Government of Sierra Leone
Ministry of Health and Sanitation
National Malaria Control Programme

Guidelines for Case Management of Malaria

Fourth Edition

2015

FOREWORD

The first edition of the treatment guidelines was published in 2000 and subsequently in 2005 (2nd edition) and 2010 (3rd edition). This edition of the guideline replaces the 2010 third edition.

The move towards universal diagnostic testing of malaria is a critical step forward in the fight against the disease as it will allow for targeted use of ACTs for those who actually have malaria. This aim is to reduce the emergence and spread of drug resistance and to help identify patients who have fever, but do not have malaria, so that alternative diagnosis can be made and appropriate treatment provided. This paradigm shift has occurred in response to a growing need for more accurate parasitological diagnosis to assure improved patient case management and the availability of more robust diagnostics test that is easy to use even at community level outside of formal health facilities. This document provides guidance for the diagnosis and treatment of malaria in line with the updated recommendations of WHO.

It is expected that these guidelines will standardize the management of malaria at all levels of the health services throughout the country.

I wish to take this opportunity to acknowledged the invaluable assistance provided by, WHO, (Country office, WHO/IST, WHO /HQ), UNICEF, other partners and the National Malaria Control Programme in the formulation of these guidelines. It is hoped that this collaborative work and cooperation will continue.

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ACKNOWLEDGEMENT

The development of the Guidelines for Case Management of Malaria was a long and painstaking process in which many individuals and institutions/organizations were actively involved. Their invaluable contributions towards the successful conclusion of this exercise cannot be over emphasized.

At this juncture, it is proper and fitting that the Ministry of Health and Sanitation and the National Malaria Programme acknowledge with thanks the support and contribution from development partners, non-governmental organizations and private sector who have in diverse ways contributed to the successful development of this guidelines.

Finally, it is my fervent hope that this document will become the single most important point of reference on issues pertaining to the control of malaria for the next five years. I hope together we can achieve our Roll Back Malaria (RBM) targets and Millennium Development Goals (MDGs)/SDGs.

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3 | Page

Table of Contents

List of Tables

List of Boxes

List of Annexes

EXECUTIVE SUMMARY

The Government of Sierra Leone recognizes malaria as a health and socio-economic burden as stated in the National Health Sector Strategic Plan (NHSSP 2010-2015) which considers malaria control a priority. Malaria case management entails early diagnosis and prompt treatment with effective antimalarial medicines remains a vital component of the malaria control strategies.

The general objective of this guideline is to provide a set of recommendations and regulations for the care of patients with malaria based on the current anti-malarial treatment policy in view of improving the quality of care in Sierra Leone.

The guideline stipulates that all suspected malaria cases should be confirmed parasitologically prior to prompt and appropriate treatment. Treatment of uncomplicated malaria is the same at all levels of the health care delivery services

The medicine of choice for the treatment of uncomplicated malaria is Artemether plus Lumefantrine (AL), Artesunate plus Amodiaquine (AS+AQ) can be used as an alternative option. For severe malaria, parenteral artensunate is the medicine of choice and in areas where parenteral treatment of severe malaria is not feasible, rectal artesunate should be used as a pre-referral treatment as the patient is referred to a facility where parenteral artesunate can be administered.

1.0 INTRODUCTION

1.1 EPIDEMIOLOGICAL SITUATION AND PARASITE DISTRIBUTION

Malaria is an acute disease caused by protozoa of the genus Plasmodium, which is transmitted to humans through the bite of an infected female anopheline mosquito.

The country has a varied terrain, ranging from coastline swamps, through inland swamps and rain forest to one of the highest mountains in West Africa, the Bintumani at 2200m. The secondary palm-bush is the main vegetation and it is interspersed with numerous swamps that are mostly cultivated for rice. These swamps provide ideal breeding places for the Anopheline vectors of malaria. The coastal line of the country has several mangrove swamps, which provide the breeding sites for *anopheles melas* mosquitoes, which is one of the major vectors of malaria besides *anopheles gambiae* and *anopheles funestus*.

In Sierra Leone, malaria is endemic with seasonal variations at the start and end of the rainy season. It is presently the leading cause of morbidity and mortality amongst children under five years of age. *Plasmodium falciparum* is the dominant parasite mainly responsible for over 90% of malaria cases and all the severe forms of the disease. The entire populace is at risk of developing the disease accounting for over 40.3% of outpatient morbidity, but the most vulnerable groups are under-five year old (U5) children and pregnant women.

The 2013 SLMIS is the first MIS that is inclusive of rapid diagnostic testing (RDT) and microscopy to determine the national malaria prevalence among children under five years of age. This survey revealed that, one-third (33%) of children under age 5 had fever during the two weeks preceding the survey, with a higher proportion of rural children (37%) than urban children (32%) having fever (MIS, 2013). Of these children, 63 percent sought advice on treatment. Among children that had a fever, 37 percent took any ACT, the recommended malaria treatment in Sierra Leone. A large proportion of children under age 5 with fever who received antimalarials for treatment were given artesunate + amodiaquine (ASAQ) (84 percent),
When tested for malaria, 46% of the children age 6-59 months were positive based on Rapid Diagnostic Tests (RDTS). Analysis of the blood smears by microscopy revealed a slightly lower prevalence of 43% of children tested positive for malaria.

Reports from health facilities obtained through the routine health management information system (HMIS) indicate an increasing trend in the number of total outpatient department (OPD) cases, with the malaria cases per 1,000 population increasing from 250 cases in year 2,000 to about 437 cases per 1,000 population in 2014 (figure 7). This can be attributed to a number of factors including improved data capture (HMIS).
The parasite testing rates of suspected malaria cases in the country stagnated from 2005 to 2007 but saw a steady increase from 18% in 2007 to 35% in 2012

Malaria is presently the leading cause of morbidity and mortality amongst children under five years of age with a mortality attributed to suspected malaria of 38.3% among children aged five years and below and 25.4% for all ages [Situation Analysis of malaria (MoHS) 2004]. Malaria is a major threat to the socio-economic development of the country with an estimated 7-12 days lost on the average per episode of malaria.

1.2 NATIONAL DRUG RESISTANCE PATTERN

Plasmodium falciparum has developed resistance to almost every class of antimalarial compounds. As a result of this, the World Health Organization has recommended artemisinin-based combination therapy as first line treatment for falciparum malaria. There is however need for the continuous monitoring of the efficacy of these antimalarials in order to provide timely information on trends of the emergence of resistant

strains. We assessed the therapeutic efficacy of oral artesunate –amodiaquine and artemether-lumefantrine combinations in the treatment of uncomplicated falciparum malaria in four District Hospitals in Sierra Leone.

Table 1:**Therapeutic efficacy of artesunate+amodiaquine in four sites and artemether+lumefantrine in four sites, Sierra Leone.**

Treatment outcome	**Artesunate+amodiaquine**		**Artemether+lumefantrine**	
	Kenema (n=101)	**Rokupa (n=8)**	**BO (n=106)**	**Makeni (n=105)**
% Early Treatment failure (95% CI)	0.0 (0.0-3.7)	0.0 (0.0-36.9)	0.0 (0.0-3.6)	0.0 (0.0-3.5)
% Late Clinical Failure(95% CI)	0.0 (0.0-3.7)	0.0 (0.0-36.9)	0.0 (0.0-3.6)	0.0 (0.0-3.5)
% LateParasitologicalFailure(95% CI)	0.0 (0.0-3.7)	0.0 (0.0-36.9)	0.0 (0.0-3.6)	0.0 (0.0-3.5)
% Adequate Clinical & Parasitological response(95% CI)	100 (96.3-100)	100 (63.1-100)	100 (96.4-100)	100 (96.5-100)
Kaplan-Meier Cumulative Treatment Failure *Rate*	0.0	0.0	0.0	0.0

PCR corrected responses.

When corrected for PCR on the other hand, a 100% adequate clinical and parasitological response was obtained for the two drugs in all four study sites. Results from this study indicate that both artesunate-amodiaquine and artemether-lumefantrine combinations remain highly efficacious in Sierra Leone with presently no observed emergence of resistant strains to both drugs.

The unadjusted results shows (uncorrected for PCR[1] analysis) 96% (95% CI: 902 – 989) and 100% (95% CI:63.1 – 100) response were obtained in Kenema and Bo respectively with Artesunate-amodiaquine combination whilst 94.3% (CI 95 : 88.1 – 979) and 100% (95% CI: 96.5 – 100) were obtained using Artemether-lumefantrine combination in Bo and Makeni respectively.

