National guidelines for diagnosis, treatment and prevention of malaria for health workers in Kenya

Ministry of Health
Division of Malaria Control, Republic of Kenya

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REPUBLIC OF KENYA
MINISTRY OF HEALTH

NATIONAL GUIDELINES FOR
DIAGNOSIS, TREATMENT AND PREVENTION OF

M A L A R I A

FOR HEALTH WORKERS IN KENYA
Correct citation:

January, 2006
ACKNOWLEDGMENTS

The Ministry of Health wishes to acknowledge the special contributions to its discussions and to the drafting of the guidelines made by the following members of the Drug Policy Technical Working Group as stipulated in National Malaria Strategy; Prof. K.Bhatt, University of Nairobi, Dr. B.Ogutu, KEMRI WRP, Dr. E. Juma, KEMRI-KISUMU, Prof. G.Kokwaro, Prof. R.Snow, Dr. D.Zurovac, all of KEMRI/Welcome Trust, Nairobi; Dr.G.Tetteh, MSH-RPM Plus, Dr. J.Carter of AMREF Nairobi, Dr.S.Ocholla, Dr.W.Akhwale and Dr. D.Memusi of the Division of Malaria Control.

The Ministry of Health also acknowledges the immense technical contribution by Dr.Peter Olumesee of WHO/HQ, Dr. Tom Sukwa WHO/AFRO, Dr.A.Ngindu and J. Greenfield of WHO/KCO.

We also acknowledge suggestions by the Provincial Medical Officers of Health as well as several clinicians and pharmacists countrywide.

The revision and updating of these guidelines could not have been successfully completed without encouragement and technical support of Dr. J.Nyikal, the Director of Medical Services and the administrative support given by the office of the Permanent Secretary, Ministry of Health.
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PREFACE

Malaria remains a leading cause of morbidity and mortality in Kenya, especially in young children and pregnant women. It accounts for 30% of outpatient attendances and 19% of admissions to health facilities. Malaria is the most important cause of death in children under 5 years of age and is estimated to cause 20% of all deaths in this age group. In spite of this situation, malaria is a preventable and curable disease. The Ministry of Health have prioritized malaria control via the National Malaria Strategy (NMS) 2001-2010 with the National Health Sector Strategic Plan II (2005-2010) laying emphasis on scaling up implementation of activities for the reduction of morbidity and mortality due to malaria.

One of the key strategic interventions of the NMS is to provide early diagnosis and prompt treatment of malaria using effective medicines aimed at achieving the Abuja targets and the Millennium Development Goals (MDGs). The biggest challenge to the implementation of this intervention is the emergence of parasite resistance to commonly used and relatively cheap antimalarials. Kenya formally abandoned the use of chloroquine in 1998 as its first line therapy in favor of an easier to use drug, sulphadoxine-pyrimethamine (SP). There has however been a precipitous decline in the efficacy of SP at the same time there is evidence of declining efficacy of amodiaquine the current second line treatment.

Based on this scientific information and WHO recommendations of changing to combination therapy, the Ministry of Health has adopted the use of Artemesinin based Combination Therapy (ACT) as 1st line treatment of uncomplicated malaria. There is therefore need to implement a new antimalarial treatment policy using ACTs. The Ministry of Health has developed these guidelines for malaria diagnosis, treatment and prevention with an aim of improving malaria case management by health workers and having a harmonized approach in efforts aimed at the reduction of morbidity and mortality due to malaria.

It should be noted that the pattern of malaria disease is changing from time to time and that there will be need to update and revise the guidelines periodically. We have carefully considered the cost effectiveness of recommended interventions but expect users to continually give feedback regarding the use of relevant sections of the guidelines.

Finally, I wish to express my sincere gratitude to all those who participated in the revision and updating of these guidelines. I 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.

Dr. James W. Nyikal  MBS

DIRECTOR OF MEDICAL SERVICES
ABBREVIATIONS

ACT        Artemisinin Based Combination Therapy
AIDS       Acquired Immune Deficiency Syndrome
AL         Artemether - Lumefantrine
ANC        Antenatal Clinic
BCC        Behavioural Change Communication
CHW        Community Health Worker
DOMC       Division of Malaria Control
DPTWG      Drug Policy Technical Working Group
EDL        Essential Drugs List
Hb         Haemoglobin
HIV        Human Immune-deficiency Virus
IEC        Information Education Communication
IM         Intramuscular
IPT        Intermittent Preventive Treatment
IV         Intravenous
KEMRI      Kenya Medical Research Institute
KEMSA      Kenya Medical Supplies Agency
NG         Nasogastric
PHC        Primary Health Care
RDTs       Rapid Diagnostic Tests
SP         Sulfadoxine or sulfalene/pyrimethamine
WHO        World Health Organization
WHO/AFRO   WHO Regional Office for Africa
1. WHAT IS MALARIA?

Malaria is a disease caused by the parasite Plasmodium. The infection is usually transmitted by the bite of an infected female Anopheles mosquito. *Plasmodium falciparum* is the commonest species in Kenya and is associated with significant morbidity and mortality. Other species include *P. malariae* and *P. ovale* which sometimes occur as mixed infections with *P. Falciparum* whilst *P. vivax* is very rare.

1.1 OCCURRENCE AND DISTRIBUTION OF MALARIA IN KENYA

The level of endemicity of malaria in Kenya varies from region to region and there is a big diversity in risk largely driven by climate and temperature (including the effects of altitude). Based on malaria risk, districts in Kenya can be broadly categorized into one of five classes of malaria ecology (see figure 1). The five categories include:

1. **Lakeside endemic**: Among many districts close to Lake Victoria, malaria transmission is common every year, immunity is acquired by the community before adulthood and the risks of disease and death from malaria are concentrated amongst children and pregnant women. Transmission is perennial and the parasite prevalence amongst childhood communities often exceeds 50%.

2. **Coastal endemic**: The coast is similar in endemicity to the Lakeshore with parasite prevalence’s often exceeding 50%, however, the transmission and maximal disease risk period exhibit stronger seasonality and the intensity of transmission is lower toward the Somali border.

3. **Highland**: A common feature of malaria in highland districts is that whilst there is always a potential for limited transmission lending itself to an overall low disease risk on an average year, variations in rainfall and ambient temperatures between years can lead to epidemics affecting all members of the community. The parasite prevalence is low in these districts but varies widely over small spatial distances.

4. **Arid, seasonal**: Several districts in a large part of North Eastern, North Western and Central areas of the country only experience malaria where communities are located to water. The arid and rainfall limited effects upon transmission lend the transmission of parasites only to a few months of the year or absent during occasional years. Other districts might experience transmission every year for a few months. Overall all districts in this category will support low infection prevalence rates in childhood.

