate change are likely to increase the areas suitable for malaria vector breeding with the introduction of malaria transmission in areas where it had not existed before.

In 2015, a model-based map of the intensity of *p. falciparum* transmission in Kenya as defined by the proportion of infected children aged **6 months -14** years in the community was produced. Based on the malaria risk map and the eco-epidemiology of malaria in Kenya, subcounties have been stratified into four categories: Lake stable endemic & Coast seasonal stable endemic; Highland epidemic-prone subcounties; Seasonal low transmission including arid and Semi arid subcounties; low risk subcounties.

Figure 1: Kenya malaria endemicity map



3. Clinical features and classification of malaria

Malaria can be classified as either uncomplicated or severe based on clinical presentation.

3.1 UNCOMPLICATED MALARIA

This is characterized by fever in the presence of peripheral parasitaemia. Other features may include chills, profuse sweating, muscle pains, joint pains, abdominal pain, diarrhoea, nausea, vomiting, irritability and refusal to feed. These features may occur singly or in combination.

3.2 SEVERE MALARIA

This is a life threatening manifestation of malaria, and is defined as the detection of *p. falciparum* in the peripheral blood in the presence of any one or more of the clinical or laboratory features listed below:

- Prostration (inability or difficulty to sit upright, stand or walk without support in a child normally able to do so, or inability to drink in children too young to sit)
- Alteration in the level of consciousness (ranging from drowsiness to deep coma)
- Cerebral malaria (unrousable coma not attributable to any other cause in a patient with *falciparum* malaria)
- Respiratory distress (acidotic breathing)
- Multiple generalized convulsions (2 or more episodes within a 24 hour period)
- Shock (circulatory collapse, septicaemia)
- Pulmonary oedema
- Abnormal bleeding (Disseminated Intravascular coagulopathy)
- Jaundice
- Haemoglobinuria (black water fever)
- Acute renal failure – presenting as oliguria or anuria
- Severe anaemia (Haemoglobin ≤5g/dl or Haematocrit ≤15%)
- Hypoglycaemia (blood glucose level <2.2mmol/l)
- Hyperlactataemia

4. Parasitological diagnosis of malaria

The recommended confirmatory tests to detect the presence of malaria parasites and parasite products are microscopy or rapid diagnostic tests (RDTs). Quality assurance of microscopy and RDTs is vital for ensuring the reliability of test results.

4.1 MICROSCOPY

- Microscopy is the gold standard method for parasitological diagnosis of malaria. This is performed by examining a stained thick or thin blood smear for the presence of malaria parasites.
- Thick films are recommended for parasite detection and quantification and can be used to monitor response to treatment.
- Thin films are recommended for species identification.
- Quality assurance microscopy should be assured through slide rechecking and proficiency assessments.

4.1.1 Recommended procedure for microscopy

- Make a thick and thin blood film on a clean microscope slide
- Stain using giemsa stain
- Examine under power 100 oil immersion objective lens starting with the thick followed by the thin film
- Report the type of parasite(s) seen, developmental stage and parasite count as parasites per 200 WBCs or parasites per microlitre of blood
- Ensure you always use relevant Standard Operating Procedures (SOPs) for all processes

4.2 RAPID DIAGNOSTIC TESTS

Rapid diagnostic tests (RDTs) are immunochromatographic tests based on detection of specific parasite antigens. Tests which detect histidine-rich protein 2 (HRP2) are specific for *P.falciparum* while those that detect parasite lactate dehydrogenase (pLDH) or aldolase have the ability to differentiate between *P.falciparum* and non-*P.falciparum* malaria (*vivax, malariae and ovale*). With the appropriate training, support supervision and mentorship, RDTs are simple to use and sensitive in detecting low parasitemia RDTs are simple to use and sensitive in detecting low parasitaemia.

The use of RDTs is however not recommended for follow-up of previously confirmed cases as most of the tests remain positive for between 2 to 3 weeks following effective antimalarial treatment and clearance of parasites. RDTs cannot be used to determine parasite density.

When using RDTs, it is important to adhere strictly to the manufacturer's instructions especially the time of reading amount of blood and the test results. Remember to observe safe medical waste disposal at all times. RDTs for use in Kenya are based on the annual recommendations of the WHO.

There is no need to confirm an initial RDT Positive with microscopy. Microscopy should be used for all treatment follow up.

4.2.1 Quality assurance of RDTs

The following key steps are involved in quality assurance of RDTs to ensure quality/ accurate results.

QA process	QA location
GMP in production	Manufacturer
Product evaluation	FIND/WHO
Lot testing (Pre-shipment/post-shipment)	In-country
Positive control wells	At end-user point
Post Market Surveillance	In-country

4.3 OTHER PARASITE DETECTION METHODS

Other parasite detection techniques include:

1. Detection of antibodies to malaria parasites and
2. Detection of parasite DNA, by use of polymerase chain reaction (PCR).

The above two methods are not used for routine clinical management in Kenya. The first is non-specific while the second is highly sensitive and very useful for detecting mixed infections, in particular at low parasite densities. PCR is mainly used in drug efficacy studies.

5. Management of uncomplicated malaria

5.1 DIAGNOSIS

Patients presenting with signs and symptoms of uncomplicated malaria should be tested for malaria. Only those who test positive should be treated for malaria. Patients should also be assessed for other conditions that may cause fever and be managed accordingly.

5.2 TREATMENT OF UNCOMPLICATED FALCIPARUM MALARIA

5.2.1 First line treatment in all age groups

The recommended first line treatment for uncomplicated malaria in Kenya is artemether-lumefantrine (AL). It is currently available as a co-formulated tablet containing 20mg of artemether and 120mg of lumefantrine in varying strengths. Child friendly dispersible tablets are also available. AL is administered as a 6-dose regimen given over three days (See Table 1 below).

Table 1: Dosing schedule for Artemether-lumefantrine

Weight	Age in years	Dose of AL to be administered at 0hrs, 8hrs, 24hrs, 36hrs, 48hrs and 60hrs
0 < 15 kg	0 < 3years	20mg Artemether and 120mg Lumefantrine
15 < 25 kg	3 < 8 years	40mg Artemether and 240mg Lumefantrine
25 < 35 kg	8 < 12years	60mg Artemether and 360mg Lumefantrine
≥ 35 kg	≥12 years	80mg Artemether and 480mg Lumefantrine

- In children below 5kg, if appropriate weight for age, evaluation of other causes of fever including malaria should be undertaken. Where malaria is confirmed, the current recommended treatment is one tablet of AL given according to the schedule in table 1 under close supervision[3].
- For children < 24kg, dispersible tablets should be administered where available. Place the tablet in a cup or spoon, add a little water to it, wait a few minutes for tablets to disperse and then administer the resulting suspension to the child.
- Directly observe the first treatment dose at the health facility.

5.2.3 Counselling and follow up

- Show all caregivers of young children how to prepare the dispersible tablet prior to administration. Ensure she/he understands how to administer the same to the child prior to leaving the facility.

[3] World Health Organization 2015. *Guidelines for the treatment of malaria 3rd edition.* WHO-GMP Geneva.

- If vomiting occurs within 30 minutes after drug administration, the dose should be repeated. And if vomiting persists, the patient should return to the facility for review
- Explain the dosing schedule, use probing questions to confirm the patient's understanding.
- Emphasize that all 6 doses must be taken over 3 days even if the patient feels better after a few doses.
- Advise patients to return immediately to the nearest health facility if the condition deteriorates at any time or if symptoms have not resolved after 3 days.

5.2.4 Supportive treatment

- **Fever management**: Administer paracetamol as the recommended antipyretic for fever. Other methods for reducing temperature like exposure, fanning and tepid sponging may be used.
- **Encourage adequate fluids and food**: Caregivers should be encouraged to give extra fluids and where applicable continue breastfeeding. Food and fluid should be administered in small quantities at frequent intervals especially when the child is still very sick.

5.3 TREATMENT FAILURE

Treatment failure can be defined as a failure to achieve the desired therapeutic response after the initiation of therapy. Treatment failures should be suspected if patient deteriorates clinically at any time or symptoms persists 3-14 days after initiation of drug therapy in accordance with the recommended treatment regimen. Whenever possible, treatment failure must be confirmed parasitologically preferably by blood-slide examination. Use of RDTs is not recommended.[4]

Treatment failure may result from poor adherence to treatment, unusual pharmacokinetic properties in that individual or drug resistance. In evaluating a patient with treatment failure, it is important to determine from the patient's history whether he or she vomited previous treatment or did not complete a full treatment course. Treatment failure is not synonymous with drug resistance.

Development of symptoms 14 days after initiation of therapy where there has been prior clearance of symptoms should be considered as a new infection and be treated with the first line drug.

5.3.1 Management of suspected treatment failure

Confirmed cases of treatment failure should be treated with the 2nd line ACT dihydroartemisinin-piperaquine. Other potential differential diagnosis should be sought for and adequately managed. In centres with no microscopy facilities, patients with suspected treatment failures should be referred. In cases of non-adherence with or non-completion of medicine, repeat a full course of the first line drug.

[4] World Health Organization 2015. *Guidelines for the treatment of malaria 3rd edition.* WHO-GMP Geneva.

5.3.2. Second line treatment in adults and children of all age groups

There commended secondline treatment for uncomplicated malaria in Kenya is dihydroartemisinin-piperaquine(DHA-PPQ).This is currently available as a fixed-dose combination with adult tablets containing 40mg of dihydroartemisinin and 320mg of piperaquine and paediatric tablets containing 20mg dihydroartemisinin and160mg of piperaquine.These are administered once daily for three days as shown in table2 below.

Therapeuticdose and range: A target dose(range) of 4(2-10)mg/kg bw/day of dihydroartemisinin and 18 (16-27) mg/kg bw/day of piperaquine once a day for 3 days for adults and children weighing ≥ 25kg. The target dose and ranges for children weighing <25kg are 4 (2.5-10) mg/kg bw/day dihydroartemisinin and 24 (20-32)mg/kg bw/day piperaquine once a day for 3 days.

Children weighing <25kg treated with dihyroartemisinin+piperaquine should receive a minimum of 2.5mg/kg bw per day of dihydroartemisinin and 20mg/kg bw per day of piperaquine daily for 3 days.

Table 2: Dosing schedule for dihydroartemisinin-piperaquine

Body weight (kg)	Dihydroartemisinin + piperaquine dose (mg) given daily for 3 days
5 to <8	20 + 160
8 to <11	30 + 240
11 to <17	40 + 320
17 to <25	60 + 480
25 to <36	80 + 640
36 to <60	120 + 960
60 <80	160 + 1280
>80	200 + 1600

5.4 TREATMENT OF UNCOMPLICATED *VIVAX* MALARIA

The recommended treatment for vivax malaria is AL. It is vital to have confirmed lab diagnosis of *p. vivax* malaria before commencing treatment. Unlike *p. falciparum, p. vivax* has dormant liver stages which require treatment. In order to achieve a radical cure and prevent relapses, Primaquine, must also be given. Primaquine causes abdominal discomfort when taken on an empty stomach; it should always be taken with food. Primaquine may also cause haemolysis in patients with glucose-6-phosphatase dehydrogenase (G6PD) deficiency. Stop treatment immediately bleeding is observed.

Therapeutic dose: Primaquine dose ranges between 0.25 and 0.5mg/kg/day once a day for 14 days.