Table 2:Therapeutic efficacy of artesunate + amodiaquine in two sites and artemether+lumefantrine in two sites, Sierra Leone. PCR uncorrected responses.

TREATMENT OUTCOME	**ARTESUNATE+AMODIAQUINE**		**ARTEMETHER+LUMEFANTRINE**	
	Kenema (n = 101)	**Rokupa (n = 8)**	**Bo (n = 106)**	**Makeni (n = 105)**
% Early Treatment Failure (95% CI)	0.0 (0.0-3.6)	0.0 (0.0 – 36.9)	0.0 (0.0 – 3.4)	0.0 (0.0 – 3.5)
% Late Treatment Failure (95% CI)	1.0 (0.0 – 5.4)	0.0 (0.0 – 36.9)	0.9 (0.0 – 5.1)	0.0 (0.0 – 3.5)
% Late Parasitological Failure (95% CI)	3.0 (0.6 – 8.4)	0.0 (0.0 – 36.9)	4.7 (1.5 – 10.7)	0.0 (0.0 – 3.5)
% Adequate Clinical & Parasitological Response (95% CI)	96.0 (90.2 – 98.9)	100 (63.1 – 100)	94.4 (88.1 – 97.9)	100 (96.5 – 100)
Kaplan-Meier Cumulative Treatment Failure Rate	0.0	0.0	5.6 (2.6 – 12.1)	0.0

[1] Polymerase Chain Reaction

1.3 GENERAL OBJECTIVE

The general objective of the guideline is to provide a set of recommendations and regulations for the care of patients with malaria based on the current anti-malarial treatment policy with the aim of improving the quality of care.

1.4 SPECIFIC OBJECTIVE

To guide stakeholders at all levels of the health care delivery system in the management of malaria cases, particularly:

- Make a prompt and correct diagnosis of malaria.
- Provide timely appropriate treatment.
- Recognize very early, the danger signs of severe malaria
- Ensure prompt referral of cases to the appropriate level equipped to provide adequate support services and care.
- Equip all levels of the health delivery system including at the community level -Community Case Management of Malaria (CCMm).
- Educate mothers/caregivers to recognize fever and other signs and symptoms of malaria and appropriate care seeking behavior.

1.5 TARGET GROUP

The guidelines targets all parties engaged in malaria control including but not limited to the following: health professionals in the public and private sector, non-governmental organizations, research and health training institutions, the pharmaceutical industry and other agencies working as partners in health or malaria control.

1.6 HEALTH CARE LEVELS

The Ministry of Health and Sanitation is charged with the responsibility of providing Health Care Services in Sierra Leone which is delivered at three levels .This classification is based on the level which determines the population served, competences, equipment and volume and quality of support services available as described in the Basic Package of Essential Health Services for Sierra Leone 2015.

(i) Primary level - all persons /institutions offering primary care. It includes Peripheral Health Units – Community Health Centres, Community Health Posts, Maternal and Child Health Posts, Community Health Workers and Private Practitioners without in-patient facilities.
(ii) Secondary level: Satellite clinics, District and Mission Hospitals manned by Medical Officers, Nursing Staff with support services including a laboratory for diagnosis and monitoring malaria parasitaemia.
(iii) Tertiary level comprising the larger district hospitals and the National Referral Hospitals.

2.0 DIAGNOSIS OF MALARIA

RECOMMENDATION: All cases of suspected malaria should have a parasitological test (with either microscopy or rapid diagnostic test kit -RDT) or Rapid diagnostic test (RDT)) to confirm the diagnosis.

2.1. CLINICAL DIAGNOSIS OF MALARIA

Malaria manifest clinically either as an uncomplicated disease or as severe disease. A careful assessment of the patient with suspected malaria is essential in order to differentiate between the acute uncomplicated and severe disease, as this has treatment and prognostic implications.

2.1.1 UNCOMPLICATED MALARIA

Fever is the most common feature of malaria. Headache, aching joints and general discomfort usually accompany this. The onset of malaria symptoms may resemble an influenza-like illness especially in infants and young children, where early symptoms may be limited to poor appetite, restlessness, cough and/or diarrhoea, and loss of normal interest in the surroundings.

2.1.2 SEVERE MALARIA

Severe manifestations of malaria are usually associated with *P. falciparum* infections. Severe malaria is defined as *P. Falciparum* infection in the presence of any life threatening condition. These include:

- Generalized Convulsions (fits)- 2 or more episodes in a 24 hour period
- Altered consciousness(change of behaviour, confusion,delirium,coma persisting for over 30min after convulsion)
- Severe anaemia (extreme pallor) -Hb<5g/dl or PCV < 15%
- Hypogylcaemia (blood glucose <2.2 mmol/l or <40mg/dl)
- Spontaneous unexplained bleeding (DIC)
- Haemoglobinuria (dark urine)
- Acute renal failure (failure to make urine or making very little quantity of urine)
- Shock or circulatory collapse (cold limbs, weak rapid pulse)
- Jaundice(yellow coloration of the eyes)
- Acute pulmonary oedema or difficulty in breathing (Adult respiratory distress syndrome)
- Hyperparasitaemia (>250,000*ml* or >5%)

All life threatening conditions and the presence of any danger signs in the presence of an acute febrile illness should be considered as possible severe malaria and referred to a facility where appropriate management is feasible. These danger signs would include:

- Vomiting everything
- Inability to drink or breast feed for infants
- Extreme weakness (Prostration)

Table 3: Clinical features of uncomplicated and Severe malaria

UNCOMPLICATED MALARIA	
• Fever	• Vomiting and/or diarrhoea
• Headache	• Chest pain
• Joint pains	• Poor appetite
• Malaise	• Body weakness

SEVERE MALARIA	
• Convulsions • Altered consciousness • Acute renal failure • Severe anaemia • Haemoglobinuria	• Bleeding tendency (DIC) • Jaundice • Pulmonary oedema • Hypoglycaemia • Shock

2.2 PARASITOLOGICAL DIAGNOSIS

Parasitological confirmation of malaria should be part of good clinical practice to improve the quality of care of patients. Routinely, the definitive diagnosis of malaria can only be made with microscopy in the presence of malaria parasites in the blood. Rapid Diagnostic Tests (RDTs) can also be used at all levels of the health care delivery system including at the community level by Community Health Workers to confirm diagnosis of malaria.

The results of parasitological diagnosis should be available within a short time (2 hours) of the patient presenting. Both microscopy and RDTs must be supported by a quality assurance programme. Antimalarial treatment should be limited to cases with positive tests, and patients with negative results should be reassessed for other common causes of fever and treated appropriately

3.0 MANAGEMENT OF UNCOMPLICATED MALARIA

RECOMMENDATION: Treat all cases of uncomplicated malaria with artemether + lumefantrine (AL). Artesunate plus amodiaquine (AS+AQ) can be used as an alternative.

3.1 CASE DEFINITION

Uncomplicated malaria is defined as symptomatic infection with malaria parasitaemia without signs of severity or evidence (clinical or laboratory) of vital dysfunction.

SIGNS AND SYMPTOMS

The signs and symptoms of uncomplicated malaria are non-specific. Malaria is, therefore, suspected clinically mostly on the basis of fever or a history of fever.
The patient suffering from uncomplicated malaria commonly complains of:

- Fever (37.5°C or higher) a history of fever for 2-3 days
- Chills or feeling unusually cold.
- Rigors or shivering
- Headache

Other features include:

- Generalized body and joint pains
- Nausea
- Vomiting
- Loss of appetite
- Sweating

The presentation of malaria varies and may resemble other locally important diseases such as pneumonia, meningitis, typhoid fever, Lassa fever, yellow fever and septicemia. In the case of malaria, the fever may be initially intermittent. Young children may be anaemic and their liver and spleen may be palpable. Pregnant women may also be anaemic.

3.2. TREATMENT OBJECTIVES

- To cure the infection as rapidly as possible (Cure is defined as the elimination from the body of the parasite that causes the illness).

- To prevent progression to severe disease, and additionally morbidity associated with treatment failure.

3.3. TREATMENT RECOMMENDATIONS

Confirmed malaria cases (clinical and parasitological) should be given prompt and appropriate treatment. Treatment solely on the basis of clinical suspicion should only be considered when a parasitological diagnosis is not accessible or possible.
The first line drug for uncomplicated malaria is the same at all levels of the health care delivery services.