5. **Low Malaria Risk**: These areas cover highlands within Central Province and Nairobi province. Parasitological surveys in these areas on the whole suggest low parasite prevalence among children aged 0-14 years. Several areas will experience almost no malaria risk, for example the central areas of Nairobi, Nyeri and Nakuru.

For clinical management purposes the above ecological zones are classified as follows:-
**High malaria risk areas**: Lakeside, coastal, highland and arid areas (categories 1-4).
**Low malaria risk areas**: Highlands within central province (category 5).
Figure 1: ENDEMICITY OF MALARIA IN KENYA
1.2 CLINICAL FEATURES AND CLASSIFICATION OF MALARIA

The clinical course of malaria may present as uncomplicated or severe.

1.2.1 Uncomplicated malaria
This is usually characterized by fever in the presence of peripheral parasitemia. 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

1.2.2 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 of the clinical or laboratory features (singly or in combination) listed below:

Features and definitions of severe malaria
- 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)
- Circulatory collapse (shock, septicaemia)
- Pulmonary oedema
- Abnormal bleeding (Disseminated Intravascular Coagulopathy)
- Jaundice
- Haemoglobinuria (black water fever)
- Acute renal failure – presenting as oliguria or anuria
- Severe anaemia (Hb <5g/dl or Hct < 15%)
- Hypoglycaemia (blood glucose level < 2.2 mmol/l)
- Hyperparasiteamia (parasitaemia of >200,000/µl - in high transmission area, or 100,000/µl in low transmission area)
- Hyperlactataemia
2. PARASITOLOGICAL DIAGNOSIS OF MALARIA

The commonly used confirmatory tests to detect the presence of malaria parasites are microscopy or rapid diagnostic tests (RDTs). Quality assurance of microscopy and RDTs is vital for the sensitivity and specificity of the results.

2.1 MICROSCOPY:
- Microscopy is the standard method for parasitological diagnosis of malaria. This is done 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.

Microscopic examination of stained blood films has a sensitivity range of 86-98% with a lower sensitivity in detecting low parasitaemias (≤ 320/µl). Various factors such as the stage of the malaria infection and previous medication may reduce parasitaemia below the detectable threshold and necessitate repeat examination.

Parasites are quantified by counting ring forms against white blood cells. The results are expressed as parasite count/200WBCs or parasite counts/µl of blood (assuming a WBC count of 8000/µl or using the measured WBC counts of the patient where available).

2.2 RAPID DIAGNOSTIC TESTS
RDTs are immunochromatographic tests based on detection of specific parasite antigens, either *Plasmodium* lactate dehydrogenase (pLDH) activity or the presence of Histidine-Rich Protein (HRP). Most of the RDT tests available are specific for *P. falciparum*, however, there are a few tests with the ability to differentiate between *P. falciparum* and non-*P. falciparum* malaria (*vivax, malariae and ovale*). RDTs are simple to use and are sensitive in detecting low parasitaemia. Use of RDTs is not recommended for follow-up as most of the tests remain positive for up to two weeks following effective antimalarial treatment and clearance of parasites. They also cannot be used to determine parasite density.
3. MANAGEMENT OF UNCOMPLICATED MALARIA

3.1 DIAGNOSIS

3.1.1 Children Under-5 Years Old

- In high malaria endemic areas, any child with fever or history of fever should be presumptively classified and treated as malaria. The use of parasitological diagnosis is not a prerequisite for treatment.
- In low malaria endemic areas, any child with fever or history of fever in the absence of measles, running nose or any other identifiable cause of fever should be presumptively classified and treated as having malaria. The use of parasitological diagnosis is recommended where possible.

3.1.2 Older Children >5 Years of age and Adults

- In all patients 5 years and above 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, patient with fever or history of fever in whom the health worker strongly suspect malaria and has eliminated other possible causes of fever, should be presumptively classified and treated as malaria.

4. TREATMENT OF UNCOMPLICATED MALARIA

4.1 FIRST LINE TREATMENT FOR ALL AGE GROUPS

The recommended first line treatment for uncomplicated malaria in Kenya is artemether-lumefantrine currently available as a co-formulated tablet containing 20 mg of Artemether and 120 mg of lumefantrine. This is administered as a 6 dose regimen given over three days (See table below)

Dosing schedule for artemether-lumefantrine

<table>
<thead>
<tr>
<th>Body weight</th>
<th>No. of tablets recommended at approximate timing (hours) of dosing(^a) (each tablet contains 20mg A and 120mg L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 h</td>
</tr>
<tr>
<td>5–14 kg (&lt;3 y)</td>
<td>1</td>
</tr>
<tr>
<td>15–24 kg (4–8 y)</td>
<td>2</td>
</tr>
<tr>
<td>25–34 kg (9–14 y)</td>
<td>3</td>
</tr>
<tr>
<td>&gt;34 kg (&gt;14 y)</td>
<td>4</td>
</tr>
</tbody>
</table>

The regimen can be expressed more simply for ease of use at the program level as follows: the second dose on the first day should be given anytime between 8 and 12 h after the first dose. Dosage on the second and third days is twice a day (morning and evening).
*Malaria patients with HIV/AIDS should be managed according to the same regimen above.
*In children below 5 kg (under 2 months of age), malaria is not a common cause of fever. Evaluation of other causes should be undertaken. Where malaria is diagnosed, the recommended treatment is oral quinine.

4.1.1 Management of fever at the community level
Since most of the cases of fever occur at the community level, it is essential to train health care providers and care-takers where applicable on early recognition with and prompt initiation of treatment at the community level. This includes not only the use of the appropriate antimalarial, but also the use of other methods to control the fever. The patients should be taken immediately to a health facility if there are any features of severity as described in the section on severe malaria below.

4.1.2 Counseling and follow up
For all patients the following counseling messages should be provided (see Annex 3):

- Explain dosing schedule, use probing questions to confirm patient’s understanding
- Emphasize that all 6 doses must be taken over 3 days even if patient feels better after few doses.
- Directly observe the first treatment dose
- If vomiting occurs within 30 minutes after drug administration, the dose should be repeated
- Artemether-lumefantrine should be taken preferably with a meal.
- Advise patients to return immediately to the nearest health facility if the condition deteriorates at anytime, or if symptoms have not resolved after three days

4.1.3 Supportive treatment
- Fever management: In cases of hyperpyrexia (temp >39.5°C) administer an antipyretic. The recommended options are: paracetamol or ibuprofen. Aspirin may be used in adults, BUT is contraindicated in children. Other mechanical methods for reducing temperature include exposure, fanning or tepid sponging.
- Encourage adequate fluids and nutrition: Care givers should be encouraged to give extra fluids and where applicable continue breast feeding. Feeds and fluid should be administered as small quantities in frequent intervals especially when the child is still very sick.