In mild-to-moderate G6PD deficiency, Primaquine 0.75 mg base/kg body weight should be given once a week for 8 weeks. In severe G6PD deficiency, primaquine is contraindicated

and should not be used.

The decision to give or withhold Primaquine should depend on the posibility of giving the treatment under close medical supervision, with ready access to health facilities with blood transfusion services.

5.5 M & E INDICATORS

i. Proportion of patients with fever presenting to health facility who are managed in accordance with national malaria treatment guidelines.

ii. Proportion of patients presenting to health facility with fever and ACT prescribed, to whom counselling and ACT dispensing tasks were performed according to national guidelines.

iii. Number of confirmed malaria cases treated with ACT.

6. Management of severe malaria

Severe malaria is a medical emergency and should be managed in a facility with inpatient services. In the absence of this, pre-referral management should be initiated and patients referred to facilities that are able to comprehensively manage the patients. (Refer to section 6.5). Delay in diagnosis and inappropriate treatment, especially in infants, children and non-immune adults leads to rapid deterioration of the situation which is often fatal. The key to effective management is early recognition, assessment, appropriate antimalarial and supportive therapy. The commonest cause of severe malaria is *p. falciparum.* In rare circumstances *p.vivax* may also manifest as severe disease.

6.1 DIAGNOSIS

The clinical manifestations of malaria severity depend on various factors including age and the levels of malarial immunity. In children the common presentations of severe malaria are severe anaemia, respiratory distress and cerebral malaria. Severe malaria can occur in the absence of fever. An outline of the presentations, their frequency of occurrence is summarized in the table below.

6.1.1 Clinical features of severe *falciparum* malaria

The clinical features of severe malaria are outlined in Table 3.

Table 3: Signs and symptoms of severe malaria in adults and children

Sign or symptom	Adults	Children
Duration of illness	5-7 days	Shorter (1-2 days)
Respiratory distress/ deep breathing (acidosis)	Common	Common
Convulsions	Common (12%)	Very common (30%)
Posturing (decorticate/decerebrate and opisthotonic rigidity)	Uncommon	Common
Prostration/obtundation	Common	Common
Resolution of coma	2-4 days	Faster (1-2 days)
Neurological sequelae after cerebral malaria	Uncommon (1%)	Common (5-30%)
Jaundice*	Common	Uncommon
Hypoglycaemia*	Less common	Common
Metabolic acidosis*	Common	Common
Pulmonary oedema	Uncommon	Rare
Renal failure*	Common	Rare
CSF opening pressure*	Usually normal	Usually raised
Bleeding/clotting disturbances*	Up to 10%	Rare
Invasive bacterial infection (co-infection)*	Uncommon (<5%)	Common (10%)

*Laboratory confirmation required

For epidemiological purposes, severe malaria is defined as one or more of the following parameters, occurring in the absence of an identified alternative cause and in the presence of *p. falciparum* asexual parasitaemia.

Table 4: Clinical Parameters

Clinical state	Definition
Impaired Consciousness	Glasgow coma scale <11, Blantyre coma Scale <3 in children
Prostration	Generalized weakness so that the person is unable to sit, stand or walk without assistance
Multiple convulsions	More than 2 episodes within 24 hours
Pulmonary oedema	Radiologically confirmed oxygen saturation <92% on room air with respiratory rate >30/minute often with chest indrawing and crepitations on auscultations.
Significant bleeding	Including recurrent or prolonged bleeding from the nose, gums or venepuncture sites; haematemesis or malaena
Shock	Compensated shock is defined as capillary refill≥3s or temperature gradient on leg (mid to proximal limb), but no hypotension. Decompensated shock is defined as systolic blood pressure <70mmHg in children or 80mmHg in adults, with evidence of impaired perfusion (cool peripheries or prolonged capillary refill).

Table 5: Clinical Chemistry Parameters

Laboratory parameters	Definition
Acidosis	A base deficit of >8mEq/L or, if not available, plasma bicarbonate level<15mmol/L or venous plasma lactate ≥5mmol/L. Severe acidosis manifests clinically as respiratory distress (rapid, deep, labored breathing).
Hypoglycaemia	Blood or plasma glucose <2.0mmol/L (<40mg/dL)
Severe malaria anaemia	Haemoglobin concentrations ≤5g/dL or haematocrit of ≤15% in children<12 years of age (<7g/dL and <20%, respectively in adults) with a parasite count >10,000/µL
Renal impairment	Plasma or serum creatinine >265 µ/L (3g/dL) or blood urea >20mmol/L
Jaundice	Plasma or serum bilirubin >50 µ /L (3mg/dL) with a parasite count of 100,000/ µL
Hyperparasitaemia	Plasmodium falciparum >10%

- In all patients with suspected severe malaria the use of parasitological diagnosis is recommended irrespective of whether the patient had fever or history of fever
- Do not withhold antimalarial treatment if parasitological diagnosis is not possible. Start presumptive treatment immediately while efforts to confirm diagnosis are ongoing.
- Frequent monitoring of the parasitemia (every 12 hours) is important during the first three days of treatment in order to monitor parasite response to treatment with antimalarial medicine. A negative RDT result may be indicative of another cause of infection.
- Other investigations to determine severity and prognosis to be undertaken where feasible.

In all suspected cases of severe malaria, a parasitological diagnosis of malaria is recommended. In the absence of or delay in obtaining a parasitological diagnosis, patients should be treated for severe malaria on clinical grounds.

6.1.2 Clinical features of severe *p. vivax* malaria

Severe *vivax* malaria may present with some symptoms similar to those of severe *p. falciparum* malaria and can be fatal. Prompt and effective treatment and follow-up should be the same as for severe *falciparum* malaria.

6.2 EVALUATION OF SOME CLINICAL MANIFESTATIONS

Along with other clinical and laboratory evaluation for severe malaria, the following are to be undertaken as the minimal investigation package for the different clinical scenarios described below:

6.2.1 Cerebral malaria

Clinical assessment

a. Assess level of consciousness using coma score (Annex 4).
b. Determine the presence of severe anaemia by examining for pallor on the palms and conjunctiva.
c. Determine presence of respiratory distress (deep and fast breathing, chest in-drawing).
d. Determine hydration status (check for sunken eyes, loss of skin stugor, dry tongue and measuring blood pressure).
e. Assess for renal insufficiency (oliguria).
f. Assess for evidence of disseminated intravascular coagulopathy (spontaneous bleeding from the gums, injection sites, or any other site.
g. Check for clinical signs of meningitis (stiff neck, Kernig's sign in children, photophobia) cerebral malaria does not cause menigism although patients may present with opisthotonus.

Laboratory Tests

Eliminate other causes of alteration in the level of consciousness including Cerebral Spinal Fluid (CSF) analysis to rule out meningitis, blood glucose levels to rule out hypoglycaemia, and other common causes of coma.

6.2.2 Severe anaemia

Clinical assessment

a. Determine the presence of severe anaemia by examining for pallor on the palms and conjunctiva.
b. Determine presence of respiratory distress (deep and fast breathing, chest in-drawing).
c. Assess for evidence of disseminated intravascular coagulopathy (spontaneous bleeding from the gums, injection sites, or any other site).
d. Assess for evidence of cardiac failure (respiratory distress, tachycardia, peripheral oedema).

Laboratory tests

a. Determine haemoglobin levels, Packed Cell Volume (PCV), peripheral blood film assessment and blood group and cross match where applicable.
b. Liver Function Tests (LFTs), Renal Function Tests and Blood Culture.

6.2.3 Hypoglycaemia

Clinical assessment

Assess the level of consciousness

Laboratory test

Determine the blood glucose level.

6.3 TREATMENT OF SEVERE MALARIA

The recommended treatment for severe malaria is **parenteral artesunate**. The preferred route of administration is intravenous (IV). However intramuscular (IM) can be used as an alternative where the intravenous route is not feasible. In the absence of artesunate, parenteral quinine or IM artemether should be administered.

6.3.1 Artesunate

Artesunate is dispensed as a powder of artesunic acid. This must be dissolved in sodium bicarbonate (5%) to form sodium artesunate. The solution is then diluted in approximately 5ml of normal saline and given by intravenous(IV) injection or by intramuscular(IM) maximum 5ml per site. The solution should be freshly prepared prior to administration and should be used within 1hour. The solution should NEVER be stored.

Administer artesunate as follows:

Dosage:

- For children <20kg administer 3.0 mg/kg
- For patients >20kg administer 2.4 mg/kg
- A dosing schedule for parenteral artesunate based on body weights and dose (ml) is given in Annex 3: Table 21

Administer Artesunate as follows:

6.3.1.1 Intravenous

- Intravenous route is preffered.
- Weigh the patient to determine the dosage needed and therefore the number of vials required.
- Dissolve each vial of artesunic powder with all the 5% sodium bicarbonate solution provided with each vial. Shake gently until the resultant solution is clear.
- Dilute resultant solution in each vial with 5ml normal saline or 5% dextrose*.
- The final solution has a strength of 10mg/ml.
- Calculate the volume of solution containing the required amount to be given see *skill on calculation of artesunate pg 64*.
- Administer by slow IV over 3-5 minutes.

6.3.1.2 Intramuscular

- Weigh the patient to determine the dosage needed and therefore the number of vials required.
- Dissolve each vial of artesunic powder with all the 5% sodium bicarbonate solution provided with each vial. Shake gently until the resultant solution is clear.
- Dilute resultant solution with 2ml normal saline or 5% dextrose*.
- The final solution has a strength of 20mg/ml.
- Calculate the volume of solution containing the required amount to be given see *skill on calculation of artesunate pg 64*.
- Administer by IM route.
- Spread the doses of more than 2ml over different sites for babies and 5ml for adults.

* This refers to 60mg artesunate. For all other strengths refer to product insert for diluent volume.

Artesunate should be administered at 0hrs, 12hrs, 24hrs, then once a day until patient can take orally (Maximum of 7 days). When the patient can take orally give a full course of AL. The first dose of AL should be administered 8 to12 hours after the last injection of artesunate. **Water for injection is not an appropriate diluent.**

Artesunate powder

Sodium Bicarbonate solution

Saline Solution

6.3.2 Artemether

Artemether is dispensed as a clear oily solution of differing concentrations. Artemether must only be given by intramuscular(IM) injection.

<u>Administer artemether as follows:</u>

- Artemether is administered by the intramuscular route at a loading dose of 3.2mg/kg IM stat then 1.6mg/kg IM once every 24 hrs until the patient is able to tolerate oral medications (Maximun of 7 days).
- Thereafter a complete course of artemether-lumefantrine is given.

6.3.3 Quinine administration

- Quinine should only be given as an intravenous infusion and **NEVER** given as an intravenous (bolus) injection.
- Loading dose should be omitted if patient have received quinine in the last 24 hours or have received mefloquine in the last 7 days.
- Quinine is not contraindicated in severe anaemia.
- In renal insufficiency the dose of quinine should be reduced by a ⅓ rd to 10mg/kg every 12hours.
- In hepatic insufficiency, the dose of quinine should be reduced by 25%. Hypoglycaemia is a potential side effect of quinine administration particularly in pregnant women and should therefore be administered in a glucose containing infusion.

6.3.3.1 Quinine administration in children

Give child doses every 8 hours to standadise practice and comply with WHO guidelines.