3.3.1 FIRST LINE TREATMENT:

THE MEDICINE OF CHOICE for the treatment of all cases of uncomplicated malaria is *Artemether plus lumefantrine (AL) except for pregnant women in the first trimester .*

In situations where AL is not available or the drug is not tolerated, the alternative recommended medicine for the treatment of uncomplicated malaria is *Artesunate plus amodiaquine (ASAQ) .*

Treatment of Malaria in Pregnancy:

- First trimester: Treat pregnant women with uncomplicated malaria in the first trimester of pregnancy with oral quinine plus clindamycin (for 7 days). If however, quinine is not available or the adherence with a 7 day treatment of oral quinine plus clindamycin cannot be guaranteed, treat with ACT (AL first option with AS+AQ as alternative).
- Second and third trimester of pregnancy: Treat pregnant women in the second and third trimester presenting with uncomplicated malaria as non-pregnant adults using AL or AS+AQ as alternative.

Treatment of infants weighing less than 5 kg:

- Treat infants weighing < 5 kg with uncomplicated malaria with AL at the same dose as for children weighing 5 kg. Malaria is an unlikely cause of fever in this age group. Management in this age group should be under medical supervision with the ability to make a firm confirmation and exclude all other more likely and dangerous causes of fever in this age group. Children less than 5kg of weight presentation to a CHW should be referred to a health facility for appropriate evaluation and treatment. **They should not be treated by CHWs**.

Table 3: Dosage schedule for Artemether-Lumefantrine treatment

Weight (Kg)	Age	20/120mg					
		Day 1		Day 2		Day 3	
		Morning	Evening	Morning	Evening	Morning	Evening
< 14	>3yrs	1 tab/dose	1 tab/dose	1 tab/dose	1 tab/dose	1 tab/dose	1 tab/dose
15-24	4-8yrs	2 Tabs/dose	2 Tabs/dose	2 Tabs/dose	2 Tabs/dose	2 Tabs/dose	2 Tabs/dose
25-34	9-14yrs	3 tabs/dose	3 tabs/dose	3 tabs/dose	3 tabs/dose	3 tabs/dose	3 tabs/dose
>35	(>14yrs	4 tab/dose	4 tab/dose	4 tab/dose	4 tab/dose	4 tab/dose	4 tab/dose
>35	1 tablet AL 80/480mg fixed dose, twice per day						

AL 80/480mg fixed dose. A higher strength of AL that has 6 tablets instead of 24 for a complete dosing regimen.

Note: Absorption of lumefantrine is enhanced by co-administration with a fatty meal. It is recommended that this ACT should be taken immediately after food or a fat containing drink (e.g. milk), particularly on the second and third days of treatment.

Table 4: Dosage schedule for fixed combination of ASAQ treatment

Age	*Weight in kg*	*Dosage*
< 11 months	≥4.5kg to < 9 kg	1 tablet (25mg artesunate/67.5 mg amodiaquine) per day for 3 days
1 to 5 years	≥9kg to <18kg	**1 tablet (50mg artesunate/135 mg amodiaquine)** per day for 3 days
6 to 13 years	≥18kg to <36kg	**1 tablet (100mg artesunate/270 mg amodiaquine)** per day for 3 days
14 years and above	≥ 36kg	**2 tablets (100mg artesunate/270 mg amodiaquine)** per day for 3 days

The patients should be advised to come immediately if symptoms get worse or develop the following danger signs:

- **Convulsions**
- **Lethargy or unconsciousness**
- **Excessive Sleepiness or drowsiness**
- **Abnormal breathing**

- **Protracted vomiting**
- **Unable to eat, drink or breast feed**
- **Non-response to home treatment after 48 hours or starting treatment.**

The patient should be advised to come back in two days for follow-up.
The first dose should be given in the clinic under supervision. If vomiting occurs within 30 minutes, the dosage should be repeated. If vomiting stops, you can give the patient the second and third doses to take home if you are sure that your instructions will be followed. If not, ask the patient to return to the clinic for the second and third doses.

If vomiting persists, this is an indication for **REFERRAL. Administer pre-referral treatment (see section on pre-referral).**

3.3.2 RECURRENT FALCIPARUM MALARIA

Recurrence of *P. falciparum* malaria can result from re-infection or recrudescence (treatment failure). Treatment failure may result from drug resistance or inadequate exposure to the drug due to sub-optimal dosing, poor adherence, vomiting, unusual pharmacokinetics in an individual or substandard medicines. It is important to determine from the patient's history whether he or she vomited the previous treatment or did not complete a full course of treatment.

When possible, treatment failure must be confirmed parasitologically or LDH-based RDTs, as *P. falciparum* histidine-rich protein-2 (PfHRP2)-based tests may remain positive for weeks after the initial infection, even without recrudescence.

Treatment Failure

When fever persists or symptoms continue for more than three days after starting treatment in recommended dosage and the presence of malaria parasites in blood.

FAILURE WITHIN 28 DAYS

Where there is failure to the first line medicine (AL), within 28 days of treatment the alternative ACT (AS+AQ) should be used for treatment. Similarly if the initial treatment was with AS+AQ and there is failure within 28 days, AL should be used for re-treatment. It is most unlikely that there will be failure to the 2 ACT options at the same time.

FAILURE AFTER 28 DAYS

Recurrence of fever and parasitaemia > 4 weeks after treatment may be due to either recrudescence or a new infection. The distinction can be made only by PCR genotyping of parasites from the initial and the recurrent infections. As PCR is not routinely used in patient management, all presumed treatment failures after 4 weeks of initial treatment should, from an operational standpoint, be considered new infections and be treated with the first-line ACT (AL).

3.3.3 SUPPORTIVE TREATMENT

- If the patient has an axillary temperature of > 37.5 °C or feels very feverish on day of examination give an antipyretic preferably paracetamol especially in children. (see table 4,5&6).
- Tepid sponge children with high fever.
- Advise mothers/ caregivers to give extra fluids i.e. breast milk, drinking water, diluted fruit juices, coconut water, ORS, zinc supplement, etc.

- **Feed** the child during illness.
- Advise mothers/caregivers when to return immediately (example when the situation worsens).
- Advise mothers/caregivers to report any adverse event that is suspected to be associated with the medicine.
- In severe reaction stop medication, and refer the patient.

Table 5: Treatment schedule for Paracetamol tablets 500mg

Age (years/months)	Weight (Kg)	Dose
2mths to 12 months	**4 up to 10**	¼
1 to 5 years	**10 up to 14**	½
6 to 9 years	**19 up to 35**	1
10 to 14 years	**35 up to 45**	11/2
15 and above	Over 45	2

- ❖ Paracetamol tablets should be administered every 6 hours
- ❖ **Paracetamol syrup containing 125 mg/5mls may be given at a dose of 10mg/kg every 6 hours till temperature is normal**.

Table 6 : PARACETAMOL SYRUP 125mg/5ml.

Age (Months/years)	*Dose*
0-6months	2.5mls (½ teaspoon)
7months -11months	5 mls (1 teaspoon)
1-2years	7.5mls (1 ½ teaspoons)
2-4yeasr	10mls (2 teaspoons)

Table 7: NUMBER OF PARACETAMOL TABLETS 100MG.

TABLETS	AGE IN MONTHS/YEARS				
100 mg	0 - 6 months	7 – 11months	1 –2 years	2 – 4 years	4 - 9 years
Number of tablets	½	1	1 ½	2	3

- ❖ **Acetylsalicylic acid tablets can also be used as an antipyretic. Do not give Asprin to children below 15years, Asthmatic patients, ulcer patients, patients with bleeding disorders, pregnant women, etc.**

Table 8: Treatment schedule for Acetylsalicylic acid tablets 300mg (Aspirin tablets)

Age (years/months)	*Weight (Kg)*	*Dose*
15 and above	Over 45	2

- **To be given every 4 hours.**

3.3.4 CRITERIA FOR REFERRAL

These essentially include two elements, namely; **severe disease and failure to respond to recommended therapy (first line and/or second line treatment)**. One or more of the following criteria listed below is an indication for referral to a higher level of care especially to a hospital:

- Altered consciousness (confusion, change in behaviour, delirium, coma persisting for over 30 minutes after convulsion).
- Convulsions (fits)
- Repeated vomiting and inability to retain oral medication, food and fluids.
- Persistent hypothermia
- Severe dehydration
- Persistent hyperpyrexia in children within 24hours to 48 hours (axillary temperature > 38.5°C)
- Severe anaemia (Extreme pallor).
- Circulatory collapse or shock, (feeble, weak, rapid pulse and cold limbs).
- Acute renal failure(failure to pass urine or passing very little quantity of urine)
- Obvious Jaundice (yellowness of the eyes).
- Pregnancy with persistent high-grade fever > 39.° C not responding to treatment.
- Failure to respond to initial treatment within two to three days.
- Severe reaction to antimalarials medicines.
- Other conditions that cannot be managed locally.