4.1.4 Treatment failure
Treatment failure can be defined as a failure to achieve the desired therapeutic response after the initiation of therapy. Treatment failure is not synonymous with drug resistance. Treatment failure may result from poor adherence to treatment, unusual pharmacokinetic properties in that individual or drug resistance. Treatment failure could also arise due to a wrong diagnosis and thus initiating the wrong treatment. 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 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.

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.

4.1.5 Management of suspected treatment failures
Malaria microscopy should be used to assess suspected treatment failures. Use of RDTs is not recommended. Confirmed cases of treatment failure should be treated with the 2nd line medicine. Other potential differential diagnosis should be sought for and adequately managed. In centers 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.

4.2. SECOND LINE TREATMENT FOR ALL AGE GROUPS

The recommended second line treatment for uncomplicated malaria in Kenya is oral QUININE. This is administered as a daily dose of 30mg/kg in three divided doses of 10mg/kg for 7 days.

Dosing schedule for quinine tablets

<table>
<thead>
<tr>
<th>Quinine sulphate 200mg</th>
<th>Quinine 300 mg salt ( sulphate, dihydrochloride, hydrochloride)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WEIGHT IN KG</td>
<td>NO OF TABS</td>
</tr>
<tr>
<td>4 - 7 kg</td>
<td>1/4</td>
</tr>
<tr>
<td>8 - 11 kg</td>
<td>½</td>
</tr>
<tr>
<td>12 - 15 kg</td>
<td>3/4</td>
</tr>
<tr>
<td>16 - 23 kg</td>
<td>1</td>
</tr>
<tr>
<td>24 - 31 kg</td>
<td>1 ½</td>
</tr>
<tr>
<td>32 - 39 kg</td>
<td>2</td>
</tr>
</tbody>
</table>

For children below the lowest weight category, the dosage of quinine is 10mg / kg and the tablets should thus be reconstituted into syrup based on the weight of the patient.

5. MANAGEMENT OF SEVERE MALARIA

5.1 DIAGNOSIS
Severe malaria is a medical emergency. Delay in diagnosis and inappropriate treatment, especially in infants and children, leads to rapid worsening of the situation. The keys to effective management are early recognition, assessment, and appropriate antimalarial and supportive therapy.

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 malaria anaemia, respiratory distress and cerebral malaria. An outline of the presentations is summarized in the table below.

Table: Clinical features of severe malaria

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Frequency</th>
<th>Prognostic value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Children</td>
<td>Adults</td>
</tr>
<tr>
<td>Prostration</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Altered level of consciousness</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Multiple convulsions</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Respiratory distress</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Circulatory collapse</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Pulmonary oedema</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Jaundice</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Haemoglobinuria</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Abnormal bleeding</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Table: Laboratory features of severe malaria

<table>
<thead>
<tr>
<th>Laboratory features</th>
<th>Frequency</th>
<th>Prognostic value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Children</td>
<td>Adults</td>
</tr>
<tr>
<td>Severe anaemia (Hb &lt; 5 gm/dl or Hct &lt; 15%)</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Hypoglycaemia (blood sugar &lt; 2.2 mmol/l)</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Hyperparasitemia</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Acidosis</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Hyperlactatemia</td>
<td>+++</td>
<td>++</td>
</tr>
</tbody>
</table>

* Severe malaria can occur in the absence of fever.

- In all patients with suspected severe malaria with or without fever or history of fever the use of parasitological diagnosis is recommended.
Antimalarial treatment should not be withheld if parasitological diagnosis is not possible. Presumptive treatment should be started immediately while efforts to confirm diagnosis are on-going.

Other investigations to determine severity and prognosis should be undertaken where feasible.

In all suspected cases of severe malaria, a parasitological confirmation of the 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.

5.2 EVALUATION AND MANAGEMENT OF SOME SPECIFIC CLINICAL MANIFESTATIONS

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

a. Cerebral malaria

   i. Clinical assessment
   a. Assess level of consciousness using coma score (Annexe 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 (sunken eyes, skin turgor, dry tongue and measuring blood pressure).
   e. Assess for renal insufficiency (measuring urine output)
   f. Assess for evidence of Disseminated Intravascular Coagulopathy (spontaneous bleeding from the gums, injection sites, or any other site).

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

b. Severe anaemia:

   i. 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)

ii. Laboratory test.

Determine haemoglobin levels, blood group and cross match where applicable.

c. Hypoglycemia

i. Clinical assessment
Assess the level of consciousness

ii. Laboratory test
Determine the blood glucose level.

5.3 ANTIMALARIAL TREATMENT

The recommended medicine of choice for severe malaria is parenteral quinine. The preferred route of administration is the intravenous route. However the intramuscular route can be used as an alternative where intravenous route is not feasible.

Practical issues with 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 24hr or have received mefloquine in the last 7 days
- Quinine is not contraindicated in severe anaemia
- In renal insufficiency the dose of quinine remains unchanged
- 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. Provide glucose supplement to these patients.

5.3.1 Quinine administration in Children.

Parenteral quinine is given as an initial loading dose in infusion of 15mg (salt)/kg and then followed by a maintenance dose of 10mg/kg every 12 hours until patient can tolerate oral medication. Thereafter quinine is continued orally at 10mg/kg every 8 hours to complete a total (parenteral + oral) of 7 days or a complete course of artemether-lumefantrine is given.
Intravenous quinine is administered as follows:

- Put up IV quinine drip 15mg/kg body weight loading dose in 15mls/kg of isotonic solution (5% dextrose or normal saline) to run over 4 hours.
- 12 hours from commencement of the initial dose of quinine, give 10mg/kg in 10mls/kg of isotonic solution (5% dextrose or normal saline) to run over 4 hours.
- Repeat 10mg/kg quinine infusion every 8 hours until the patient can take medication orally.

Intramuscular quinine is administered as follows:

* Note: The dose of quinine through the intramuscular route is same as for intravenous route.

- Quinine MUST be diluted (maximum concentration is 60mg/ml) before intramuscular injection.
- A loading dose of 15mg/kg of quinine (diluted to a maximum 60mg/ml) is given by intramuscular injection (preferably the anterior thigh). A maximum of 3ml should be injected into one site. If the amount to be injected exceeds 3 mls, multiple sites should be used.
- 12 hours after the loading dose, give 10mg/kg (diluted to a maximum 60mg/ml) as intramuscular injection every 12 hours until the patient can take medication orally.

*An example of body weights and dose (ml) of injection is given in Annex 3, Table 2).

5.3.2 Quinine administration in Adults

Parenteral quinine is given as an initial loading dose of 20mg (salt)/kg (maximum of 1200mg) of quinine and then followed by a maintenance dose of 10mg/kg (maximum 600mg) every 8 hours until patient can tolerate oral medication. Thereafter quinine is continued orally at 10mg/kg (maximum 600mg) every 8 hours to complete a total (parenteral + oral) of 7 days or a complete course of artemether-lumefantrine is given.