Administer quinine as follows:

- Put up IV quinine drip 20mg/kg body weight loading dose in 15mls/kg of 5% dextrose or normal saline to run over 4 hours to run at a rate not exceeding 5mg salt/kg bodyweight per hour.
- Calculate the number of drops per minute to deliver the quinine in 4 hours - see *skill on calculation of drops/min pg 61*.
- 8 hours from commencement of the initial dose of quinine, give 10mg/kg in 10ml/kg of isotonic solution (5% dextrose or normal saline) to run at the same rate as the previous one.
- Repeat 10mg/kg quinine infusion every 8 hours until the patient can take medication orally. Thereafter give a complete course of artemether-lumefantrine (AL).
- Alternatively, treat with oral quinine given at 10mg/kg every 8 hours to complete a total of 7 days.

6.3.3.2 Quinine administration in adults

Administer quinine as follows:

- A loading dose of quinine 20mg/kg (maximum 1,200mg) diluted in 15ml/kg (maximum 500ml) of isotonic solution (5% dextrose or normal saline) is given intravenously to run over 4 hours to run in a way not to exceed 5mg salt/kg body weight per hour.
- Calculate the number of drops per minute to deliver the quinine in 4 hours - see *skill on calculation of drops/min pg 61*.
- 8 hours from commencement of the initial dose of quinine, give 10mg/kg (maximum 600mg) diluted in 10ml/kg (maximum 500ml) of isotonic solution (5% dextrose or normal saline) to run over 4 hours at the same rate as previous one.
- Repeat 10mg/kg quinine infusion every 8 hours until the patient can take medication orally.
- Thereafter a complete course of artemether-lumefantrine (AL) is given.
- Alternatively oral quinine is continued at 10mg/kg (maximum 600mg) every 8 hours to complete a total of 7 days treatment, in combination with clindamycin or doxycycline also for 7 days.

In the absence of injectable artemisinins or quinine, patients, particularly children with severe malaria who are able to tolerate orally, should be given AL or other available ACT to initiate treatment. If the patient is unable to take oral medications, a **nasogastric tube** should be used to administer AL.

Note: In the case of severe *p.vivax* malaria, once the patient has completed treatment, a full dose of primaquine should be administered to clear liver stages.

6.3.4 Severe malaria patients who may be able to tolerate oral treatment

Patients with the following features:

- Severe anaemia (haemoglobin level of <5g/dl or haematocrit of <15%, or
- Two or more convulsions within a 24hr period, or
- Hyperparasitaemia and who are stable but show none of the features of prostration, respiratory distress (acidotic breathing) or alteration in the level of consciousness:

Can be treated with AL, DHA-PPQ, or oral quinine where ACT is not available. They should however be treated as in-patients for close monitoring. Thus any emerging complications of severe malaria should be managed promptly and appropriately.

6.4 SUPPORTIVE TREATMENT

Supportive treatment is crucial in reducing the high mortality associated with severe malaria. The table below highlights specific management for manifestations or complications of severe malaria.

Table 6: Supportive treatment for manifestations of severe malaria

Manifestation/Complication	Immediate Management[a]
Coma (cerebral malaria)	Maintain airway, place patient on their side, manage other treatable causes of coma; avoid harmful ancillary treatment, such as corticosteroids, heparin and adrenaline; intubate if necessary. Provide proper nursing care to avoid aspiration and pressure sores.
Hyperpyrexia	Administer tepid sponging, fanning, a cooling blanket and antipyretic drugs (Paracetamol is preferred).
Convulsions	Maintain airways; treat promptly with: Diazepam (0.3mg/kg IV, or 0.5mg/kg by rectal administration) or phenobarbitone (15mg/kg IM loading dose then a maintenance dose of 4-8mg/kg/day for 48 hours) if convulsions persist. Phenytoin (18mg/kg loading dose then maintenance dose of 5mg/kg/day for 48 hours) may be used instead of phenobarbitone. Check blood glucose and control temperature.
Hypoglycaemia	Check blood glucose, correct hypoglycaemia with glucose (IV or oral), and ensure adequate caloric intake (nutritional support) thereafter. Hypoglycaemia (≤3mmol/l) should be corrected with 500mg/kg of glucose. Using parenteral dextrose, immediately give 5ml/kg of 10% dextrose through a peripheral line, followed by a slow intravenous infusion of 5 ml/kg per hour of 10% or 10ml/kg per hour of 5% to prevent recurrence of hypoglycaemia.
Severe anaemia	Transfuse with screened fresh whole blood as per national blood transfusion guidelines[B]. With paediatric patients transfuse for severe malarial anaemia when Hb<4g/dl and that if Hb is between 4-5g/dl. Transfuse if signs of respiratory distress or cardiac failure are present.

Manifestation/Complication	Immediate Management[a]
Fluid and electrolyte imbalance	Ensure adequate fluid and electrolyte balance. Note that strict fluid management is vital in the comatose patient. Fluid used in administration of antimalarials and any other transfusions (e.g. blood transfusion) must be calculated as part of the total fluid requirement of the patient.
Acute pulmonary oedema[c]	Prop patient up at an angle of 45°, give oxygen, give a diuretic, stop intravenous fluids, intubate and add positive end-expiratory pressure/ continuous positive airway pressure in life-threatening hypoxaemia.
Acute renal failure	Exclude pre-renal causes, check fluid balance and urinary sodium; if in established renal failure refer for specialised care.
Spontaneous bleeding and coagulopathy	Transfuse with screened fresh whole blood (cryoprecipitate, fresh frozen plasma and platelets, if available); give vitamin K injection.
Metabolic acidosis	Exclude or treat hypoglycaemia, hypovolaemia and septicaemia. If severe, refer for haemofiltration or haemodialysis.
Shock	Suspect septicaemia, take blood for cultures; give parenteral broad-spectrum antimicrobials, correct haemodynamic disturbances.

a. It is assumed that appropriate antimalarial treatment will have been started in all cases.
b. http://www.fhi360.org/sites/default/files/media/documents/Guidelines%20for%20the%20Appropriate%20Use%20of%20Blood%20and%20Blood%20Products.pdf.
c. Prevent by avoiding excess hydration.

6.5 PRE-REFERRAL MANAGEMENT OF SEVERE MALARIA

Since severe malaria is a medical emergency, treatment of a patient with severe malaria should begin in the primary health facility (while waiting for referral) so that life-saving therapy is not delayed.

The risk for death from severe malaria is greatest in the first 24 hours, therefore, upon recognition of severe malaria, pre-referral treatment should be initiated at the peripheral facility using IM artesunate or rectal artesunate. In the absence of artesunate, IM artemether should be used. All efforts should be made to move the patient to a centre where the expertise and infrastructure exist for the adequate management of severe malaria.

In patients with alteration in the levels of consciousness, parenteral antibiotics (ceftriaxone) should also be administered along with the antimalarial.

If for any reason referral is not possible or delayed, treatment for severe malaria with the use of IM artesunate should be continued. Health workers at such facilities should ensure that treatment continues until the patient **PHYSICALLY** moves to another facility.

NOTE
It is not enough to give a referral letter and assume that the patient has been referred. The referral letter should be as comprehensive as possible and a health worker should accompany the referred patient.

6.5.1 Administration of parenteral artemisinins

- Artesunate is dispensed as a powder of artesunic acid. This must be dissolved in 5% sodium bicarbonate (diluent) to form sodium artesunate. (Refer to 6.3.1.2 for administration instructions).

6.5.2 Administration of rectal artesunate

- Artesunate for rectal administration is presented in suppositories of different strengths. The appropriate single dose of artesunate should be administered.
- In the event that a suppository is expelled from the rectum within 30 minutes of insertion, a second suppository should be inserted. In young children the buttocks should be held together for 10 minutes to ensure retention of the rectal dose of artesunate. Patients should be transported immediately to a higher level facility where IM or IV treatment is possible. In the event that referral is not possible a single daily dose of artesunate should be administered until parenteral treatment or oral AL is instituted.
- A single dose of 10mg/kg body weight should be given to children <6 years and only when intramuscular artesunate is not available.

6.5.3 Administration of intramuscular quinine

- Quinine **MUST** be diluted (maximum concentration is 100mg/ml for adults, and 50mg/ml for children) before intramuscular injection.
- A loading dose of 20mg/kg of quinine (diluted to a maximum 100mg/ml for adults and 50mg/ml for children) is given by intramuscular injection (preferably into the anterior thigh). A maximum of 3ml should be injected into one site. If the amount to be injected exceeds 3ml, multiple sites should be used.
- An example of body weights and doses (ml) of injection is given in Annex 3, Table 20).
- Administer a stat dose of 3.2mg/kg of artemether solution by the intramuscular route to the anterior thigh.

6.5.4 Referral of the patient

- Send a clear letter or referral form about the clinical picture, including dosages, times, and route of administration for any medications given.
- Carry all blood film examination or slides (if these have been taken) to be sent along with the patient to the referral centre.
- Send potential blood donors.
- Ask the guardian to keep the child lying down on their side during the journey.
- Accompany or ask a fellow health worker to accompany the patient to the referral centre.

6.6 FOLLOW-UP OF ALL PATIENTS WITH SEVERE MALARIA

- Monitor for possible complications and manage accordingly.
- Monitor Hb levels and give haematinics as appropriate.
- Monitor and rehabilitate patients with neurological sequelae.

7. Malaria in pregnancy

Pregnancy increases the risk of malaria infection in all women. Malaria during pregnancy causes febrile illness, anaemia and increases the risk of maternal illness and death, miscarriage, stillbirth, low birth weight and neonatal death. All pregnant women living in malaria risk areas should be advised on malaria prevention measures and clinical cases of malaria treated promptly with effective antimalarials. Women in their first and second pregnancies, and all HIV infected women are at greatest risk of the effects of malaria.

7.1 MANAGEMENT OF UNCOMPLICATED MALARIA

7.1.1 Diagnosis

Table 7: Symptoms and signs of uncomplicated malaria in pregnant women

TYPE OF MALARIA	SIGNS AND SYMPTOMS USUALLY PRESENT	SIGNS AND SYMPTOMS SOMETIMES PRESENT
Uncomplicated malaria	Fever Shivering/chills/rigors Headache Muscle/joint pain nausea and vomiting False labor pain (uterine contractions)	Enlarged spleen

- In all pregnant women with fever or history of fever the use of parasitological diagnosis is recommended.
- At health facilities where malaria diagnostics (microscopy or RDT) are not available, patients suspected to have malaria should be treated for malaria.

Pregnant women at most risk of malaria infection
- First or second pregnancy in malaria endemic areas.
- Immigrants or visitors from areas of low or no malaria transmission.
- HIV infected.

7.1.2 Treatment

7.1.2.1 First trimester

The recommended treatment for uncomplicated malaria in the first trimester is a 7-day therapy of oral quinine. Do not withhold artemether-lumefantrine or any other treatment in 1st trimester if quinine is not available. Malaria if untreated can be fatal to the pregnant woman.

7.1.2.2 Second and third trimesters

Artemether-lumefantrine is the recommended treatment in the 2nd and 3rd trimesters. Oral quinine may also be used but compliance must be ensured. Dose regimens for quinine and AL are as given in the uncomplicated malaria section.

7.1.3 Supportive care

- Prevent hypoglycaemia (particularly if taking quinine).
- Foetal monitoring.
- Treatment of anaemia[5].
- Antipyretics.

7.1.4 Follow-up management

Antenatal Care[6]

7.2 MANAGEMENT OF SEVERE MALARIA IN PREGNANCY

Severe malaria in pregnancy is a medical emergency that puts the lives of both the mother and unborn baby at high risk. Aggressive management is essential.