REFERRAL TO A HIGHER LEVEL:

When sending the patient, remember to:

- Start initial treatment before referral. (first dose of IM artesunate or rectal artesunate).
- include a referral note about the clinical picture, the type of treatment given, dosages, times and route of administration for any medications given
- Send a staff member with the patient if possible
- Continue feeding if possible
- Send potential blood donors with the patient.

4.0 MANAGEMENT OF SEVERE MALARIA

RECOMMENDATION: Treat adults and children with severe malaria (including infants, pregnant women in all trimesters and lactating women) with intravenous or intramuscular artesunate for at least 24 h and until they can tolerate oral medication. Once a patient has received at least 24 h of parenteral therapy and can tolerate oral therapy, complete treatment with 3 days of ACT (AL or AS+AQ).

Severe Malaria is a Medical Emergency!!!

Delay in diagnosing and inappropriate treatment of malaria especially in infants, young children may lead to the rapid development of severe malaria. Severe malaria mostly occurs in children under five years of age, pregnant women and individuals with low immune status.

Severe malaria is mainly caused by *Plasmodium falciparum* infection. It is important to confirm the diagnosis of severe malaria by finding asexual forms of *Plasmodium falciparum* in the blood.

4.1 CASE DEFINITION

In a patient with P. falciparum, asexual parasitaemia and other cause of symptoms, the presence of one or more of the following **clinical** or **laboratory** symptoms classifies the patient as suffering from severe malaria.

CLINICAL FEATURES:

- Impaired consciousness or unrousable coma (change of behaviour, confusion, delirium, coma persisting for over 30 mins after convulsion).
- Prostration i.e. generalized weakness so that the patient cannot walk or sit without assistance
- Failure to feed (vomiting everything)
- Multiple convulsions (fits)- 2 or more episodes in a 24 hour period
- Deep breathing , respiratory distress (acidotic breathing) Circulatory collapse or shock, systolic blood pressure less than 70mm Hg in adults and less than 50mm Hg in children (cold limbs, weak rapid pulse).
- Clinical jaundice (yellow coloration of the eyes)plus evidence of other vital organs dysfunction.
- Signs of haemoglobinuria (dark urine).
- Abnormal spontaneous bleeding. (Disseminated Intravascular Coagulation).
- Pulmonary oedema (Radiological).

LABORATORY FINDINGS

- Hypoglycaemia , (blood sugar- <2.2mmol or <40mg/dl)
- Metabolic acidosis (plasma bicarbonate less than 15mmol / litre)
- Severe normocytic anaemia (Hb <5g/dl, packed cell volume <15%)
- Haemoglobinuria
- Hyper parasitaemia (>5% or 250,000/ µ**l).**
- Hyperlactataemia (lactate >5mmol/l)
- Renal impairment (serum creatinine >265 µmol/l)

4.2 TREATMENT OBJECTIVES

- To prevent the patient from dying.
- To prevent disabilities.
- To restore previous physical and mental state.

4.3 TREATMENT RECOMMENDATIONS

The most common complications of severe malaria responsible for most deaths particularly in children under five years of age are:

- **Cerebral malaria – Prolonged coma not attributed to any other cause in a patient with *falciparum* malaria.**
- **Respiratory distress (acidosis)**
- **Severe anaemia(Extreme pallor)**
- **Hypoglycaemia**

Children with fever who are suspected of having severe malaria should be examined for other causes of fever eg. ARI (Pneumonia), septicemia, meningitis, Lassa fever etc and appropriately managed.

ALL CASES DIAGNOSED AS SEVERE MALARIA SHOULD BE REFERRED FOR HOSPITALIZATION.

4.4. Management of severe malaria

For the management of severe malaria, the following should be followed:

- **Initial emergency treatment**
- **Specific antimalarial treatment**
- **Adjunctive therapy and supportive care**

As severe malaria is a medical emergency it demands urgent clinical assessment and treatment. If the facility does not have the capacity, the patient should be referred. The patient, especially if comatose, should be managed in a special observation unit or an intensive care unit (ICU).

4.4.1 Initial emergency treatment

The initial management of severe malaria should be done as per following table.

Box 1: Initial Management of Severe Malaria

1. Clear and maintain airway, where indicated
2. Position semi-prone or on side, if comatose
3. Weigh patient (particularly children), if possible, and calculate dosage per body weight
4. Make rapid clinical assessment and look for signs of meningitis and other conditions
5. Take blood for diagnostic smear/slide or RDT, haematocrit and other laboratory tests.
6. Exclude hypoglycemia and monitor blood glucose (2-4 hourly)
7. Obtain specimens to exclude meningitis and other conditions where indicated
8. Start anti-malarial chemotherapy
9. Start treatment for hypoglycemia, meningitis and other conditions where indicated
10. Monitor urine output. If necessary insert urethral catheter
11. Plan first 8 hours intravenous intravenous fluids, including, glucose therapy and blood transfusion, if necessary
12. If auxiliary temperature exceeds 38.5°C, take measures to lower temperature.
13. Start anticonvulsant therapy in case of convulsions and monitor patient closely

Note:
The patient's fluid requirements should be assessed regularly. Look for evidence of fluid depletion or overload. Calculate the appropriate rate of infusion. Children with metabolic acidosis may benefit from a resuscitation bolus of fluid, preferably a plasma expander such as normal saline. Naso-gastric infusion is an alternative route.

4.4.2. SPECIFIC ANTIMALARIAL TREATMENT

THE DRUG OF CHOICE for the initial treatment of all severe malaria is parenteral artesunate. Where artesunate is not available, parenteral artemether or quinine in that order of preference may be used. The parenteral treatment should be given for a minimum of 24hours (irrespective of the patient's ability to tolerate oral medication). After 24hours and when the patient is able to tolerate oral medication, give a full course of AL Dosing Schedule

Box 2: Parenteral Artesunate dosage schedule

Children: Children less than 20kg body weight (5 years of age) should receive artesunate 3.0 mg/kg BW IV or IM given on admission (time = 0), then at 12 h and 24 h, then once a day is the recommended treatment.

Older children and adults: Children weighing more than 20kg and adults should receive artesunate 2.4 mg/kg BW IV or IM given on admission (time = 0), then at 12 h and 24 h, then once a day is the recommended treatment.

This should be given for at least 24 hours, then once the patient is able to tolerate oral medication, complete treatment with a full course of AL by the oral route.

The dosage schedule for the alternative artemether and quinine where artesunate si not available is provided below:

Box 3: Treatment using parenteral Artemether

Artemether
Dose: 3.2 mg/kg (loading dose) I.M followed by 1.6 mg/kg I.M daily for 6 days.

Box 4: Treatment using quinine

Quinine is given as an intravenous infusion (should never be used as an intravenous injection) at a loading dose of 20mg/kg body weight diluted in 10ml/kg of isotonic solution (preferable 5% dextrose) infused over 4 hours, then 8 hours from the start of the initial infusion continue with 10mg/kg of quinine diluted in 10ml/kg of isotonic solution over 4 hours. This is repeated every 8hours until patient is able to tolerate oral medication, then complete treatment with a full course of AL

5.0 TREATMENT OF MALARIA CAUSED BY OTHER SPECIES

Malaria caused by all other species of plasmodia (P.*Ovale* and *Malariae)* are aslo susceptible to AL. patients with other species either in combination with falciparum or in isolation should be treated with AL as for facilparum described above.

6.0 DISEASE MANAGEMENT AT THE DIFFERENT LEVELS

Prompt parasitological confirmation by microscopy or alternatively by rapid diagnostic tests (RDTs) is recommended **in all patients suspected of malaria** before treatment is started. Treatment solely on the basis of clinical suspicion should only be considered when a parasitological diagnosis is not accessible.
The results of parasitological diagnosis should be available within a short time (2 hours) of the patient presenting. In the absence or delay of parasitological diagnosis, patients with suspected severe malaria, and other high risk groups (children under five years of age, pregnant women, HIV positive patients, sickle cell patients, non-immune visitors, etc) should be treated immediately on clinical grounds.

6.1 MANAGEMENT OF UNCOMPLICATED MALARIA AT THE DIFFERENT LEVELS

6.1.1 Community level

The strategy of community case management of malaria will be implemented.
Management of fevers at home - Actions to be taken by mothers/caregivers:

- Early recognition of fever and promptly seek appropriate health care.
- Control of fever by the use of anti-pyretic, fanning and tepid sponging
- Continue breast feeding and oral fluids
- On recognition of danger signs before or during treatment (see below), seek appropriate care immediately from the nearest Community Health Workers or at the nearest health facility .