Intravenous quinine is administered as follows:

- A loading dose of quinine 20mg/kg (max 1200mg) diluted in 15mls/kg (maximum 500ml) of isotonic solution (5% dextrose or normal saline) is given intravenously to run over 4 hours.
- 8 hours from commencement of the initial dose of quinine, give 10mg/Kg (max 600mg) diluted in 10mls/kg (maximum 500ml) of isotonic solution (5% dextrose or normal saline) to run over 4 hours.
- Repeat 10mg/Kg quinine infusion every 8 hours until the patient can take medication orally.
Intramuscular quinine is administered as follows:
* Note: The dose of quinine through the intramuscular route is same as for intravenous route.

- Quinine MUST be diluted (maximum concentration is 60mg/ml) before intramuscular injection.
- A loading dose of 20mg/kg (maximum 1200mg) of quinine (diluted to a maximum 60mg/ml) is given by intramuscular injection (preferably the anterior thigh). A maximum of 3ml should be injected into one site. If the amount to be injected exceeds 3 mls, multiple sites should be used.
- 8 hours after the loading dose, give 10mg/kg (diluted to a maximum 60mg/ml) as intramuscular injection every 8 hours until the patient can take medication orally.

Note: In an emergency and in the absence of quinine, the following parenteral antimalarial options may be used for management of severe malaria

- Artesunate administered by the IM route at 2.4 mg/kg start then 1.2 mg/kg at 12 hrs, 24hrs then 1.2mg/kg daily for 6 days.
- Artemether administered by the intramuscular route at a loading dose of 3.2 mg/kg start then 1.6 mg/kg/daily for five days.

In patients with severe malaria and in the absence of quinine or any of the above parenteral antimalarials and the patient is able to tolerate oral feeds, then artemether-lumefantrine or any other available effective antimalarial may be used to initiate treatment (see annex 3). If the child is not able to drink, a nasogastric tube can be used to give oral medications.

5.3.3 Supportive Treatment

.1 Specific management for other severe manifestations of malaria. Some are highlighted below:

i. Hypoglycaemia – correct with glucose (IV or oral), and ensure adequate caloric intake (nutritional support) thereafter.

ii. Convulsions
   a. Treat with anti-convulsants
      i. (diazepam 0.3 mg/Kg IV, or 0.5mg/kg by rectal administration)
      ii. OR paraldehyde 0.4 ml/kg intramuscular injection.
   b. Make sure the patient has received glucose and that the temperature is controlled.
   c. If convulsions persist after initiation of antimalarial treatment, give phenobarbitone 15 mg/kg IM injection loading dose then a maintenance dose of 4 - 8mg/kg/day for 48 hours. An alternative to phenobarbitone is
IV phenytoin at a loading dose of 18 mg/kg loading dose the maintenance of 5 mg/kg/day for duration of 48 hours).

iii. Severe anaemia – treat with blood transfusion as per national blood transfusion guidelines which recommend that in the paediatric age group transfuse when Hb<4g/dl and that if Hb is between 4 and 5g/dl transfuse if signs of respiratory distress or cardiac failure are present.

iv. 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.

v. Control fever – antipyretic; mechanical methods (exposure, fanning, tepid sponging)

vi. Nursing care – management for comatose patients to avoid aspiration and pressure sores

5.3.4 Severe malaria patients able to tolerate oral treatment

Patients with the following features:
• Severe anaemia (haemoglobin level of <5g/dl or haemocrit of <15%)
• Two or more convulsions within a 24-h period
• hyperparasitaemia

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 the artemether-lumefantrine or oral quinine where AL is not available. They should however be closely monitored and other features of severity managed appropriately e.g. blood transfusion etc.

5.4 FOLLOW-UP OF ALL PATIENTS WITH SEVERE MALARIA

• Monitor Hb levels and give haematinics
• Monitor and rehabilitate patients with neurological sequelae

5.4.1 Pre- referral Management of Severe Malaria

Treatment of a patient with severe malaria should begin in the health centre/dispensary (while waiting for referral) so that life-saving therapy is not delayed:
Upon recognition of severe malaria, the medicine of choice for initiating treatment (pre-referral) at the peripheral facility is IM quinine. Quinine should be given at a loading dose of 15mg/kg body weight. All efforts should be made to move the patient to a center where the expertise and infrastructure exist for the adequate management of severe malaria.

In patients with alteration in the levels of consciousness, parenteral antibiotics (chloramphenicol) should also be administered along with the antimalarial (quinine).
If for any reason referral is not possible or delayed, treatment for severe malaria with the use of IM quinine 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.

**Intramuscular quinine is administered as follows:**

- Quinine MUST be diluted (maximum concentration is 60mg/ml) before intramuscular injection.
- A loading dose of 15mg/kg of quinine (diluted to a maximum 60mg/ml) is given by intramuscular injection (preferably the anterior thigh). A maximum of 3ml should be injected into one site. If the amount to be injected exceeds 3 mls, multiple sites should be used.

*For adults, the dose of quinine is 20mg/kg to a maximum of 1200mg.*

Note: In the absence of quinine, the following antimalarial options may be used to initiate management (pre-referral) of severe malaria

- Rectal artesunate is administered at a dose of 10mg / kg. If the rectal capsule is expelled within the first hour, another rectal capsule should be inserted. A second dose may be given after 24 hrs if patient is unable to access parenteral therapy.
- Artemether administered by the intramuscular route at a loading dose of 3.2 mg/kg start.
- Artesunate administered by the IM route at 2.4 mg/kg start.

Referral to Hospital: When sending the patient, remember:

- Send a clear letter or referral form about the clinical picture, including dosages, times, and route of administration for any medications given
- If blood film examination or slides have been taken, these should be sent along with the patient to the referral center.
- Send potential blood donors
- Ask the guardian to keep the child lying down on their side during the journey
- Send a staff member with the patient

### 6. MALARIA IN PREGNANCY

Pregnant women are at particular risk of malaria infection. Its consequences to the mother (anaemia and febrile illness) and the developing foetus and newborn (particularly low birth weight and associated infant mortality) can be grave. Although women in their first and second pregnancy, and all HIV infected women are at greatest risk of the effects
of malaria, all women should be advised on malaria prevention measures and clinical cases of malaria treated promptly with effective antimalarials.

6.1 MANAGEMENT OF UNCOMPLICATED MALARIA.

6.1.1 Diagnosis

- Clinical symptoms are as in non pregnant population.
- 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, patient with fever or history of fever in whom the health worker suspect malaria and has eliminated other possible causes of fever, should be presumptively classified and treated as malaria.