7.2.1 Diagnosis

Features of severe malaria in pregnant women are similar to those in non-pregnant women. These are detailed in Section 6.1.1. Pregnant women have an increased risk of quinine induced hypoglycaemia and also complications from severe anaemia.

Table 8: Symptoms and signs of severe malaria in pregnant women

TYPE OF MALARIA	SIGNS AND SYMPTOMS SOMETIMES PRESENT	SIGNS AND SYMPTOMS USUALLY PRESENT
Severe	Symptoms and signs of uncomplicated malaria plus one or more of the following: • Confusion, drowsiness, coma • Fast breathing/breathlessness/ difficulty in breathing • Vomiting at every feed or unable to feed • Pale conjuctivae, mucous membranes, tongue and palms • Jaundice	• Convulsions • Severe jaundice • Signs of severe dehydration, especially if woman has been vomiting repeatedly • Sudden weight loss • Sunken eyes • Reduced skin turgor • Dry mouth • Reduced amount of urine or no urine at all • Spontaneous bleeding from the gums, skin and vein puncture sites

[5] All pregnant women should receive an iron supplementation during ANC as part of the prevention of anaemia.
[6] IPTp with SP should be prescribed in high transmission areas and LLINs given during the ANC visit to all pregnant women.

Table 9: Convulsions in pregnancy

Eclampsia is a differential diagnosis in pregnant women presenting with convulsions or alteration in level of consciousness. In which case the table below should be used to differentiate between the two.

SIGNS/SYMPTOMS	SEVERE MALARIA	ECLAMPSIA
Recent history of fever, chills (from patient or family)	Yes	No
Temperature	>38°C	<38°C
Blood pressure	Diastolic < 90mm hg	Diastolic often ≥ 90mm hg
Enlarged spleen	Yes	No
Jaundice	Yes	No

Additionally, check for protein in urine which commonly occurs in Eclampsia.

Parasitologically confirm diagnosis in ALL suspected cases of severe malaria in pregnancy. If such confirmation is missing or delayed, start treatment for severe malaria immediately

7.2.2 Treatment

The recommended medicine for severe malaria in pregnancy is parenteral artesunate. In the absence of artesunate, artemether or quinine can be given. The preferred route of administration is intravenous for artesunate. However the intramuscular route can be used as an alternative where intravenous route is not feasible. Due to the increased risk of hypoglycaemia in pregnant women, a dextrose containing solution must be used for quinine administration.

NOTE:
Pregnancy is not a contraindication for the use of a loading dose of quinine

7.2.3 Pre-referral treatment for severe malaria in pregnancy

- Treatment of a patient with severe malaria should begin in the primary health facility (while waiting for referral) so that life-saving therapy is not delayed.
- Management of severe malaria in pregnancy should follow the adult dosing for artesunate. Where artesunate is not available, artemether can be administered. Management of severe malaria in pregnancy should follow the adult dosing for artesunate. A loading dose of artesunate at 2.4mg/kg body weight should be administered.
- All efforts should be made to move the patient to a centre where the expertise and infrastructure exist for the adequate management of severe malaria.
- In patients with alteration in the levels of consciousness, a parenteral antibiotic (ceftriaxone) should also be administered along with the antimalarial.

- It is not enough to give a referral letter and assume that the patient has been referred. A health worker should accompany the referred patient to the next level of health care.

7.3 PREVENTION OF MALARIA IN PREGNANCY

The goal of prevention of malaria in pregnancy is to reduce maternal and perinatal morbidity and mortality associated with malaria. The strategies in prevention of malaria in pregnancy are integrated into the overall antenatal care (ANC) package for maternal health. They include the provision of:

- Intermittent preventive treatment for malaria in pregnancy (IPTp).
- Long lasting Insecticidal Nets.
- Provision of prompt diagnosis and treatment of fever due to malaria.
- Health education.

7.3.1 Intermittent preventive treatment of malaria in pregnancy (IPTp)

IPTp is the presumptive (regardless of whether the woman is infected or not) provision of a full treatment course of the recommended antimalarial at specific intervals during pregnancy. IPTp has been shown to reduce the risk of placental infection and the associated risk of maternal anaemia, miscarriage, premature deliveries and low birthweight. The current recommended medicine for IPTp of sulphadoxine 500mg and pyrimethamine 25mg (SP).

- IPTp is recommended in areas of high malaria transmission.
- Administer IPTp with each scheduled visit starting as early as possible in the second trimester
- Women should receive a minimum of three doses of SP during Pregnancy
- IPTp should be given at an interval of at least 4 weeks (1 month).
- IPTp should be given under directly observed treatment (DOT) in the antenatal clinic and can be given on an empty stomach.
- SP as IPTp is safe up to term *(40 weeks pregnancy)* and even one dose is beneficial for women presenting late in pregnancy.
- Low dose Folic acid 0.4mg is recommended during pregnancy and can be given together with SP. If low dose folic acid is not available, high dose folic acid (5mg) tablets should NOT be administered with SP given for IPTp and if need be, may be taken 14 days following administration of IPTp.

Always ask the mother if she is allergic to sulpha-drugs or has experienced side effects to sulpha drugs before giving SP.

7.3.1.1 IPTp and HIV+ pregnant women

HIV infection during pregnancy increases the risk of the complications of malaria in pregnancy while malaria infection during pregnancy particularly placental malaria

increases the risk of mother to child transmission of HIV.

- Pregnant women who are HIV positive and are on daily cotrimoxazole chemoprophylaxis should not be given SP for IPTp.

7.3.2 Long Lasting Insecticidal Nets (LLINs)

- LLINs are key in the prevention of malaria in pregnancy.
- Each pregnant woman living in a malaria risk area should receive a LLIN at the first contact visit to the ANC.
- Each pregnant woman should be shown how to hang the LLIN correctly and encouraged to use the net each and every night during her pregnancy and thereafter.
- LLINs are not a substitute for IPTp and vice versa. Both must be used in order to achieve maximal benefits in the reduction of both maternal and perinatal morbidity and mortality.

7.3.3 Health education

- Continuous maternal health education should be provided at the ANC encouraging use of all interventions and services and encouraging the pregnant woman to attend all ANC visits as scheduled.

8. Basic techniques in managing malaria medicines

8.1 CONCEPT OF ESSENTIAL DRUGS

The WHO defines essential drugs as those that satisfy the health care needs of the majority of the population; they should therefore be available at all times in adequate amounts and in appropriate dosage forms, at a price the community can afford. Antimalarials are "essential medicines".

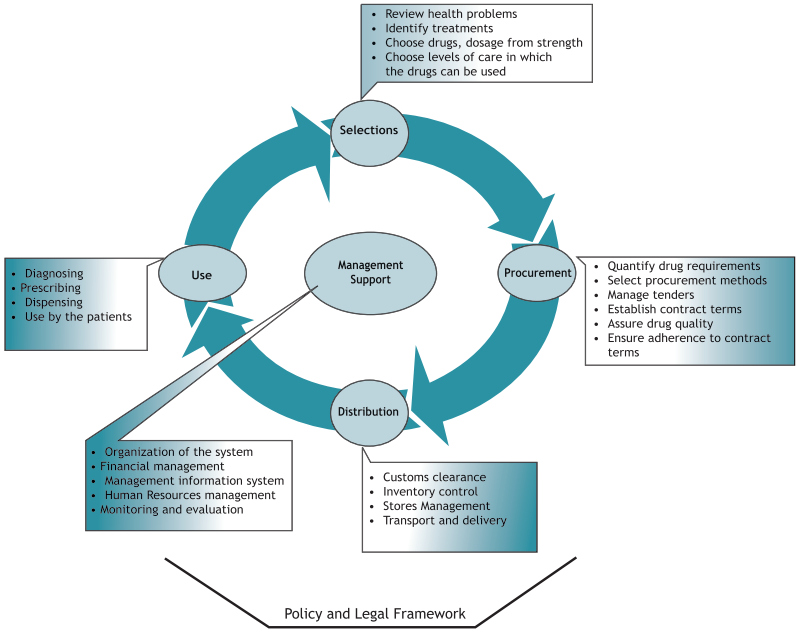
8.1.1 Pharmaceutical management

Pharmaceutical management is a set of practices aimed at ensuring the timely availability and appropriate use of safe, effective, quality medicines and related products and services in any health-care setting.

8.1.2 The Pharmaceutical Management Cycle[7]

The Pharmaceutical Management Cycle is a systematic approach to ensure that medicines at all levels of health care delivery are consistently available and appropriately used. It emphasizes the connections between four drug management activities - selection, procurement, distribution and use. The cycle is depicted below:

Figure 2: The Pharmaceutical Management Cycle



[7] The cycle was developed by the Management Sciences for Health Centre for Pharmaceutical Management in collaboration with the World Health Organization's Action Program on Essential Drugs.

8.2 QUANTIFICATION OF ANTIMALARIAL MEDICINES

Quantification is the process of estimating the quantities of antimalarials needed for a specific period of time in order to ensure an uninterrupted supply. Quantification is an important step in procurement and ordering for re-supply. Good quantification ensures the appropriate allocation of funds to enable purchase of the right medicine in the right quantity at the right time.

8.2.1 The rationale for quantification of antimalarials

- To ensure that there are sufficient quantities to meet clients' / patients' needs and avoid shortages/stock-outs.
- To avoid surpluses that may lead to over-stocking, expiries and/or wastage of commodities.
- To make informed adjustments to procurement when faced with budgetary constraints.

8.2.2 Quantification methods

This guideline focuses attention on the two most commonly used methods— consumption and morbidity. The particular method used depends on the type of data available.

8.2.2.1 Consumption method

This is the currently recommended quantification method for antimalarials. The consumption based method uses historical data on the actual medicines dispensed to patients to calculate the quantity of medicines that will be needed in the future. When using the consumption method for quantification, out of stock periods must be factored into the calculation.

8.2.2.2 Morbidity method

The morbidity-based method uses data about diseases and the frequency of their occurrence in the population (incidence or prevalence) or the frequency of their presentation for treatment. It forecasts the quantity of drugs needed for the treatment of specific diseases, based on projections of the incidence of those diseases.

8.2.3 Good inventory management

An inventory management system is a cycle of activities comprising ordering, receiving, storage and issuing of commodities.

8.2.4 Definitions of inventory terms

- **Average monthly consumption**: This refers to the average quantity of commodities consumed per month.
- **Months of stock:** The quantity on hand expressed as the number of months that quantity should last. It is calculated based on the commodity's average monthly consumption.

- **Lead time:** The time interval between when a new stock is ordered and when it is received and available for use.
- **Review period:** The routine interval of time between assessments of stock levels to determine if an order should be placed. It is also known as order interval or resupply interval.
- **Maximum stock level:** The amount of stock above which a facility should not exceed under normal circumstances, a maximum of 6 months of stock.
- **Minimum stock level:** The amount of stock below which a facility should not fall under normal circumstances, a minimum of 3 months of stock.
- **Shelf life:** The length of time a product may be stored without compromising its usability, safety, purity or potency.
- **Pipeline:** The entire chain of storage facilities and transportation links through which supplies are moved from manufacturers to clients
- **Stock out days:** The number of days that the commodity is not in stock.