Danger Signs:

- **Convulsions**
- **Lethargy or unconsciousness**
- **Excessive Sleepiness**
- **Abnormal breathing**
- **Protracted vomiting**
- **Unable to eat, drink or breastfeed**

Actions to be taken by the Community Health Workers

- Refer all infants less than 5kg body weight to the health facility for proper evaluation and treatment
- Confirm all suspected malaria cases using an RDT
- Treat uncomplicated malaria with AL
- Give first dose as DOT (Directly Observe treatment) and explain to mothers/caregivers how to complete treatment at home.
- Encourage and advice family members especially mothers and children sleep under ITNs.
- Identify danger signs
- Pre-referral treatment with rectal artesunate and immediate referral to the nearest health facility. Follow-up patients during and after treatment.
- Ensure good storage of antimalarials medicines and other supplies (RDTs)

- Record few details of patient s treated ,medicines given ,outcome of treatment and any other adverse drug reaction

NB – These function should be carried out under the supervision of the nearest Peripheral Health Unit staff.

6.1.2 Management of uncomplicated malaria at the Maternal and Child Health Post (MCHP)

- Confirm all suspected malaria cases using RDT
- Administer drug of choice (AL) for uncomplicated malaria except for pregnant women during the first trimester
- Refer all infants less than 5kg to a health facility for proper evaluation and treatment.
- Administer oral quinine to pregnant women during the first trimester and infants less than 5kg.
- Control of fever with the use of anti-pyretic.
- Early recognition of symptoms and signs defining severe malaria
- Pre-referral treatment with IM artesunate or rectal artesunate and immediate referral to the nearest community health centre (CHC).

6.1.3 Management of uncomplicated malaria at the Community Health Post (CHP)

Confirm all suspected malaria cases using RDT

- Administer drug of choice (AL) for uncomplicated malaria except for pregnant women during the first trimester
- Refer all infants less than 5kg.
- Administer oral quinine to pregnant women during the first trimester.
- Refer suspected treatment failure cases to the next level.

6.1.4 Management of uncomplicated malaria at the Community Health Centre (CHC)

- Confirm all suspected malaria cases using mRDT or microcopy confirmation.
- Administer first line drug (AL) for uncomplicated malaria except for pregnant women during the first trimester.
- Administer oral quinine to pregnant women during the first trimester.
- Treat confirmed treatment failure cases with recommended 2nd line treatment, if not possible refer to the next level.
- Diagnose and treat severe malaria cases, if not possible give pre-referral treatment with intramuscular artesunate and immediate referral to hospital**.**

6.1.5 Management of uncomplicated malaria in hospital

- Treat confirmed uncomplicated malaria cases (clinical and laboratory) according to the National Malaria Case Management Treatment Guidelines.
- Manage treatment failure cases

6.2 Management of Severe Malaria at Different Levels

6.2.1 Community level

Management of Severe Malaria at Home and by the Community Health Workers

- Early recognition of symptoms and signs of severe illness.
- Pre-referral treatment with rectal artesunate and immediate referral to the nearest health facility.

6.2.2 Management of severe malaria at the Maternal and Child Health Post (MCHP)

- Early recognition of danger signs of severe malaria based upon a complete history physical examination.
- Administer pre – referral treatment urgently and refer to the next level.

6.2.3 Management of Severe malaria at the Community Health Post (CHP)

- Early recognition of danger signs of severe malaria based upon a complete history and physical examination.
- Provision of pre-referral treatment and refer to the next level**.**

6.2.4 Management of Severe malaria at the Community Health Centers (CHC)

- Early recognition of danger signs of severe malaria based upon a complete history and physical examination, blood smear examination if available or mRDT.
- Start treatment whilst waiting for laboratory results.
- Immediate referral to the next level if the condition is deteriorating.

6.2.5 Management of severe malaria at Hospital

- Early diagnosis of severe malaria based upon a complete history, physical examination and blood smear examination for malaria parasites. Treatment must be started whilst waiting for laboratory results.
- Provision of appropriate treatment according to the National Malaria Case Management Treatment Guidelines.
- Refer to tertiary hospitals in the event of complications that cannot be managed.

DIAGNOSIS

a) Assess the patient by looking for:

i) Dehydration
ii) Repeated convulsions or history of convulsion
iii) Signs of shock and collapse
iv) Anaemia (Extreme Pallor)
v) Pulmonary Oedema
vi) Level of consciousness
vii) Hyperpyrexia.
viii) Urine output

b) Do the following laboratory tests immediately:

i) Thick and thin blood film for malaria parasites
ii) Heamoglobin (Hb)and Haematocrit HCT (If HCT < 15% or Hb<5gm/dl, do blood group, cross match for possible transfusion).
iii) Lumbar puncture to exclude meningitis and other causes of coma
iv) Urea /creatine, and electrolytes
v) Blood glucose for hypogylceamia (<2.2 mmol or <40mg/dl)

c) Other laboratory tests

The following investigations are not essential to management but if available may be helpful or of prognostic value:

i). **Chest Xray**. May identify pulmonary oedema or lobar consolidation. It may be of value in assessing respiratory distress syndrome.

ii) **Full Blood Count and differential white cell count**. Sometimes these may indicate the possibility of an additional diagnosis

iii) **Urea, creatinine and electrolytes**. These are most valuable when acute renal failure threatens or develops.

d) Start treatment whilst waiting for results of laboratory investigations.

THE MEDICINE OF CHOICE FOR TREATING SEVERE MALARIA IS PARENTERAL ARTESUNATE PREFERABLY GIVEN AS INTRAVENOUS INJECTION.

(see box 2 for dosage)

SUPPORTIVE TREATMENT

- Reduce fever by tepid sponging or fanning patient and give antipyretics preferably paracetamol especially in children.
- Correct dehydration – give ORS. Unconscious patients should receive ORS by nasogastric tube.

7.0 MALARIA CHEMPROPHYLAXIS

Malaria prophylaxis is not necessary in persons living in a malarious area because it may lower ones resistance to the disease. However, it may be used in pregnancy, sickle cell anaemia and in non- immune visitors because of risk for severe disease, but it is not 100% protective.
It is the regular use of anti-malarial drugs to prevent development of malarial parasites following infection.

Malaria chemoprophylaxis is recommended for use in the following special groups:

- Non immune visitors to areas of malaria transmission
- Patients with sickle cell anaemia
- Non immune pregnant women visiting areas of malaria transmission

7.1 CHEMOPROPHYLAXIS FOR NON-IMMUNE VISITORS

- The optioins available for chemoprophylaxis includes : mefloquine, atovaquone-proguanil (malarone) and doxycycline. The choice fromthese options is determined by tolerability as all these options are efficacious in Sierra Leone.
- **Mefloquine (Lariam)** should be started at least 2 weeks before the arrival to ensure that the individual can tolerate and also to have acheieved the desired blood levels of the drug before arrival in a malaria endemic area. Also it should be continued for a 4 weeks period after departure and return to country of origin. Mefloquine is dosed weekly. .

  Atovaquone-proguanil can be started 24 hours before arrival and stopped immediately on departure. It is however dosed daily.

Information to patients and caregivers

Health Workers should stress the importance of:

- Seeking prompt treatment for all cases of fever on presumption of malaria especially in the under 5 year old and pregnant women
- Antipyretics and fluids in managing episodes of fever especially for young children.

- Full compliance with the recommended treatment and regimen.
- Early attendance by pregnant women at antenatal clinics.
- An early start and meticulous compliance with IPT during pregnancy to prevent severe disease and protect the baby.
- Education on early recognition of symptoms and signs of malaria.
- Promotion of prompt and effective home treatment and care of suspected cases of malaria
- Promotion of early and appropriate health care seeking behaviour
- Combining treatment for malaria with personal protection against mosquitoes using insecticide treated nets.
- Promotion of Personal protection (bednets, screens on windows, repellents, coils) and community participation and involvement (Environmental Sanitation)

Women (especially mothers) in our communities play a key role in malaria case management in the home where the first step in managing the disease very often starts. Health care workers must especially target this sub-population.

7.3 ANNEXES

Annex 1: MALARIA DIAGNOSIS

REPORTING OF BLOOD SMEAR RESULTS

Two methods are commonly used in reporting blood smear results.