6.1.2 Treatment

a. ANTIMALARIALS
The recommended treatment for uncomplicated malaria in all trimesters of pregnancy is a 7 day therapy of oral quinine. However, artemether-lumefantrine can also be used in the 2nd and 3rd trimesters. Do not withhold artemether-lumefantrine in 1st trimester if quinine is not available Dose regimens for quinine and AL are as given in the uncomplicated malaria section (see annex 3)

b. SUPPORTIVE
   Prevent hypoglycaemia
   Foetal monitoring
   Treatment of anaemia
   Antipyretics

c. FOLLOW UP
   ANC
6.2 MANAGEMENT OF SEVERE MALARIA.

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

6.2.1 Diagnosis

- Features of severe malaria in pregnant women are similar to the non pregnant population. These are detailed in Section 2…………. However, pregnant women have an increased risk of hypoglycaemia and severe anaemia.
- Note that eclampsia is a differential diagnosis in pregnant women presenting with convulsions or alteration in level of consciousness.

| In all suspected cases of severe malaria, a parasitological confirmation of the 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. |

6.2.2 Treatment

The recommended medicine of choice for severe malaria is parenteral quinine. The preferred route of administration is the intravenous route. However the intramuscular route can be used as an alternative where intravenous route is not feasible.

The dosage regimen for quinine is as given in annex 3…………

However, because of the increased risk of hypoglycaemia in pregnant women, 5% dextrose is the preferred infusion solution for quinine administration.

*Note: Pregnancy is not a contraindication for the use of a loading dose regimen of quinine.*
7. MALARIA PREVENTION

7.1 INTERMITTENT PREVENTIVE TREATMENT in pregnancy (IPTp)
Pregnant women are at a particular risk of malaria infection. The consequences of malaria in pregnancy include anaemia and febrile illnesses in the mother, fetal loss, and low birth weight. Women in their first and second pregnancy are at greatest risk. All pregnant women at risk should be advised on malaria prevention measures as follows;

• IPT is recommended in areas of high malaria transmission
• The current recommended medicine for IPT is Sulphadoxine 500mg/Pyrimethamine 25mg given as a dose of three tablets
• Administer IPT with each scheduled visit after quickening to ensure women receive at least 2 doses.
• Women known to be HIV-infected or with unknown HIV status living in areas of high HIV prevalence (>10% among pregnant women) should receive at least 3 doses of IPT.
• IPT should be given at an interval of at least 4 weeks (1 month).
• Pregnant women who are HIV positive and are also taking antiretroviral therapy for PMTCT should receive IPT.
• Pregnant women who are HIV positive and are on daily cotrimoxazole chemoprophylaxis should not be given SP.
• IPT should be given under directly observed therapy (DOT) in the antenatal clinic and can be given on an empty stomach.

7.2 INSECTICIDE TREATED NETS (ITNS)
The use of ITNs is encouraged for all, but particularly in populations living in high transmission areas. It is recommended that all pregnant women and children under five years of age sleep under an ITN. ITN use should be encouraged early and consistently throughout pregnancy, and after delivery.

7.3 CHEMOPROPHYLAXIS IN THE NON-IMMUNE POPULATION.
Chemoprophylaxis is recommended for the following high risk groups

1. Non-immune visitors (mefloquine or atovaquone-proguanil or doxycycline)

2. Patients with sickle cell disease (proguanil).

3. Patients with tropical splenomegaly syndrome/hyperimmune malaria splenomegaly (proguanil).
Note:
- Travelers are encouraged to use other barrier methods to prevent or reduce bites from mosquitoes.
- 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.
- Travelers should carry a full course of artemether-lumefantrine (standby treatment) for use in the event they develop a fever and have no immediate access to health services.

8. 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 behaviors, the environment and resources available. The community should actively participate in the implementation of these vector control measures. Inter-sectoral collaboration involving line ministries, NGOs and the private sector is encouraged. The following strategies are available:

Reduction of transmission
- Use of ITMs/ITNs especially the vulnerable groups (Pregnant Women, Children under 5, HIV, economically disadvantaged).
  - Applicable in all epidemiological zones with malaria transmission
- Indoor Residual Spraying and selective larviciding in specific sites
  - Applicable in epidemic prone areas especially in highlands with regular periodicity of malaria upsurges.
- Screening of house inlets with wire mesh to reduce entry of mosquitoes
  - Applicable in all epidemiological zones with malaria transmission
- Environmental management for source reduction of vector density e.g. canal re-canalization, clear blocked drainages etc.
  - Applicable in all epidemiological zones with malaria transmission
- Biological control measures where feasible
  - Applicable in epidemic prone areas especially in highlands with regular periodicity in malaria upsurges
- Repellents and fumigants
  - Applicable in all epidemiological zones with malaria transmission
9. EPIDEMIC PREPAREDNESS AND RESPONSE

- Strengthening routine surveillance of:
  - Epidemiological indicators i.e. vectors, parasite rates,
  - Meteorological data
- Buffer stocks – chemicals, spray pumps, medicines among others.
- Logistic support
- Advocacy and social mobilization,
- Plans for epidemic response

10. BEHAVIORAL CHANGE COMMUNICATION

Health information, education and communication are a critical intervention for behavioral change towards improved health practices. The following important information should be provided to the patient, caretaker and community members

- seek prompt treatment of fevers
- Recognition of symptoms and signs of severe disease
- Adherence to treatment plan
- Use of appropriate prevention measures
ANNEX 1: IMCI flow chart showing danger signs, assessment and classification of child
1.2 ANNEX 2

MALARIA OUTPATIENT ALGORITHM FOR OLDER CHILDREN (>5 YRS) AND ADULTS

**FEVER**  
(History of fever in last 48h or axillary T ≥ 37.5°C)

- Assess patient for signs of severe malaria

  - If Yes
    - Manage as severe malaria

  - If No
    - Is there any other obvious cause of fever?

  - If No & microscopy/RDT NOT available
    - Do not request blood slide/RDT

  - If No & microscopy/RDT available
    - Request blood slide/RDT

    - Blood slide or RDT positive
      - Treat for uncomplicated malaria

    - Blood slide or RDT negative
      - Do not treat for malaria
        - Treat with antipyretic
        - Treat other cause of fever

  - If Yes & regardless of availability of microscopy/RDT
    - Do not request blood slide/RDT

**ANNEX 3: THE PHARMACOLOGY OF ANTIMALARIALS**

A. Antimalarials for uncomplicated malaria
1. Artemether-Lumefantrine (AL)

Formulation
Tablets containing 20mg Artemether and 120 mg Lumefantrine

Dose
AL is administered as a six dose treatment over a 3 day period. The first dose is taken at the time of initial diagnosis (0hr), the dose is repeated again after 8hrs, then twice a day for the next 2 days.
The number of tablets per dose for different age categories is given in the table below:

Dosing Schedule

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Age of patient in yrs</th>
<th>Number of tablets per dose (to be administered at 0h,8h,24,36h,48h, and 60h)</th>
<th>Content of Artemether (A) + Lumefantrine (L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 – 14 kg</td>
<td>Under 3 yrs</td>
<td>1</td>
<td>20mg A + 120 mg L</td>
</tr>
<tr>
<td>15 – 24 kg</td>
<td>4 – 8 yrs</td>
<td>2</td>
<td>40mg A + 240 mg L</td>
</tr>
<tr>
<td>25 – 34 kg</td>
<td>9 – 14 yrs</td>
<td>3</td>
<td>60mg A + 360 mg L</td>
</tr>
<tr>
<td>35 +</td>
<td>Above 14 yrs</td>
<td>4</td>
<td>80mg A + 480 mg L</td>
</tr>
</tbody>
</table>

* Absorption of Lumefantrine is increased when the drug is taken with food.