8.2.4.1 Ordering

The facility should order supplies periodically from the central medical store using a standard order form. The formula below is used to derive the amount of medicines to order:

Quantity to Order = (Average Monthly Consumption X review period in months) less stock on hand

8.2.4.2 Receiving

The facility should counter-check commodities received against the standard order form and delivery note, and record the receipts on a stock/bin card.

8.2.4.3 Storage

Malaria medicines and commodities such as RDTs should be stored under optimal conditions to ensure their safety and efficacy in accordance with the principles of good storage practices:

- Good arrangement.
- Quality maintenance (appropriate temperature, light and humidity).
- Assured security.
- Good inventory control and stock rotation (First in First Out/First Expiry First Out).
- Good record keeping.

8.2.4.4 Issuing

The facility should issue supplies to various points of use, using an issue/requisition voucher (S11/S12) and must record the issue on the bin card.

8.2.4.5 Disposal

Disposal of unusable stock should be carried out according to the guidelines for disposal of pharmaceuticals and biosafety guidelines for medical waste.

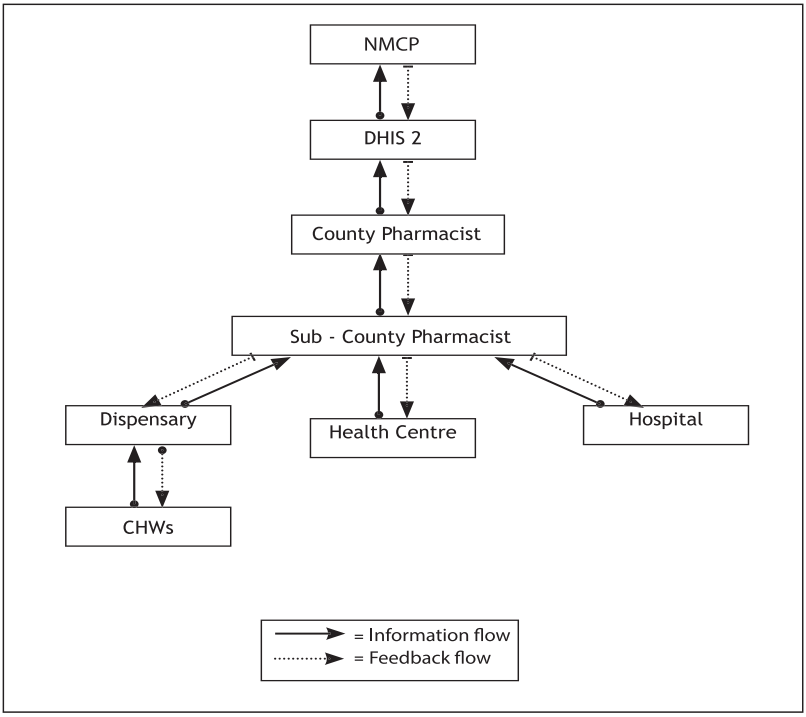
8.2.5 Types of inventory records

Various forms are used for requisitioning and issuing medicines, financial accounting, and preparing consumption and stock balance reports.

Table 10: Types of inventory records

Record type	Source document	Information
Stock keeping records	Bin cards, stock ledger card	Stock at hand Receipts, losses and adjustments
Transaction records	Issue and receipt voucher –(S12 , S11), KEMSA delivery notes, standard order form	Orders, issues and receipts
Consumption records	Daily activity register, health facility monthly summary	Consumption data Stock out days Patient numbers

Figure 3: Flow of logistics management information



8.2.6 M & E LMIS Indicators

- National reporting rate.
- Proportion of health facilities having no stock-out of all ACTs in a month.
- Number of patients treated with ACTs.
- Proportion of health facilities having no stock-out of RDTs in a month.

8.3. RATIONAL USE OF ANTI-MALARIAL MEDICINES

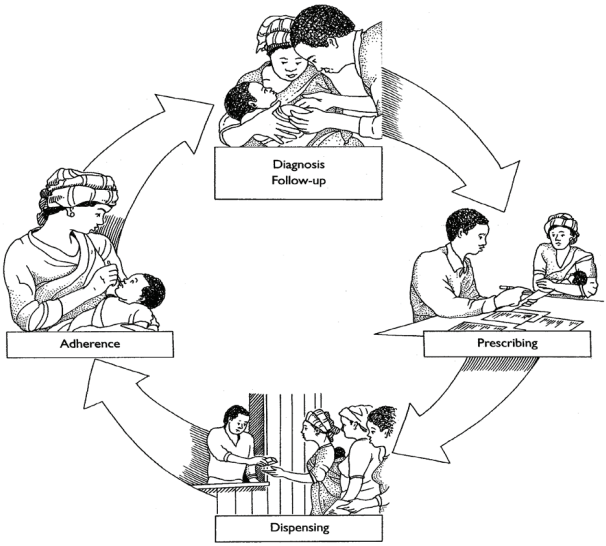
8.3.1. Definition of rational use

The rational use of medicines requires that patients receive medicines appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and the community[8]

8.3.2. Factors affecting rational use of medicines

- **Diagnosis** – correct diagnosis based on parasitologically confirmed diagnosis.
- **Prescribing** – prescribing /administering the recommended medicine based on the correct diagnosis.
- **Dispensing** – correct dispensing (quantity, packaging and labelling) of the prescribed medicine.
- **Patient compliance** - patients' adherence to health worker and label instructions.

Figure 4: The medicine use cycle



[8] World Health Organization, 1988

8.3.3 Implications of irrational use of medicines

- Irrational medicine use can destroy the benefits of a good pharmaceutical management system and also reduce the therapeutic useful life of an effective medicine.
- Resources spent on procurement are lost if the correct drugs are not prescribed and dispensed to the right patient.

8.3.4 Minimum dispensing information

- Directly observed treatment for first dose of AL and SP.
- Instructions on how long to take the medicine.
- Instruction on what to do if the patient vomits within 30 minutes of taking the medication.
- The common adverse drug reactions and instructions to report any suspected adverse drug reactions (ADR).
- Clear label with appropriate patient and medicine information.

8.3.5 M & E Indicators

i. Proportion of patients with fever presenting to health facility who are managed in accordance with national malaria guidelines.

ii. Proportion of patients presenting to health facility with fever and ACT prescribed, to whom counselling and ACT dispensing tasks are performed according to national guidelines.

8.4 PHARMACOVIGILANCE

8.4.1 Pharmacovigilance

WHO defines pharmacovigilance as the science of collecting, monitoring, researching, assessing and evaluating information from healthcare providers and patients on the adverse effects of medicines, biological products, herbals and traditional medicines, with the view to identifying new information about hazards, and preventing harm to patients.

Ultimate goals of Pharmacovigilance

- The rational and safe use of medicines.
- The evaluation of and communication of the risks and benefits of drugs on the market.
- Education and information of patients.

8.4.2 Adverse drug reaction (ADR)

This is a response to a drug which is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis or therapy of disease. Adverse drug reactions may also be called side effects.

Report ALL suspected ADRs with medications, especially those where the patient outcome is:

- Death.
- Life-threatening.
- Hospitalization (initial or prolonged).
- Disability (significant, persistent or permanent).
- Congenital anomaly.
- Required intervention to prevent permanent impairment or damage.

Report even if:

- You are not certain if the drug caused the ADR.
- You do not have all the details.

8.4.3 Counterfeit

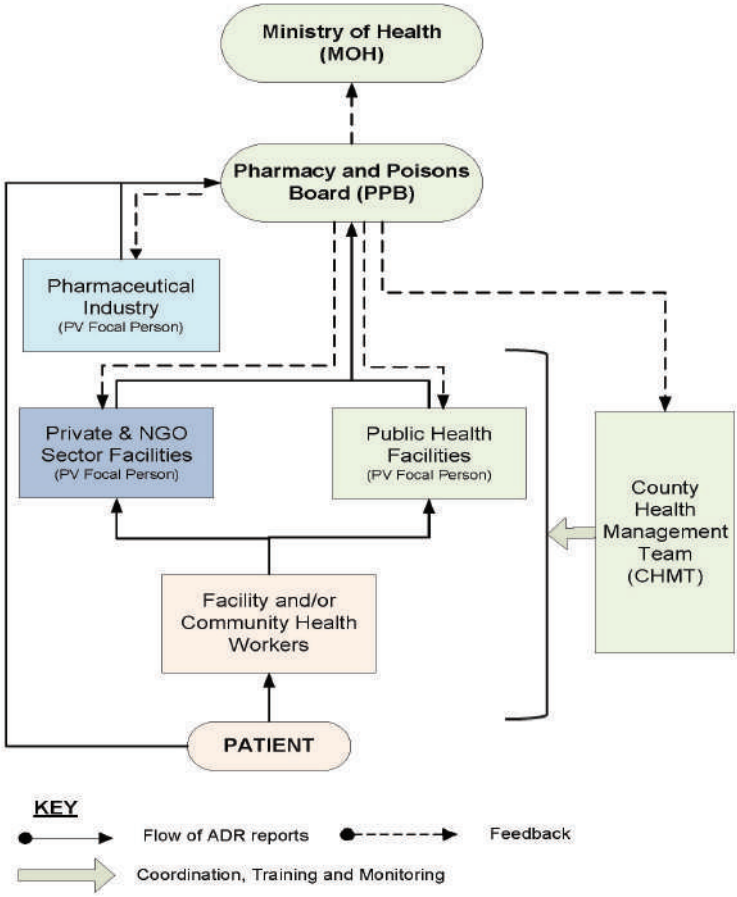
WHO defines a counterfeit pharmaceutical product as a product that is deliberately and fraudulently mislabelled with respect to identity and or source.

8.4.4 Tools for reporting side effects, adverse drug reactions and poor quality medicines

Reporting of ADRs is done using the forms below: (These forms are also available online at the Pharmacy and Poisons Board website www.pharmacyboardkenya.org

- PV 1: Yellow form - to capture all suspected adverse drug reactions.
- PV 4: White alert card - to report life threatening drug reactions.
- PV 6: Pink form - to report poor quality medicinal products.

Figure 5: Flow of information on adverse drug reactions



- Feedback to all levels of the system is the responsibility of the Pharmacy and Poisons Board (PPB).
- ADR reports may be submitted to the PPB Pharmacovigilance Center as follows:
  - Manually: Hard copies may be sent by courier or hand delivered to PPB.
  - Electronically: *either* via the PV Electronic Reporting Systen on the PPB website - http://www.pv.pharmacyboardkenya.org/; *or* via the mobile phone applications that can be downloaded from the same link.

8.4.5 M & E Indicator

Number of adverse drug reactions reports received.

9. Malaria prevention

9.1 CHEMOPROPHYLAXIS FOR NON-IMMUNE POPULATIONS

Chemoprophylaxis is recommended for the following high-risk groups:

9.1.1. Non-immune visitors (tourists)

The recommended medicines for chemoprophylaxis for non-immune persons visiting a malarious area are mefloquine, atovaquone-proguanil or doxycycline.

Note

- Chemoprophylaxis and other preventive measures are not 100% effective. Early medical care should be sought if they develop fever within 3 months of travel to an endemic area, even if adequate prophylaxis has been taken.
- Travellers are encouraged to use other barrier methods (LLINs, insecticide treated materials and repellents) to prevent or reduce bites from mosquitoes.
- Travellers should carry a full course of artemether-lumefantrine (as standby treatment) for use in the event they develop a fever and have no immediate access to health services.