(a) **Parasites per microlitre of blood:**

In this method it is assumed that 1 microlitre (ul) of blood contains 8,000 white blood cells (WBC). The number of parasites counted relative to the number of leucocytes counted can thus be converted to the number of parasites per ul of blood by the simple formula given below:

$$\frac{\textit{Number of parasites x 8000 WBC}}{\textit{Number of leucocytes counted}} = \textbf{Parasite count per ul}$$

In practice, this means that if 200 leucocytes are counted (denominator in the formula), the number of parasites should be multiplied by 40 and if 500 hundred are counted, the number of parasites is multiplied by 16. This is the preferred method of reporting.

Annex 2: ADJUNCTIVE THERAPY

CONVULSIONS

Convulsions are common in children with severe *P. falciparum* but are relatively rare in adults. The general principles for the care of patients with convulsions should be followed: maintenance of a clear airway urgently, abort the seizure with an anticonvulsant, monitoring of vital signs and nursing the patient in a semi-prone position.

Drugs: Treat with diazepam or paraldehyde or phenobarbitone.

Diazepam:

Give a slow bolus of IV diazepam 0.15mg/kg (maximum 10mg for adults)

If IV access is not possible, the rectal route should be used. Give at a dose of 0.5-1.0mg/kg. For rectal administration, withdraw the IV preparation into a syringe, and then remove the needle. Insert about 5cm length of a nasogastric tube into the rectum, inject the diazepam into the nasogastric tube and thereafter flush

with the 5 mls water. If a nasogastric tube is not available, use a syringe **without a needle.** If convulsions persist after 10 minutes repeat rectal diazepam treatment as above. Should convulsions continue despite a second dose, give a further dose of rectal diazepam or **phenorbarbitone** 15 mg.kg or IV after another 10 minutes (maximum 200mg for adults).

NB: for children rectal administration of diazepam is preferable.

Diazepam should not be used in infants below one month of age instead use phenorbabitone 20mg/kg IM or IV. If convulsions persist, repeat phenorbabitone 10mg/kg after 30 minutes.

Intramuscular injection of paraldehyde (0.1ml/kg body weight) can be used as an alternative to control convulsions.(See table 13).

INTRAMUSCULAR PARALDEHYDE – 1gm in1 ml

WEIGHT KG	AGE IN MONTHS/YEARS	PARALDEHYDE (1gm = 1ml)
1.5kg – <4kg	0 – 2 months	0.5ml
4kg – <6kg	2 – 4 months	1.0ml
6kg – <10kg	4 months – 1 year.	1.5ml
10kg – <14kg	1year – 3 years	2.0ml
14kg – <19kg	3years – 5years	2.5ml

COMA

Clear and maintain airway; nurse on side; exclude other causes of coma (hypoglycaemia, bacterial meningitis), monitoring of vital signs. (See coma scale in annexe),

HYPOGLYCAEMIA

It is common in patients with severe malaria. This is usually partly secondary to the anorexia and vomiting following the disease, especially for young children who may have not eaten for as long as 24 hours before presenting to the health facility.
Hypoglycaemia may be present in pregnant women on admission or may occur after quinine infusion. Features of hypoglycemia include, restlessness, alteration in levels of consciousness with frank coma in some cases, convulsions among others. Hypoglycemia complicating severe malaria is a poor prognostic indicator and should be aggressively looked for and urgently appropriately managed.

Management of Hypoglycemia: Give 50mls of 50% glucose by IV bolus injection rapidly (for children give 25% glucose, use 1ml/kg body wt.). Follow with IV infusion of 10% glucose. Until the blood glucose stabilizes at normal levels or through a nasogestric tube to an unconscious patient.

If injectable glucose is not available, give glucose solutions by mixing 20 gm of sugar (4-levels tea spoons) with 200ml of clean water.50 ml of this solution is given orally or through a nasogestric tube to an unconscious patient.

HYPERPYREXIA

Tepid sponging and fanning.
Give Paracetamol at 15mg/kg body wt. every 6 hours.

DEHYDRATION

IV isotonic fluid (0.9% saline or 5% dextrose) watch for over hydration. Nasogastric tube may be preferable in children. Children are mostly affected and in such a situation, the rehydration plan B (mild to moderate dehydration with ORS) or C (severe dehydration with Ringers lactate) should be applied. (See annexe V&V1 for details on plan B and Plan C).

PULMONARY OEDEMA:

Check for over hydration and stop all intravenous fluids. Prop up patient at an angle of 45°, give oxygen, give diuretic (Furosemide, 1-2mg /kg of body weight for children and up to a maximum of 40mg by intravenous injection for adults. If there is no response, increase the dose progressively to a maximum of 200mg). Intubate and add positive end – expiratory pressure / continuous positive airway pressure in life threatening hypoxaemia (or in case of severe respiratory distress).

SEVERE ANAEMIA

Anaemia is a major cause of the high morbidity and mortality associated with malaria. It is especially serious in young children and pregnant women. During the course of malaria infection parasitized red cells are destroyed. Repeated or chronic malaria infection which may follow inadequate treatment, will result in chronic and possibly severe anaemia. The presence of anaemia from other causes such as hookworm infestation and dietary deficiencies worsens the prognosis of anemia in malaria. For this reason an understanding of the association between anaemia and malaria , the recognition of anaemic patients, and prompt treatment when it is diagnosed are essential if the burden of morbidity and mortality inflicted by malaria is to be reduced.

Classifying Anaemia
In areas of high transmission there is high association between malaria and anaemia .Every patient, especially pregnant women and young children presenting to a health facility should be checked for anaemia.

Look for:

- Pale palms, pale nail beds, pale inner eyelids and tongue
- People who become tired
- Infants and children who are unable to feed and drink well
- People in heart failure , swelling of feet or around eyes, rapid and weak pulse, large ad painful liver
- Children or pregnant women who have a history of eating soil.

Use the adapted IMNCI chart below to guide management. Where available a blood slide for malaria parasites and haemoglobin level should be done and should further inform decision process.

SEVERE ANAEMIA

Signs: S**evere pallor, rapid difficult breathing, increased effort in order to breath, unable to feed, extreme tiredness.**

This is a medical emergency. Patients with these signs must be admitted to a hospital as an emergency. Give urgent blood transfusion to patients with severe pallor/anaemia in heart failure (Give5-10mls of packed cells or 10- 20mls of whole blood/kg body wt in patients with Hb <4g/dl or Hb <6g/dl in-patient with signs of heart failure (dyspnoea, enlarged liver, gallop rhythm).Where blood is not available give pre-referral treatment and refer urgently to a health facility with blood transfusion services.

Follow-up after discharge

Continue with folic acid and ferrous sulphate and review after 14 days to check haemoglobin or haematocrit level. Encourage patients to sleep under an insecticide treated net (ITN).

ACUTE RENAL FAILURE

Exclude pre-renal causes, maintain strict fluid balance if in established renal failure, then you can carry out peritoneal dialysis (or haemodialysis if available).

CIRCULATORY COLLAPSE

Suspect gram – negative septiceamia: Take blood for culture. Correct hypovolaemia. Give parenteral antimicrobials. Give broad spectrum antibiotics

CAUTION: Avoid the following:

- Drugs that increase gastrointestinal bleeding.
- Corticosteroids.
- Other anti-inflamatory agents NSAID (NON-STEROIDAL ANTI-INFLAMATORY DRUGS).
- Other agents given for cerebral oedema (Urea, Manitol)

ADMINISTRATION OF VITAMIN A FOR CHILDREN UNDER 5 YEARS

For children under five years give initial dose of Vitamin A during treatment (Three doses during course of treatment i.e. day one, day two and day Fourteen according to the recommended dose) Vitamin A helps to stimulate the immune system to prevent other infections .

DOSAGE

6 – 11 months of age: 100000 IU
12 – 59 Months of age: 200000 IU

SUPPORTIVE CARE/ MONITORING OF PATIENTS WITH SEVERE MALARIA

Patients with severe malaria required intensive nursing care, preferably in an intensive care unit where possible. Clinical observation should be made as frequently as possible. This should include monitoring of vital signs, coma score, urine output.