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

Contraindications
- Pregnancy – 1st trimester and lactation. There is limited data on use in pregnancy.
- Persons with severe malaria
- Persons with known hypersensitivity to either of the components.

2. Amodiaquine plus artesunate

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

3. Mefloquine plus artesunate

- 4 mg / kg once a day for 3 days plus Mefloquine (25 mg of base per kg) given as a single or split dose on second or third day.

B. Antimalarials for severe malaria

Quinine
Formulation

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

For practical purposes one (300mg) quinine sulphate tablet = one (300 mg) quinine dihydrochloride = one (300 mg) quinine hydrochloride tablet = one and a half (300 mg) quinine bisulphate tablets

Similarly one (300 mg) quinine bisulphate tablet = one (200 mg) quinine sulphate tablet.

Injectable solutions of quinine hydrochloride, quinine dihydrochloride or quinine sulphate containing 82% 82% and 82.6% quinine base respectively. The ampoules are usually 300mg / ml and come as 600 mg (salt) / 2ml or 300mg (salt) / ml.

Dose
Quinine is administered as a seven day dose of 10 mg /kg salt three times a day every 8 hourly

Dosing schedule for quinine tablets

<table>
<thead>
<tr>
<th>Quinine sulphate 200mg</th>
<th>Quinine 300 mg salt ( sulphate, dihydrochloride, hydrochloride)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WEIGHT IN KG</td>
<td>NO OF TABS</td>
</tr>
<tr>
<td>4 - 7 kg</td>
<td>1/4</td>
</tr>
<tr>
<td>8 - 11 kg</td>
<td>1/2</td>
</tr>
<tr>
<td>12 - 15 kg</td>
<td>3/4</td>
</tr>
<tr>
<td>16 - 23 kg</td>
<td>1</td>
</tr>
<tr>
<td>24 - 31 kg</td>
<td>1 1/2</td>
</tr>
<tr>
<td>32 - 39 kg</td>
<td>2</td>
</tr>
</tbody>
</table>

For children below the lowest weight category, the dosage of quinine is 10mg / kg and the tablets should thus be reconstituted into a syrup based on the weight of the patient.

Quinine intramuscular injection

The dosage of IM quinine injection is a loading dose of 15mg/kg and maintenance of 10mg/kg body weight.
How to give the intramuscular injection

- Weigh the patient (if the he/she cannot be weighed the following formula can be used to estimate the Weight: (Age (in years) X 2) + 8 = Wt in kg)

- Use a 10 ml sterile syringe. Draw up 5 ml of sterile water for injection. Then into the same syringe, draw up 300 mg (1 ml) from an ampoule of quinine. The syringe now contains 50 mg 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 300 mg.

- In all situations a maximum of 3ml should be injected into one injection site. If the amount to be injected exceeds 3 mls, half the amount should be injected into each injection site (refer to table below for number of sites).

- Give 10 mg (0.16 ml) per kg body weight by intramuscular injection.

An example of body weights and dose (ml) of injection is given in the table below;
<table>
<thead>
<tr>
<th>Body weight</th>
<th>Volumes of diluted quinine injection (ml) to be administered</th>
<th>Number of injection sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>under 5 kg</td>
<td>1.0ml</td>
<td>one</td>
</tr>
<tr>
<td>5.1 - 7.5 kg</td>
<td>1.5ml</td>
<td>one</td>
</tr>
<tr>
<td>7.6 - 10 kg</td>
<td>2.0ml</td>
<td>one</td>
</tr>
<tr>
<td>10.1 - 12.5 kg</td>
<td>2.5ml</td>
<td>one</td>
</tr>
<tr>
<td>12.6 - 15 kg</td>
<td>3.0ml</td>
<td>one</td>
</tr>
<tr>
<td>15.1 - 17.5 kg</td>
<td>3.5ml</td>
<td>two</td>
</tr>
<tr>
<td>17.6 - 20 kg</td>
<td>4.0ml</td>
<td>two</td>
</tr>
<tr>
<td>20.1 - 22.5 kg</td>
<td>4.5ml</td>
<td>two</td>
</tr>
<tr>
<td>22.6 - 25 kg</td>
<td>5.0ml</td>
<td>two</td>
</tr>
<tr>
<td>25.1 - 27.5 kg</td>
<td>5.5ml</td>
<td>two</td>
</tr>
<tr>
<td>27.6 - 30 kg</td>
<td>6.0ml</td>
<td>two</td>
</tr>
<tr>
<td>30.1 - 32.5 kg</td>
<td>6.5ml</td>
<td>three</td>
</tr>
<tr>
<td>32.6 - 35 kg</td>
<td>7.0ml</td>
<td>three</td>
</tr>
<tr>
<td>35.1 - 37.5 kg</td>
<td>7.5ml</td>
<td>three</td>
</tr>
<tr>
<td>37.6 - 40 kg</td>
<td>8.0ml</td>
<td>three</td>
</tr>
<tr>
<td>40.1 - 42.5 kg</td>
<td>8.5ml</td>
<td>three</td>
</tr>
<tr>
<td>42.6 - 45 kg</td>
<td>9.0ml</td>
<td>three</td>
</tr>
<tr>
<td>45.1 - 47.5 kg</td>
<td>9.5ml</td>
<td>four</td>
</tr>
<tr>
<td>47.6 - 50 kg</td>
<td>10.0ml</td>
<td>four</td>
</tr>
<tr>
<td>50.1 - 52.5 kg</td>
<td>10.5ml</td>
<td>four</td>
</tr>
<tr>
<td>52.6 - 55 kg</td>
<td>11.0ml</td>
<td>four</td>
</tr>
<tr>
<td>55.1 - 57.5kg</td>
<td>11.5ml</td>
<td>four</td>
</tr>
<tr>
<td>57.6 - 60 kg</td>
<td>12.0 ml</td>
<td>four</td>
</tr>
<tr>
<td>60.1 - 62.5 kg</td>
<td>12.5 ml</td>
<td>four</td>
</tr>
<tr>
<td>62.6 - 65 kg</td>
<td>13.0 ml</td>
<td>four</td>
</tr>
<tr>
<td>65.1 - 67.5 kg</td>
<td>13.5 ml</td>
<td>four</td>
</tr>
<tr>
<td>67.6 - 70.0 kg</td>
<td>14.0 ml</td>
<td>four</td>
</tr>
<tr>
<td>70.1 - 72.5 kg</td>
<td>14.5 ml</td>
<td>four</td>
</tr>
</tbody>
</table>
Quinine intravenous infusion

Intravenous quinine is administered in isotonic fluid; either 5% dextrose or normal saline as follows

**Adult**

1. The first dose 20 mg/Kg in 500mls of isotonic fluid given over 4 hours (max 1,200 mg).
2. Then 8 hours after commencing the initial dose give 10mg/Kg in 500mls of isotonic fluid over 4 hours (max 600mg).
3. Repeat 10mg/Kg 8 hourly until the patient can take orally.
4. Change to a full course of oral artemether/lumefantrine full course (6 doses) or oral quinine to complete 7 days of quinine.