9.1.2 Patients with sickle cell disease

The currently recommended prophylactic medicine for those with sickle cell disease is still proguanil. Although there is increasing documented resistance to anti-folate drugs, no studies on the effectiveness of proguanil in sickle cell disease have been conducted to recommend otherwise. It is important for patients with sickle-cell disease to consistently use other malaria prevention methods and to promptly seek treatment for any febrile illness.

9.1.3 Patients with Tropical Splenomegaly Syndrome (TSS)

The currently recommended malaria prophylactic medicine for those with TSS is proguanil. Although there is increasing documented resistance to anti-folate drugs, no studies on the effectiveness of proguanil in this group have been conducted to recommend otherwise.

9.1.4 Medicines for malaria chemoprophylaxis

9.1.4.1 Mefloquine

Mefloquine is available as tablets of 274mg mefloquine hydrochloride containing 250mg base or tablets of 250mg mefloquine hydrochloride containing 228mg base (United States only). Mefloquine is administered as a weekly dose of 250mg for adults, or 5mg base/kg body weight for persons below 36kg.

It is recommended that mefloquine prophylaxis is started 2–3 weeks before arrival in a malaria risk area, taken throughout the stay and continued for 4 weeks after leaving the area.

Table 11: Dosing schedule for mefloquine

Weight	Age	Number of tablets per day
<5 kg	<8 months	Not recommended
5 – 12 kg	8 months – 3 years	¼
13 – 24 kg	4 – 7 yrs	½
25 – 35 kg	8 – 10 yrs	¾
36 and above	11 yrs and above	1

Side effects

Nausea, vomiting, abdominal pain and diarrhoea are most common but are dose related and self-limiting. Other CNS related ones include dysphoria, dizziness, ataxia, headache, some visual and auditory disturbances, sleep disturbances and nightmares and convulsions.

Contraindications

- The first trimester of pregnancy.
- Do not administer to patients less than 5 kg.
- Avoid use in history of seizures and in severe neuro-psychiatric disturbance.
- Do not administer concomitantly with quinine and avoid quinine use after administration of mefloquine.

Caution

- Mefloquine can compromise adequate immunisation with the live typhoid vaccine.
- Mefloquine should not be taken <12 hours after last dose of quinine.
- Care should be taken when administering concomitant medications that interfere with cardiac function.

9.1.4.2. Proguanil

Proguanil is available as tablets of 100mg of proguanil hydrochloride containing 87mg of proguanil base.

Dose

Proguanil is administered at a daily dose of 3mg/kg daily. Often, the average daily dose is 200mg/day for adults and 100mg/day for children for the duration recommended by the physician.

Table 12: Dosing schedule for proguanil

Weight	Age	Number of tablets per day
5 – 8 kg	<8 months	¼
9 – 16 kg	8 months – 3 years	½
17 – 24 kg	4 – 7 yrs	¾
25 – 35 kg	8 – 10 yrs	1
36 – 50 kg	11 – 13 yrs	1 ½
50 + kg	14+ yrs	2

Side effects

Low doses – nausea, diarrhoea, rarely, hair loss and mouth ulcers. High doses - vomiting, haematuria and diarrhoea. Symptoms are treated as they appear. There is no specific antidote for proguanil overdose.

Contraindications

The use of proguanil is contraindicated in persons with liver or kidney dysfunction.

Caution

Antacids like magnesium trisilicate decrease absorption of Proguanil.

9.1.4.3 Atovaquone – proguanil (Malarone®/Malanil®)

Atovaquone–proguanil is available as film coated adult tablets containing 250mg atovaquone and 100mg proguanil hydrochloride or paediatric tablets containing 62.5mg atovaquone and 25mg proguanil hydrochloride.

Dose

It is administered as a daily dose of 1 tablet commencing 1 day before departure to a malaria endemic area, throughout the stay and continuing 7 days after leaving. Adults and children >40kg should take 1 adult tablet daily. The drug should be taken with food or milk at the same time each day.

Table 13: Dosing schedule for atovaquone-proguanil for children

Weight	Number of paediatric tablets
<11 kg	Not recommended
11 – 20 kg	1
21 – 30 kg	2
31 – 40 kg	3

Side effects

Abdominal pain, nausea, vomiting, diarrhoea, headache, anorexia and coughing.

Contraindications

- Persons with hypersensitivity to atovaquone and/ or proguanil.
- Pregnancy (because of lack of data).
- Do not use atovaquone-proguanil for prophylaxis in patients with severe renal impairment (creatinine clearance <30ml/min).

9.1.4.4. Doxycycline

Doxycycline is commonly available as capsules containing 100mg doxycycline hydrochloride. Tablets containing 100mg doxycycline hydrochloride may be available.

Dose

Doxycycline is administered as a daily dose of 100mg salt or 1.5mg salt per kg daily. It is taken 1 day before departure to a malaria endemic area and continued daily throughout the stay and for 4 weeks after departure.

Table 14: Dosing schedule for doxycycline tablets for children aged 8-13 yrs.

Weight	Age in years	No of tablets
<25 kg	<8	Contraindicated
25 – 35 kg	8 – 10	½
36 – 50 kg	11 - 13	¾
>50 kg	14+	1

Side effects

GIT irritation, increased vulnerability to sun-burn (phototoxic reaction), transient depression of bone growth and discoloration of teeth, vaginal candidiasis.

Contraindications

Doxycycline shouldn't be used in:

- Children under 8 years of age.
- Pregnant and lactating mothers.
- Persons with hepatic insufficiency.
- Persons with known hypersensitivity to tetracyclines.

Caution

Doxycycline should not be used for prophylaxis for periods exceeding 4 months. Antacids and milk impair absorption of tetracycline and concurrent administration should be avoided.

9.2 VECTOR CONTROL

Integrated vector management is one of the recommended methods to augment other malaria control interventions to reduce transmission of malaria. Vector control must be selective, targeted, site specific and cost effective. The selection of vector control methods should be based on intensity of the disease transmission, vector, human behaviours, the environment and resources available. The community should actively participate in the implementation of these vector control measures especially measures to reduce mosquito breeding within their environments. Inter-sectoral collaboration involving line ministries, NGOs and the private sector is encouraged in this respect.

The following vector control strategies are available:

- Use of long lasting insecticidal nets: The use of LLINs is encouraged for all persons living in malaria endemic areas.
- Indoor residual spraying – both in endemic and epidemic prone areas.
- Larviciding - in focalized breeding sites.
- Screening of house inlets with wire mesh to reduce entry of mosquitoes.

- Environmental management for source reduction of vector density e.g. drainage of breeding sites.
- Biological control measures where feasible – larvivorous fish, growth regulators, BTI (*Bacillus thuringiensis var israeliensis)*.
- Repellents and fumigants.

9.2.1 M & E Indicators

i. Proportion of households who own at least 2 LLINs.
ii. Proportion of households in targeted areas sprayed in the last 12 months.
iii. Proportion of household members who use LLIN.

9.3 EPIDEMIC PREPAREDNESS AND RESPONSE

Malaria interventions are reducing malaria prevalence in many areas, converting them into areas at risk of malaria epidemics; therefore there is need to:

- Strengthen routine surveillance of:
  - Epidemiological & entomological indicators, i.e. parasite rates (sentinel facilities, community), vectors.
  - Meteorological data.
- Ensure availability of buffer stocks for all medicines for uncomplicated and severe malaria, chemicals, spray pumps and LLINs.
- Plan for logistics support.

In case of an epidemic threat:

- Conduct advocacy and social mobilization.
- Mobilize health workers to provide active surveillance and prompt treatment of cases.
- Warn referral facilities about potential patient influx and strengthen referral systems.
- Conduct indoor residual spraying and net hanging campaigns.

9.3.1 M & E Indicator

Proportion of targeted subcounties with functional Epidemic Preparedness and Response (EPR) teams and logistics.

9.4 PREVENTION OF MALARIA INFECTION THROUGH BLOOD TRANSFUSION

All donated blood should be screened before transfusion using a sensitive diagnostic method. The Ministry of Health is developing guidelines on blood transfusion transmissible infections for further guidance.

9.5 ADVOCACY COMMUNICATION AND SOCIAL MOBILIZATION

Advocacy communication and social mobilization is a critical intervention for behavioural change towards improved health practices. The following important information should be provided to patients, caretakers/guardians of young children and community members to:

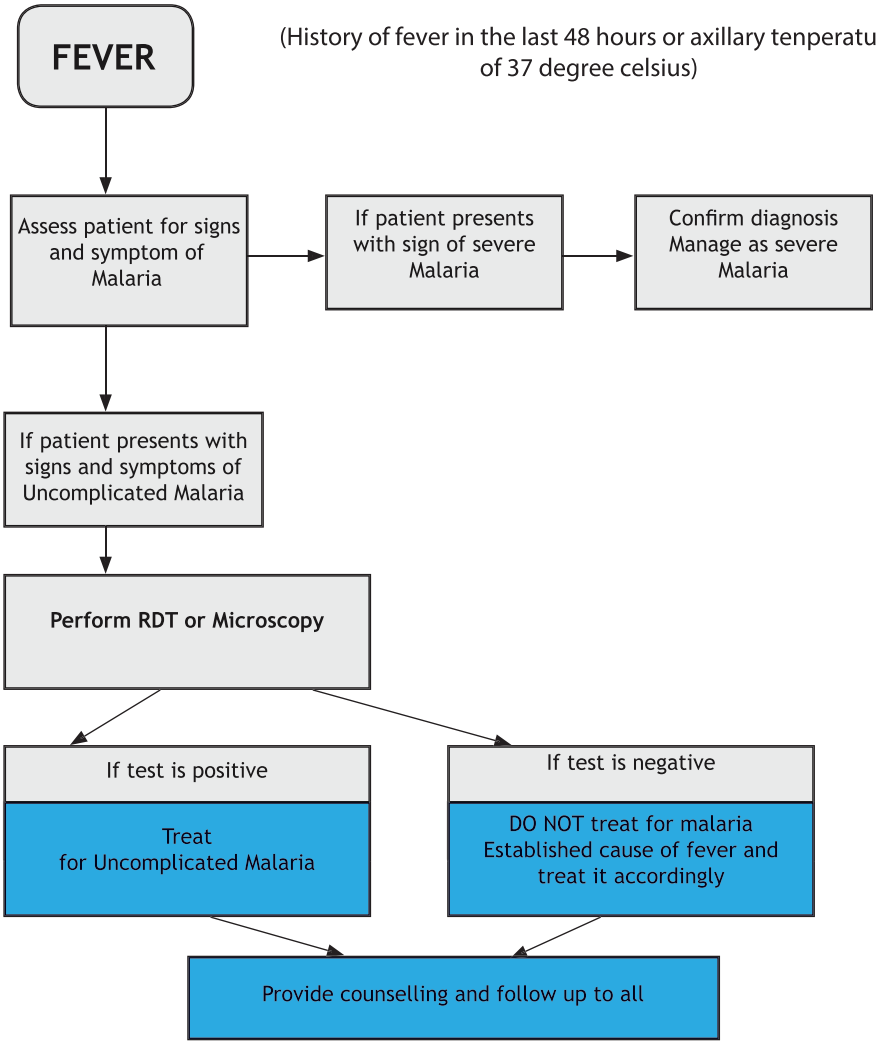
- Seek prompt diagnosis and correct treatment of all fevers within 24 hours of onset of symptoms.
- Recognize symptoms and signs of malaria and severe malaria.
- Test before treating.
- Adhere to dosing instructions and complete all prescribed medicines.
- Use appropriate prevention measures especially to sleep under LLIN every night.
- Pregnant women in endemic areas to get a minimum of 2 doses of IPTp.