The following should be monitored:

1 Level of consciousness Fluid intake/output and speed of infusion of fluids.
2 Urine volume (hourly) and specific gravity. If necessary insert urethral catheter. (Oliguria<17ml/hr in an adult or <0.3ml/kg/hr in infants and children)
3 Blood glucose 4-hourly while patient is unconscious : falls below 2.2 mmol/l (<40 mg/dl)
4 Blood pressure : Falls (<90mm hg systolic in an adult, <50mm Hg in infants and children)
5 Core temperature(>-38.5ºC): If temperature remains high or increases despite treatment with quinine
6 Respiratory rate 4 hourly (Increased respiratory rate: <2months : 60 or more per minute, 2-11 months: 50 or more per minute, 1 year and abov e: 40 or more per min. or difficulty in beathing.
7 Patients with secondary pneumonia or with clear evidence of aspiration should be given appropriate treatment.
8 Parasitaemia: Remains high 2-3 days or remains positive for 5 days. Parasitaemia commonly remains at the initial level for 12-24 hours even if drugs are fully effective.
9 Haemoglobin (Hb) if anaemia is suspected to be worsening.: Falls below 5g/dl or Haematocrit <15%
10 Occurrence of convulsions. These can recur or develop for the first time during treatment and may be due to hyperpyrexia, abnormal blood glucose or electrolyte imbalance.
11. Bleeding from vene-puncture sites or spontaneous haemorrhage
12. Uterine contractions and fetal heart rate in pregnant women.

ASSESSMENT OF RECOVERY

.

Absence of sequelae indicates a good recovery from treatment of severe malaria .Assessment of patient for possible neurological sequelae of the disease or the treatment is important especially in children, in which 10% develop neurological sequelae after they recover from cerebral malaria.

a. Assess

(i) Vision
(ii) Hearing

b. Repeat on 7th and 14th day:

(i) Thick and thin blood films
(ii) Haematocrit
(iii) Haemoglobin

c. For children recovering from severe anaemia

- Give iron and folic acid for two months
- If child has sickle cell disease, give folic acid only
- Advice on correct feeding recommendation according to the child's age .
- Give anthelmentics if the child is over one year and has not received a dose of Albendazole/Mebendazole for the past six months.
- Encourage to sleep under ITNs.

d If neurological defects occur refer for physiotherapy

FOLLOW ON TREATMENT

Following initial parenteral treatment for at least 48 hrs, and once the patient can tolerate oral therapy thereafter, it is essential to continue with oral Quinine plus Clindamycin or oral Quinine plus Doxcycline inorder to complete the full seven days of treatment. Alternatively a full course of Artemether plus Lumefrantrine or Artesunate plus Amodiaquine can be administered to complete the treatment

PRE REFERAL TREATMENT OPTIONS

The risk of death from severe malaria is greatest in the first twenty four hour, yet in most cases the transition time between referral and arrival at health facilities able to properly manage severe malaria cases is usually prolonged .This delays the commencement of appropriate ant malarial treatment . As during this time the patient may deteriorate or die, it is recommended that the patient be treated with first dose of one of the recommended treatment before referral. The recommended pre referral treatment options are as follows:

- **A**dministration of the first dose of intra-muscular artesunate . Where this is not available or possible, intramuscular artemether can be used *(refer to page 39 for dosage schedule*).
- In situations where parenteral administration is not possible (CHWs), rectal artesunate should be used as pre-referral treatment. (*refer to table No 7*)
- In suspected severe malaria where meningitis and septicaemia cannot be ruled out, a broad – spectum antibiotic should be administered (for children less than 5 years of age, refer IMNCI treatment chart)**.**
- Control of fever by use of anti-pyretic, tepid sponging, etc.

Dosage schedules for Artesunate suppositories as pre-referral malaria treatment
10mg/kg body weight daily

Weight (Kg)	Age (Years)	Number of 100 mg capsules	Number of 400mg capsules
10-19	1-5	1	
20-2	6-7	2	
30-39	8-12	3	
40-49	>12		1
50-90	>12		2
>90	>12		3

NB: If, however, referral is impossible or delayed (e.g. due to logistics reasons etc) continue the treatment with rectal Artesunate or IM Artesunate (as applicable) until the patient can tolerate oral medication. At this point, continue with the follow-on treatment recommendation.

In case of underfive children, refer to IMNCI guidelines in situation where referral is not possible.

TREATMENT OF MALARIA CAUSED BY OTHER SPECIES

Malaria caused by all other species of plasmodia (P.*Ovale* and *Malariae)* are aslo susceptible to AL. patients with other sepcies either in combination with falciparum or in isolation should be treated with AL as for facilparum described above.

Annex 3: THE GLASGOW COMA SCALE

Criteria		score
Eyes opening (4)	Spontaneously	4
	To speech (verbal stimuli)	3
	To pain only	2
	No response	1
Best verbal response (5)	Oriented , appropriate	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds or Non-specific sounds	2
	No response	1
Best motor response(6)	Obeys commands	6
	Localizes painful stimulus	5
	Withdraws in response to pain	4
	Flexion in response to pain	3
	Extension in response to pain	2
	No response	1
Total		**3 –15**

To obtain the Glasgow coma score, obtain the score for each section, then add the three figures to obtain a total.

Annex 4: THE BLANTYRE COMA SCALE

This score has been modified to be applicable to children, including those who have not learned to speak.

Eye movements	Directed (e.g. Follow mothers face)	1
	Not directed	0
Verbal response	Appropriate cry	2
	Moan or inappropriate cry	1
	None	0
Best motor response	Localizes pain stimulus	2
	Withdraws limb from pain	1
	None specific or absent response	0
	Total	**0 – 5**

a) Rub knuckles on patient's sternum.
b) Firm pressure on thumb nail with horizontal pencil.

Annex 5: HOW TO GIVE INTRAMUSCULAR QUININE:

1. **If a child:**
   a. Weigh.
   b. Calculate the volume to be given based on the body weight (See table 10).
   c. Use a 10ml sterile syringe and needle to draw up 5mls of sterile water for injection or saline (**not dextrose**). Then draw into the same syringe 300mg (1ml) from an ampoule of quinine. The syringe now contains 50mg quinine per ml. Give 10mg (0.2ml) per kg/ body weight by intramuscular injection to the upper outer thigh (anterior thigh). If the volume exceeds 3mls, inject half the dose into each thigh.

Note: Intramuscular Injection should be given with maximum sterile precautions into the anterior thigh not the buttock

Body weights and doses (ml) of Quinine injection.

BODY WEIGHT KG	VOLUME OF QUININE DIHYDROCHLORIDE INJECTION (ML)
< 5	1.0 ml
5.1 – 7.5	1.5 ml
7.6 – 10.0	2.0 ml
10.1 – 12.5	2.5 ml
12.6 – 15.0	3.0 ml
15.1 – 17.5	3.5 ml – half to each thigh
17.6 – 20.0	4.0 ml – half to each thigh
20.1 – 22.5	4.5 ml – half to each thigh
22.6 – 25.0	5.0 ml – half to each thigh
25.1 - 27.5	5.5 ml – half to each thigh
27.6 – 30.0	6.0 ml – half to each thigh

2. **In the case of adults,** the dilution in sterile water or saline (**not dextrose**) should be 120mg/ml.
   a. Draw 2mls of quinine 600mg and 3mls of sterile water or saline (**not dextrose**) and administer by deep intramuscular injection.

INTRAVENOUS QUININE:

- Give an initial **loading dose** of 20mg quinine dihydrochloride salt/kg body weight by constant rate infusion over 4 hours, in 5% dextrose (5-10ml/kg body weight depending on the patient's overall fluid balance).
- This is followed by 10mg/kg in 5-10ml/kg 5% Dextrose over 4 hours every 12 hours in children and 8 hours in adults.
- A loading dose should not be used if the patient received quinine for this illness. Within 24 hours. The first dose of IV infusion should be 10mg/kg given over 4 hours.
- Continue treatment with intravenous quinine until patient can take orally, then change to oral quinine 10mg salt/kg (every 8 hours) to complete the 7 days treatment **OR**
- Give a three days course of ACT according to guidelines if patient cannot tolerate oral quinine.

Annex 6:INTEGRATED MANAGEMENT OF CHILDHOOD ILLNESS

ASSESS **CLASSIFY**
IDENTIFY TREATMENT

Check For General Danger Sign	
ASK: **Is the child able to drink or breastfed?** **Does the child vomit everything?** **Has the child had convulsion?**	**LOOK:** **See if the child is lethargic or unconscious** **See if the child is convulsing now**
If the child is convulsing n ow, treat current convulsion with diazepam. Then rapidly assess, classify and provide other treatment before referring to hospital **A child with any danger sign needs URGENT attention: complete the assessment and any pre-referral treatment immediately so referral is not delayed**	

Does the child have fever?