Assessment of fluid status should be monitored regularly including urine output.

* If patient cannot be weighed – IV quinine loading dose should be 900 mg. Followed by 600 mg 8 hourly.

**Children**

1. Put up IV quinine drip (15mg/Kg body weight loading dose in 15mls/kg of isotonic fluid) to run over 4 hours.
2. Fluid intake should be calculated according to weight, bolus 20 mls/kg (minimum 10mls/Kg) and maintenance 4-6 mls/kg/hr.
3. 12 hours after commencing the initial dose of quinine, give 10mg/Kg in 10mls/kg of isotonic fluid.
4. Repeat 10mg/Kg 12 hourly until the patient can take medication orally.

A full course of artemether/lumefantrine can be given or quinine should 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, hypoglycemia 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.

Hypoglycemia is due to the stimulative effect of quinine on the β cells of the pancreas. It is common in pregnancy and very prolonged and severe infection.

**Other side effects are:**
GIT: nausea, vomiting, diarrhoea,
Vision: blurred vision, distorted color perception, photophobia, diplopia and night blindness
Cutaneous flushing, pruritus, rashes, fever, dyspnoea
Black water fever has been observed in patients with G6PDH enzyme deficiency. It is characterized by hemolysis, hemoglobinuria and renal failure

**Artemether**

**Formulations**

1. Ampoules of injectible solution for intramuscular IM injection containing 80mg / ml and 20mg / ml for paediatric patients.
2. Capsules containing 40 mg Artemether
3. Tablets containing 50 mg Artemether

**Dose**

1. Severe malaria

3.2 mg / kg by the intramuscular route as a loading dose on the first day then 1.6 mg / kg daily for a minimum of 3 days or until the patient can take oral therapy to complete a 7 day course.

**Artesunate**

**Formulations**

1. Ampoules for intramuscular or intravenous injection containing 60 mg sodium artesunate in 1 ml of injectable solution
2. Tablets containing 50 mg sodium artesunate or 200 mg sodium artesunate.
3. Rectal capsules containing 100 mg or 400 mg sodium artesunate.
4. Suppositories of sodium artesunate.

**Dose**

**Severe malaria**

By the IM route, the dose is 2.4 mg / kg followed by 1.2 mg / kg at 12 hrs and 24 hrs then 1.2 mg / kg daily for 6 days.

By the intravenous route (IV) the dose is 2.4mg/kg on the first day followed by 1.2 mg / kg body weight daily until patient can take another effective antimalarial drug.
Rectal artesunate

Formulation

1. Capsules containing 100mg sodium artesunate.
2. Capsules containing 400mg sodium artesunate.

Dose

Rectal artesunate is administered as pre referral treatment at a dose of 10mg / kg. If the rectal capsule is expelled within the first hour, another rectal capsule should be inserted. A second dose may be given after 24 hrs if patient is unable to access parenteral therapy.

Dosage schedule for artesunate suppositories.

<table>
<thead>
<tr>
<th>Weight</th>
<th>Age</th>
<th>Number of 100 mg capsules</th>
<th>Number of 400 mg capsules</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 – 19 kg</td>
<td>1 – 5 yrs</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>20 – 29 kg</td>
<td>6 – 7 yrs</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>30 – 39 kg</td>
<td>8 – 12 yrs</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>40 – 49 kg</td>
<td>&gt; 12 yrs</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>50 – 92 kg</td>
<td>&gt; 12 yrs</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Above 92 kg</td>
<td>&gt; 12 yrs</td>
<td>-</td>
<td>3</td>
</tr>
</tbody>
</table>

CHEMOPROPHYLACTIC AGENTS

Mefloquine

Formulations

1. Tablets of 274mg Mefloquine Hydrochloride containing 250 mg base.
2. Tablets of 250 mg Mefloquine hydrochloride containing 228mg base.

Dose

Mefloquine is administered as a weekly dose of 250 mg for adults or 5mg base / kg body weight for persons below 36 kg.

It is recommended that Mefloquine prophylaxis is started 2 – 3 weeks before departure, throughout the stay and continued for 4 weeks after departure.
Dosing schedule

<table>
<thead>
<tr>
<th>Weight</th>
<th>Age</th>
<th>No of tablets per week</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5 kg</td>
<td>&lt; 3 months</td>
<td>Not recommended</td>
</tr>
<tr>
<td>5 – 12 kg</td>
<td>3 – 23 months</td>
<td>¼</td>
</tr>
<tr>
<td>13 – 24 kg</td>
<td>2 – 7 yrs</td>
<td>½</td>
</tr>
<tr>
<td>25 – 35 kg</td>
<td>8 – 10 yrs</td>
<td>¾</td>
</tr>
<tr>
<td>36 and above</td>
<td>11 yrs and above</td>
<td>1</td>
</tr>
</tbody>
</table>

Side effects

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

Contraindications

- Avoid in 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 only be taken 12 hours after administration of the last quinine dose.
- Care should be taken when administering concomitant medications that interfere with cardiac function.
**Proguanil**

**Formulation**

1. Tablets of 100mg of Proguanil hydrochloride containing 87mg of Proguanil base

**Dose**

Proguanil is administered at a daily dose of 3mg / kg beginning two days before travel continuing daily throughout and then continued for 4 weeks after departure.