9.4.1 M & E Indicator

Proportion of people reached by ACSM messages on malaria prevention and treatment.

10. Annexes

ANNEX 1: OUTPATIENT ALGORITHM FOR DIAGANOSIS AND MANAGEMENT OF MALARIA FOR CHILDREN AND ADULTS



ANNEX 2: THE PHARMACOLOGY OF ANTIMALARIALS

Antimalarials can be classified according to their chemical composition and mode of action. In this guideline, classification based on the mode of action is used.

Table 15: Common antimalarials classified by mode of action

Class	Definition	Examples
Blood schizonticidal drugs	Act on (erythrocytic) stage of the parasite thereby terminating clinical illness	Quinine, artemisinins, amodiaquine, chloroquine, lumefantrine, tetracycline[a], atovaquone, sulphadoxine, clindamycin[a], proguanil[a]
Tissue schizonticidal drugs	Act on primary tissue forms of plasmodia which initiate the erythrocytic stage. They block further development of the infection	Primaquine, pyrimethamine, proguanil, tetracycline
Gametocytocidal drugs	Destroy sexual forms of the parasite thereby preventing transmission of infection to mosquitoes	Primaquine, artemisinins, quinine[b]
Hypnozoitocidal drugs	These act on persistent liver stages of *P.ovale* and *P.vivax* which cause recurrent illness	Primaquine, tafenoquine
Sporozontocidal drugs	These act by affecting further development of gametocytes into oocytes within the mosquito thus abating transmission	Primaquine, proguanil, chlorguanil

[a] Slow acting, cannot be used alone to avert clinical symptoms

[b] Weakly gametocytocidal

ANNEX 3: ADDITIONAL INFORMATION ON ANTIMALARIALS

Only fixed dose ACTs should be used for the treatment of uncomplicated malaria. Not all the medicines in this reference section are recommended for use in Kenya.

1. Artemether-lumefantrine(AL)

For information on regular tablets and child friendly dispersible tablets, see Section 5.2.1. AL may also be presented as a powder for suspension. Once reconstituted, the suspension must be used as directed and discarded after 3 days.

Table 16: Dosing Schedule for AL powder for reconstitution

Body weight in kg	Dosage (in ml) to be administered once a day for three days
3	4.5
4	6
5	7
6	8
7-8	10
9-10	13
11-12	15
13-14	18
15-17	22
18-20	25
21-23	29
24-26	33
27-29	37
30	40

Side effects

Dizziness and fatigue, lack of appetite, nausea, vomiting, abdominal pain, palpitations, muscle pain, joint pain, headache and rash.

Contraindications

- There is limited data on the safety of use in the first trimester pregnancy.
- Persons with known hypersensitivity to either of the components.

2. Dihydroartemisinin-piperaquine(DHA-PPQ)

This DHA-PPQ is available as both adult and paediatric tablets administered once a day for three days. See section 5.3.2 for dosing information.

Side effects
Nausea, diarrhoea, loss of appetite, rash, pruritus.

Contraindications
- Hypersensitivity to any of the components of the combination.
- There is limited data on the safety of use in the first trimester pregnancy.

3. Amodiaquine-artesunate(ASAQ)

Is available as fixed dose combination tablets containing amodiaquine and artesunate dose

Dose
Amodiaquine 10mg/kg daily for three days plus artesunate 4mg/kg given daily for 3 days.

Side effects
Pruritus, rash, and with higher doses, syncope, spasticity, convulsions and involuntary movements.

Contraindications
- Hypersensitivity to any of the component medicines.
- Not recommended during the first trimester of pregnancy.

4. Primaquine

Dose
Primaquine is available as tablets containing 5.0, 7.5 or 15mg primaquine diphosphate. Dose 0.25-0.5mg/kg once daily for 14 days.

Side effects

The most important adverse effects are haemolytic anaemia in patients with G6PD deficiency. Therapeutic doses may also cause abdominal pain if administered on an empty stomach. Larger doses can cause nausea and vomiting. Methaemoglobinaemia may occur. Other uncommon effects include mild anaemia and leukocytosis. Overdosage may result in leukopaenia, agranulocytosis, gastrointestinal symptoms, haemolytic anaemia and methaemoglobinaemia with cyanosis.

5. Quinine

Quinine is presented as the following tablet strengths:
- 300 mg quinine dihydrochloride
- 300 mg quinine hydrochloride
- 300 mg quinine bisulphate
- 300 mg quinine sulphate
- 200 mg quinine sulphate

Table 17: Quinine tablets equivalence table

Quinine salt	Number of tablets
300 mg Quinine Dihydrochloride	1
300 mg Quinine Hydrochloride	1
300 mg Quinine Bisulphate	1.5
300 mg Quinine Sulphate	1.5

Dose

Quinine is administered in severe malaria as a seven-day dose of 10mg/kg salt three times a day every 8 hours.

Table 18: Dosing schedule for quinine 200mg tablets

Weight in kg	No of 200mg tablets
4 – 7	¼
8 – 11	½
12 – 15	¾
16 – 23	1
24 – 31	1½
32 – 39	2

Table 19: Dosing schedule for quinine 300mg tablets

Weight in kg	No of 300mg tablets
6 – 11	¼
12 – 17	½
18 – 23	¾
24 – 35	1
36 – 47	1½
48+	2

For children below the lowest weight category, the dosage of quinine is 10mg/kg and the tablets should thus be reconstituted into a suspension and given based on the weight of the patient. It is important to note that this is not an accurate method for quinine dosing and the reconstitution must be done prior to each dose as the stability of quinine in the liquid used is not known.

Injectable quinine

- Quinine hydrochloride (82% quinine base).
- Quinine dihydrochloride (82% quinine base).
- Quinine sulphate (82.6% quinine base) respectively.

The ampoules contain 300mg/ml and come as 2 ml or 1 ml ampoules.

Quinine for intramuscular injection

The dosage of IM quinine injection for pre referral treatment is a loading dose of 20mg/kg up to a maximum of 1,200mg.

How to give the intramuscular injection

- Weigh the patient (if he/she cannot be weighed the following formula can be used to estimate the weight of children under 5 years:

  (Age (in years) x 2) + 8 = wt in kg)

- Use a 10ml sterile syringe. Draw up 5ml of sterile water for injection. Then into the same syringe, draw up 300mg (1ml) from an ampoule of quinine. The syringe now contains 50mg quinine per ml. Mix the drug by shaking the syringe before injection. ***For the formulation of 600mg/2ml, only one ml is drawn out into the syringe. For the 300mg/ml the whole vial is drawn out while for the 150mg/ml, two vials will be required to make 300mg.**
- In all situations a maximum of 3ml should be injected into one injection site. If the amount to be injected exceeds 3ml, half the amount should be injected into each injection site (refer to table below for number of sites).

Table 20: Dosing schedule for IM Injections of quinine

Dilute quinine to 50mg/ml – and give based on 10mg/kg doses.

Body weight	Volumes of diluted quinine injection (ml) to be administered	Number of injection sites
Less than 5 kg	1.0ml	1
5.1 - 7.5 kg	1.5ml	1
7.6 –10kg	2.0ml	1
10.1 - 12.5 kg	2.5ml	1
12.6 - 15 kg	3.0ml	1
15.1 - 17.5 kg	3.5ml	2
17.6 – 20 kg	4.0ml	2
20.1 - 22.5kg	4.5ml	2
22.6 – 25 kg	5.0ml	2
25.1 - 27.5 kg	5.5ml	2
27.6 –30 kg	6.0ml	2
30.1 - 32.5 kg	6.5ml	3
32.6 – 35 kg	7.0ml	3

Quinine intravenous infusion

Intravenous quinine is administered in isotonic fluid; either 5% dextrose or dextrose - saline as follows. See section on treatment of severe malaria.

Adults

- The first dose 20mg/kg in 500mls of isotonic fluid given over 4 hours (maximum 1,200 mg).
- Use the formula to calculate number of drops per minute:

$$\frac{\text{Drop factor(from infusion set) x vol. to be given}}{\text{time in mins (240)}}$$

- Then 8 hours after commencing the initial dose give 10mg/kg in 500mls of isotonic fluid over 4 hours (maximum 600mg).
- Repeat 10mg/kg 8 hourly until the patient can take orally.
- Then preferably, give a full treatment course of artemether-lumefantrine or quinine may be continued orally at 10mg/kg three times a day to complete a total of 7 days treatment of quinine.
- Assessment of fluid status should be monitored regularly including urine output.
- If patient cannot be weighed – IV quinine loading dose should be 900mg. Followed by 600 mg 8 hourly.

Children

- Put up IV quinine drip (20mg/kg body weight loading dose in 15ml/kg of isotonic fluid) to run over 4 hours.
- Fluid intake should be calculated according to weight, bolus 20ml/kg (minimum 10ml/kg) and maintenance 4-6 ml/kg/hr.
- 8 hours after commencing the initial dose of quinine, give 10mg/Kg in 10mls/kg of isotonic fluid.
- Repeat 10mg/kg 8 hourly until the patient can take medication orally.
- Then preferably, give a full treatment course of artemether-lumefantrine or quinine may be continued orally at 10mg/kg three times a day to complete a total of 7 days treatment of quinine.

Side effects

The triads of quinine toxicities comprise cinchonism, hypoglycaemia and hypotension. Careful attention should be paid to these and adequate measures taken to correct them.

Cinchonism is characterized by tinnitus, high tone deafness, visual disturbances, headache, dysphoria, nausea and vomiting and postural hypotension all of which disappear on withdrawal of the drug. It is usually mild.

Hypotension is often associated with excessively rapid IV infusion or bolus injection. Hypoglycaemia is due to the stimulative effect of quinine on the ß cells of the pancreas which produce insulin. It is common in pregnancy and very prolonged and severe infection.

Other side effects include nausea, vomiting, diarrhoea, blurred vision, distorted colour perception, photophobia, diplopia and night blindness, cutaneous flushing, pruritus, rashes, fever and dyspnoea.

Black water fever is seen in patients with G6PD enzyme deficiency and malaria treated with quinine. It is characterized by haemolysis, Haemoglobinuria and in severe forms renal failure.

Pharmacology of artesunate injection

Description: Artesunate is a white crystalline powder. It is a rapidly acting blood schizontocide active against all *plasmodium* species. It is active against asexual parasites killing all stages from young rings to schizonts. In *p. falciparum* malaria, it also kills the gametocytes including stage 4 gametocytes.

Administration

- Artesunate can be administered IV or IM after reconstitution with sodium bicarbonate and dilution with normal saline or 5% dextrose.

Intravenous

- Intravenous route is preferred.
- Weigh the patient to determine the dosage needed and therefore the number of vials required.
- Dissolve each vial of artesunic powder with all the 5% sodium bicarbonate solution provided with each vial. Shake gently until the resultant solution is clear.
- Dilute resultant solution with 5 ml normal saline or 5% dextrose*.
- The final solution has a strength of 10mg/ml.
- Calculate the volume containing the required amount of drug to be given (mg) required x vol in vials/amount in mg in vials = volume containing required drug.
- Administer by slow IV over 3-5 minutes.

Intramuscular

- Weigh the patient to determine the dosage needed and therefore the number of vials required.
- Dissolve each vial of artesunic powder with all the 5% sodium bicarbonate solution provided with each vial. Shake gently until the resultant solution is clear.
- Dilute resultant solution with 2ml normal saline or 5% dextrose*.
- The final solution has a strength of 20mg/ml.

- Calculate the volume containing the required amount of drug to be given: (mg) required x vol in vials/amount in mg in vials = volume containing required drug.
- Administer by IM route.
- Spread the doses of more than 2ml over different sites for babies and 5ml for adults.

* This refers to 60mg artesunate. For all other strengths refer to product insert for diluent volume.

Precautions

- Inject immediately after reconstitution and discard if not used within 1 hour.
- Discard if the solution isn't clear.
- Do no use in an intravenous drip.
- Water for injection isn't suitable for dilution of artesunate injection.
- Sodium artesunate MUST be reconstituted with sodium bicarbonate solution to activate it.

Side effects

Dizziness, vomitting, headache, insomnia, cough, altered taste, abdominal pain, diarrhea, rash, pain at injection site.

Uncommon: Anaemia.

Contraindications

Oral artesunate should not be used during the 1st trimester of pregnancy.

Table 21: Dosing schedule for parenteral artesunate

	For Intravenous Route			For intramuscular Route		
	Concentration 10gm/ml			Concentration 20mg/ml		
	(3.0 mg x body weight) / Concentration (10mg/ml)			(3.0 mg x body weight) / Concentration (10mg/ml)		
	Example					
	Dose needed for 8kg child					
	(3.0x 8)/10= 2.4 ml rounded to 3 ml			(3.0x 8)/20= 1.2 ml rounded to 2 ml		
Less than 20 Kg	Weight	Dose				
	Kg	mg	ml	Kg	mg	ml
	6-7	20	2	6-7	20	1
	7-10	30	3	7-10	30	2
	11-13	40	4	11-13	40	2
	14-16	50	5	14-16	50	3
	17-20	60	6	17-20	60	3
	(2.4x 26)/10= 6.24 ml rounded to 7 ml			(2.4 x 26)/20 = 3.12 rounded to 4 ml		
More than 20kgs	20-25	60	6	20-25	60	3
	26-29	70	7	26-29	70	4
	30-33	80	8	30-33	80	4
	34-37	90	9	34-37	90	5
	38-41	100	10	38-41	100	5
	42-45	110	11	42-45	110	6
	46-50	120	12	46-50	120	6
	51-54	130	13	51-54	130	7
	55-58	140	14	55-58	140	7
	59-62	150	15	59-62	150	8
	63-66	160	16	63-66	160	8
	67-70	170	17	67-70	170	9
	71-75	180	18	71-75	180	9
	76-79	190	19	76-79	190	10
	80-83	200	20	80-83	200	10
	84-87	210	21	84-87	210	11
	88-91	220	22	88-91	220	11
	92-95	230	23	92-95	230	12
	96-100	240	24	96-100	240	12

Dosing schedule

Artesunate is administered at 0hrs, 12hrs, 24hrs then daily until the patient can take orally. A patient should receive a minimum of 3 doses of IV/IM artesunate before being transitioned to oral ACTs. If the patient cannot take orally, continue the artesunate injection for a maximum of 7 days then given a three day course of ACT as appropriate. **All attempts should be made to allow patients who can take orally to take a full course of AL.**

- Discard after 1 hour of reconstitution.

ANNEX 4: COMA MONITORING SCALES

The Glasgow coma scale

Table 22: The Glasgow coma scale (for adults and children over 5 yrs).

Behaviour	Response	Score
Eye Opening Response	Spontaneous: open with blinking at baseline	4
	Opens to verbal command, speech, or shout	3
	Opens to pain, not applied to face	2
	None	1
	Oriented	5
	Confused conversation, but able to answer questions	4
Verbal Response	Inappropriate responses, words discernible	3
	Incomprehensible speech	2
	None	1
	Obeys commands for movement	6
	Purposeful movement to painful stimulus	5
Motor Response	Withdraws from pain	4
	Abnormal (spastic) flexion, decorticate posture	3
	Extensor (rigid) response, decerebrate posture	2
	None	1

It is recommended to use the simpler Blantyre coma score for children. However, if the GCS is used for children under 5, adjust the verbal response according to the Table 23 below.

Table 23: Adjusted verbal response for children <5yrs.

Score	2 to 5 years	0 to 23 months
5	Appropriate words or phrases	Smiles or coos appropriately
4	Inappropriate words	Cries and consolable
3	Persistent cries and/or screams	Persistent inappropriate crying and/or screaming
2	Grunts	Grunts or is agitated or restless
1	No response	No response

To obtain the Glasgow coma score obtain the score for each section and add the three figures to obtain a total out of 15.

Interpretation of symptoms: (Severe: 8 or less; Moderate: 9-12; Mild: 13 or more).

The Blantyre coma scale

The Blantyre coma scale[9] is a modification of the Glasgow coma scale suitable for use in children not yet able to speak. The scale uses motor and crying responses to pain and includes the ability to watch. It can be used to assess young children with cerebral malaria.

Table 24: The Blantyre coma scale for children <5 years

Response	Findings	Score
Eye movement	Directed (e.g. towards mother's face)	1
	Not directed	0
Best verbal response	Appropriate cry	2
	Inappropriate cry	1
	None	0
Best motor response	Localizes painful stimuli	2
	Withdraws limb from pain	1
	Non-specific or absent response	0

Blantyre coma scale = (best motor response score) + (best verbal response score) + (eye movement score).

The score can range from 0-5. Any score < 4 is abnormal while 2 or less indicates unrousable coma. The score can be used repeatedly to assess improvement or deterioration.

[9] Molyneux ME Taylor TE et al. Clinical features and prognostic indicators in paediatric cerebral malaria: A study of 131 comatose Malawian children. Q J Med. 1989; 71: 441-459.

ANNEX 5: UPDATED IMCI ALGORITHM

The integrated management of childhood illnesses (IMCI) algorithm has been updated to reflect their recommendation for confirmation of malaria diagnosis before treatment.

ASSESS AND CLASSIFY THE SICK CHILD AGE 2 MONTHS UP TO 5 YEARS

DOES THE CHILD HAVE FEVER?

(by history or feels hot or temperature 37.5°C* or above)

IF YES:
Has the child travelled to a high risk (Malaria endemic, seasonal transmission or epidemic prone) area in the last 1 month?
Decide Malaria Risk: high or low risk.

THEN ASK:
- For how long?
- If more than 7 days, has fever been present every day?
- Has the child had signs of measles within the last 3 months?

LOOK AND FEEL:
- Look or feel for stiff neck.
- Look for runny nose.

Look for signs of MEASLES:
- Generalized rash and one of these: cough, runny nose, or red eyes.
- Look for any other cause of fever***

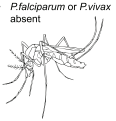
High Malaria risk:
Do a malaria test
- Endemic Zone
- Seasonal Transmission Zone
- Epidemic prone areas

Low malaria risk:
- Do a malaria test if no obvious cause of fever

NOTE: If you can't test, don't withhold treatment

TEST POSITIVE
- *P.falciparum* PRESENT
- *P.vivax* PRESENT

TEST NEGATIVE
- *P.falciparum* or *P.vivax* absent



Check for Complications of **MEASLES**

If the child has signs of measles now or within the last 3 months
- Look for mouth ulcers, are they deep or extensive?
- Look for pus draining from the eye
- Look for clouding of the cornea

CLASSIFY FEVER: HIGH OR LOW MALARIA RISK

CLASSIFY MEASLES

If MEASLES now or within the last 3 months, Classify

CLASSIFY		IDENTIFY TREATMENT
SIGNS	**CLASSIFY AS**	**TREATMENT**
• Any general danger sign or • Stiff neck. **AND** • Confirm malaria with a test.	**VERY SEVERE FEBRILE DISEASE OR SEVERE MALARIA**	• **Give first dose of Artesunate for severe malaria** • **Give first dose of Ceftriaxone** • **Treat the child to prevent low blood sugar** • **Give one dose of paracetamol in clinic for high fever (≥38.5 °C)** • **Admit or Refer URGENTLY to hospital** • **Screen for possible TB disease and check for HIV.**
• Malaria test POSITIVE**	**UNCOMPLICATED MALARIA**	• **Give Artemether + Lumefantrine (AL)** • **Give one dose of paracetamol in clinic for high fever (≥38.5 °C)** • **Give Vitamin A** • Follow up in 3 days if fever persists • If fever is present every day > 7 days assess further or refer • Screen for possible TB disease and check for HIV • Advise when to return immediately.
• Malaria test NEGATIVE	**FEVER: NO MALARIA**	• Give one dose of paracetamol in clinic for high fever (≥38.5 °C) • Assess for other possible causes of fever • Follow up in 3 days if fever persists • If fever is present every day for more than 7 days assess further or refer • Screen for possible TB disease and check for HIV • Advise mother when to return immediately.
Generalized rash of measles and • One of: cough, runny nose or red eyes	**SUSPECTED MEASLES**	• **Give Vitamin A** • Notify, take blood sample for confirmation • Screen for possible TB disease and check for HIV • Advise mother when to return immediately.
Any general danger sign or • Clouding of cornea or • Deep or extensive mouth ulcers.	**SEVERE COMPLICATIONS OF MEASLES**	• **Give Vitamin A** • **Give first dose of Ceftriaxone Antibiotic** • **If clouding of the cornea or pus draining from the eye, apply tetracycline eye ointment.** • **Notify, take blood sample for confirmation OR refer** • **Admit or refer URGENTLY to hospital** • **Screen for possible TB disease and check for HIV.**
• Pus draining from the eye or • Mouth ulcers.	**EYE OR MOUTH COMPLICATIONS OF MEASLES****	• **Give Vitamin A** • **If pus draining from the eye, treat eye infection with tetracycline eye ointment.** • **If mouth ulcers, treat with Gentian Violet** • Follow-up in 2 days • If child has no indication for referral, notify and draw blood sample for confirmation of measles • Screen for possible TB disease and check for HIV.
• No pus draining from the eye or mouth ulcers.	**NO EYE OR MOUTH COMPLICATIONS OF MEASLES**	• **Give Vitamin A if not received in the last 1 month** • If child has no indication for referral, draw blood and send for confirmation • Screen for possible TB disease immediately after the measles infection and check for HIV.

TABLE : 3

* These temperatures are based on axillary temperatue. Rectal temperature readings are approximately 0.5°C higher.
** If no malaria test available: High risk-classify as MALARIA; Low malaria risk AND NO obvious cause of fever- classify as MALARIA
*** Look for local tenderness, refusal to use a limb, hot tender swellingsed tender skin or boils, lower abdominal pain or pain on passing urine
**** Other important complications of measles - pneumonia*mastoiditis, diarrhoea, ear infection, and malnutrition - are classified in other tables.*

ANNEX 6: FIFTH EDITION GUIDELINE REVIEW TEAM

Name	Organization
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Peter Njiru	National Malaria Control Program
Kiambo Njagi	National Malaria Control Program
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James Sang	National Malaria Control Program
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Julius Kimitei	Zoonotic disease Unit
Agnetta Mbithi	PIMA Measure Evaluation
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Dejan Zurovac	KEMRI Wellcome Trust
Bernard's Ogutu	KEMRI Waltereed
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