**Dosing schedule**

<table>
<thead>
<tr>
<th>Weight</th>
<th>Age</th>
<th>Number of tablets per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 – 8 kg</td>
<td>&lt; 8 Months</td>
<td>¼</td>
</tr>
<tr>
<td>9 – 16 kg</td>
<td>8 months – 3 years</td>
<td>½</td>
</tr>
<tr>
<td>17 – 24 kg</td>
<td>4 – 7 yrs</td>
<td>¾</td>
</tr>
<tr>
<td>25 – 35 kg</td>
<td>8 – 10 yrs</td>
<td>1</td>
</tr>
<tr>
<td>36 – 50 kg</td>
<td>11 – 13 yrs</td>
<td>1 1/2</td>
</tr>
<tr>
<td>50 + kg</td>
<td>14+ yrs</td>
<td>2</td>
</tr>
</tbody>
</table>

**Side effects**

Low doses – nausea and diarrhoea
Rarely hair loss, mouth ulcers,
High dose - abdominal pain, vomiting, hematuria and diarrhoea have been reported.
*Symptoms are treated as they appear, there’s no specific antidote for over dosage of Proguanil.

**Contraindications**

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

**Caution**

Antacids like magnesium trisilicate decrease absorption of Proguanil.
**Atovaquone – Proguanil (Malarone®)**

**Formulation**

1. Adult tablets: Film coated tablets containing 250 mg atovaquone and 100 mg Proguanil hydrochloride
2. Pediatric tablets containing 62.5 mg atovaquone and 25 mg Proguanil hydrochloride

**Dosage**

Atovaquone – Proguanil is administered as a daily dose of 250 mg atovaquone and 100 mg Proguanil (1 tablet) commencing 1 day before departure to a malaria endemic area, throughout the stay and continuing 7 days after leaving.

**The table below refers to the paediatric tablet of 62.5 mg atovaquone and 25 mg Proguanil**

<table>
<thead>
<tr>
<th>Weight</th>
<th>Number of tablets</th>
<th>Daily dose Atovaquone (A) + Proguanil (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;11 kg</td>
<td>Not recommended</td>
<td></td>
</tr>
<tr>
<td>11 – 20 kg</td>
<td>1</td>
<td>62.5 mg A + 25 mg P</td>
</tr>
<tr>
<td>21 – 30 kg</td>
<td>2</td>
<td>125 mg A + 50 mg P</td>
</tr>
<tr>
<td>31 – 40 kg</td>
<td>3</td>
<td>187.5 mg A + 75 mg P</td>
</tr>
</tbody>
</table>

The drug should be taken with food or milk at the same time each day.

**Side effects**

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

**Contraindications**

- It is contraindicated in persons with hypersensitivity to atovaquone and/or Proguanil.
- It isn’t recommended for use in pregnancy because of lack of data.
- Caution is indicated in persons with severe renal failure (creatinine clearance)
**Doxycycline**

**Formulation**

1. Tablets containing 100mg doxycycline salt as hydrochloride
2. Capsules containing 100mg doxycycline salt as hydrochloride

**Dose**

Doxycycline is administered as a daily dose of 100 mg 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.

If tablets are available, fractions can be administered for patients aged 8 to 13 years.

**Dosing schedule**

<table>
<thead>
<tr>
<th>Weight in kg</th>
<th>Age in years</th>
<th>No of tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25</td>
<td>&lt; 8</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>25 – 35</td>
<td>8 - 10</td>
<td>½</td>
</tr>
<tr>
<td>36 – 50</td>
<td>11 – 13</td>
<td>¾</td>
</tr>
<tr>
<td>50+</td>
<td>14+</td>
<td>1</td>
</tr>
</tbody>
</table>

**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.
ANNEX 4: COMA MONITORING SCALES

Table 1: The Glasgow Coma Score (for Adults and Children over 12yrs)

<table>
<thead>
<tr>
<th>Eyes open</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Spontaneously</td>
<td>4</td>
</tr>
<tr>
<td>- To speech</td>
<td>3</td>
</tr>
<tr>
<td>- To pain</td>
<td>2</td>
</tr>
<tr>
<td>- Never</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Best verbal</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>- oriented</td>
<td>5</td>
</tr>
<tr>
<td>- response- confused</td>
<td>4</td>
</tr>
<tr>
<td>- in appropriate words</td>
<td>3</td>
</tr>
<tr>
<td>- incomprehensible sounds</td>
<td>2</td>
</tr>
<tr>
<td>- none</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Best motor response</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>- obeys commands</td>
<td>6</td>
</tr>
<tr>
<td>- localizes pain</td>
<td>5</td>
</tr>
</tbody>
</table>

  *flexion to pain:*
  - withdrawal        | 4     |
  - abnormal          | 3     |
| - extension to pain | 2     |
| - none              | 1     |

**Total** 3-15

To obtain the Glasgow coma score obtain the score for each section add the three figures to obtain a total.
### Table 2: The modified Glasgow Coma scale (The Blantyre Coma Scale) (for children < 12 years)

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes open</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- spontaneously</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Eyes movement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- directed</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(eg follows mothers face)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- not directed</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Verbal response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- appropriate cry</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>- moan or inappropriate cry</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>- none</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Best motor response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- localizes painful stimulus (a or c)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>- withdraws limb from pain (b)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>- non-specific or absent response</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>0 - 5</td>
</tr>
</tbody>
</table>

Press knuckles firmly on the patients sternum
Press firmly on the thumbnail bed with side of a horizontal pencil
Press firmly on the supra-orbital groove with the thumb

The scales can be used repeatedly to assess improvement or deterioration.
ANNEX 5: GLOSSARY

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).

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

CHEMOPROPHYLAXIS:
The protection from, or prevention of, disease by the use of drugs.

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

ENDEM1CITY:
Occurring frequently in a particular region or population

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

FEVER:
Arise in body temperature above the normal temperature i.e. above an oral temperature of 37.5°C.

FEBRILE CONVULSIONS:
Convulsions occurring in children aged 6/12 - 6yrs due to fever caused by infection outside the central nervous system

HYPERPYREXIA:
Temperature over 39.5°C

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

HYPERSENSITIVITY:
Prone to respond abnormally to the presence of a particular antigen, which may cause a variety of tissue reactions ranging from serum sickness to an allergy.

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 fluid for examination.

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.

PRURITUS:
Itching caused by local irritation of the skin or sometimes nervous disorders.

RECRUDESCENCE:
Renewed manifestation of infection believed due to the survival of malaria parasites in the blood.

RESISTANCE:
The ability of a parasite to multiply or survive in the presence of concentrations of a drug that normally destroys parasites of the same species or prevents their multiplication.

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

SENSITIVE:
Possessing the ability to respond to a stimulus.

STEVEN-JOHNSON SYNDROME:
An inflammatory condition characterized by fever, large blisters on the skin, and ulceration of the mucous membranes. It may be a severe allergic reaction to certain infections or drugs.

TREATMENT FAILURE:
Treatment failure can be defined as a failure to achieve the desired therapeutic response after the initiation of therapy. Treatment failure is not synonymous with drug resistance.

ZOOPROPHYLAXIS:
The prevention of disease transmission by the use of animals to attract mosquitoes to bite them instead of man. This is usually done by tethering domestic cattle and animals at night between known mosquito breeding sites and human dwellings.
REFERENCES