If yes: Then Ask: **o For how long?** **o If more than 7 days, has fever been present every day?** **o Has the child had measles within the last 3 months?**	***Look and feel*** **o Look or feel for stiff neck**	**CLASSIFY FEVER**	**. Any general danger sign** **. Stiff neck**	***VERY SEVERE FEBRILE DISEASE/ SEVERE MALARIA***	**. Give first dose of parenteral artesunate (if not available give IM arthemeter or IM quinine) for severe malaria** .Treat the child to prevent complications **Give first dose of an appropriate antibiotic** **.Treat the child to prevent low blood sugar** **.Give one dose of paracetamol in clinic for high fever (38.5°C or above)** **. Refer URGENTLY to hospital**
			. Fever (by history or feels hot or temperature 37.5ºC or above)	***UNCOMPLICATED MALARIA***	**. Treat with 1st line oral Antimalarial (AL)** **. Give one dose of paracetamol in case of high fever (38.5ºC or** **. Advise mother when to return immediately** **. Follow up in 2 days if** **. If fever is present every day for 7 days, refer for assessment**
	Malaria test NEGATIVE			**FEVER: NO MALARIA**	**.Follow-up in 3 days if fever persists** **.If fever is present every day for more than 7 days, refer for assessment** **.Give one dose of paracetamol in clinic for high fever (38.5°C or above)** **.Give appropriate antibiotic treatment for an identified bacterial cause of fever** **.Advise mother when to return immediately**

Annex 7: Classification of Anaemia

SIGNS	CLASSIFICATION	ACTION
Severe palmar pallor **Signs of heart failure** **-Rapid weak pulse** **-Breathlessness** **-Large painful liver**	Severe Anaemia	• **Give quinine (first dose)** • **Refer urgently to hospital**
Some palmar pallor	Anaemia	• **Give first line anti-malarial treatment (AL)** • **Give folic acid and iron immediately after one week** • **Advise when to return immediately** • **Counsel on personnel protection with ITNs** • **Advise that patient must be reassessed if fever persists for more than 3 days** • **Give mebendazole for a child 2 years and above, if not administered within the previous 6 months** • **Follow up in 14 days for anaemia.**
No palmar pallor	**No anaemia but malaria suspected**	• **Give first line anti-malarial drug (AQAS)** • **Counsel on feeding** • **Counsel on personnel protection with ITNs**

Annex 8: Plan B: Treat for some dehydration with ORS

➢ *Plan B: Treat for Some Dehydration with ORS*

Give in clinic recommended amount of ORS over 4-hour period

➢ **DETERMINE AMOUNT OF ORS TO GIVE DURING FIRST 4 HOURS.**

** Use the child's age only when you do not know the weight. The approximate amount of ORS required (in ml) can also be calculated by multiplying the child's weight (in kg) times 75.*

- If the child wants more ORS than shown, give more.
- For infants under 6 months who are not breastfed, also give 100-200 ml clean water during this period.

➢ **SHOW THE MOTHER HOW TO GIVE ORS SOLUTION.**

- Give frequent small sips from a cup.
- If the child vomits, wait 10 minutes. Then continue, but more slowly.
- Continue breastfeeding whenever the child wants.

➢ **AFTER 4 HOURS:**

- Reassess the child and classify the child for dehydration.
- Select the appropriate plan to continue treatment.
- Begin feeding the child in clinic.

➢ **IF THE MOTHER MUST LEAVE BEFORE COMPLETING TREATMENT:**

- Show her how to prepare ORS solution at home.
- Show her how much ORS to give to finish 4-hour treatment at home.
- Give her instructions how to prepare SSS for use at home .
- Explain the 4 Rules of Home Treatment:

1. *GIVE EXTRA FLUID*

2. GIVE ZINC SUPPLEMENTS

3. *CONTINUE FEEDING*

4. *WHEN TO RETURN*

Annex 9: Plan C: Treat Severe Dehydration Quickly

➢ *Plan C: Treat Severe Dehydration Quickly*

➢ **FOLLOW THE ARROWS. IF ANSWER IS "YES", GO ACROSS. IF "NO", GO DOWN.**

START HERE

Can you give intravenous (IV) fluid immediately?

YE S

- Start IV fluid immediately. If the child can drink, give ORS by mouth while the drip is set up. Give 100 ml/kg Ringer's Lactate Solution (or, if not available, normal saline), divided as follows:

** Repeat once if radial pulse is still very weak or not detectable.*

- Reassess the child every 1- 2 hours. If hydration status is not improving, give the IV drip more rapidly.
- Also give ORS (about 5 ml/kg/hour) as soon as the child can drink: usually after 3-4 hours (infants) or 1-2 hours (children).
- Reassess an infant after 6 hours and a child after 3 hours. Classify dehydration. Then choose the appropriate plan (A, B, or C) to continue treatment.

NO

Is IV treatment available nearby (within 30mn)?

YES

- Refer URGENTLY to hospital for IV treatment.
- If the child can drink, provide the mother with ORS solution and show her how to give frequent sips during the trip.

NO

Are you trained to use a naso-gastric (NG) tube for rehydration?

NO

Can the child drink?

YES

- Start rehydration by tube (or mouth) with ORS solution: give 20 ml/kg/hour for 6 hours (total of 120 ml/kg).
- Reassess the child every 1-2 hours:
  - If there is repeated vomiting or increasing abdominal distension, give the fluid more slowly.
  - If hydration status is not improving after 3 hours, send the child for IV therapy.
- After 6 hours, reassess the child. Classify dehydration. Then choose the appropriate plan (A, B, or C) to continue treatment.

NO

Refer URGENTLY to hospital for IV or NG treatment

NOTE:

- If possible, observe the child at least 6 hours after rehydration to be sure the mother can maintain hydration giving the child ORS solution by mouth.

If the child is 2 years or older and there is an outbreak of cholera, treat with recommended antibiotic.

Annex 10: Differences between severe malaria in adults and in children[a]

Sign or Symptom	Adults	Children
History of cough	Uncommon	Common
Convulsions	Common	Very common
Duration of illness	5-7 days	1-2 days
Resolutions of coma	2-4 days	1-2 days
Heurological sequelae	<5%	>10%
Jaundice	Common	Uncommon
Pretreatment hypoglycaemia	Uncommon	Common
Pulmonary oedema	Uncommon	Rare
Renal failure	Common	Uncommon
CSF opening pressure	Usually normal	Usually raised
Respiratory distress (acidosis)	Sometimes	Common
Bleeding/clotting disturbances	Up to 10%	Rare
Abnormality of brain stem Reflexes (e.g. oculovestibular, oculocervical)	Rare	More common

[a]Derived from studies in south-east Asian adults and children, and African children,

Annex 11: Prognostic indicators

The major indicators of a poor prognosis in children and adults with severe malaria are listed below.

Clinical indicators

Age under 3 years
Deep coma
Witnessed or reported convulsions
Absent corneal reflexes
Decerebrate/decorticate rigidity or opisthotonos
Clinical signs of organ dysfunction (e.g. renal failure, pulmonary oedema)
Respiratory distress
Papiloedema and/or retinal oedema

Laboratory indicators

Hyperparasitaemia (>250 000/ul or >5%)
Peripheral schizontaemia
Peripheral blood polymorphonuclear leukocytosis(>12 000/ul)
Mature pigmented parasites(>20% of parasites)
Peripheral blood polymorphonuclear leukocytes with visible malaria pigments (>5%)
Packed cell volume less than 15%
Haemoglobin concentration less than 5 g/dl
Blood glucose less than 2.2 mmol/l (<40 mg/dl)
Blood urea more than 60 mg/dl)
Serum creatinine more than 265 umol/l (>3.0 mg/dl)
High CSF lactic acid (>6 mmol/l) and low CSF glucose
Raised venous lactic acid (>5 mmol/l)
More than 3 – fold elevation of serum enzymes (aminotransferases)
Increased plasma 5'-nucleotidase
Low antithrombin lll levels
Very high plasma concentrations of tumour necrosis facto (TNF)

Common errors in diagnosis and management

The common errors in the diagnosis and management of severe malaria are listed below.

Errors in diagnosis

Failure to think of malaria in a patient with either typical or atypical illness

Failure to elicit a history of exposure (travel history) – including travel within a country with variable transmission
Misjudgement of severity
Failure to do a thick blood film in a non-immune patient
Failure to identify *P. falciparum* in a dual infection with *P. vivax* (the latter may be more obvious)
Missed hypoglycaemia
Failure to diagnose other associated infections (bacterial, viral, etc)
Failure to recognize respiratory distress (metabolic acidosis)
Failure to carry out an opthalmoscopic examination for the presence of papilloedema, and retinal haemorrhages in adults.

Errors in management
Inadequate nursing care
Delay in starting antimalarial therapy
Use of inappropriate therapy:
- chloroquine in areas of resistance
- unjustified withholding of an antimalarial drug
- dosage not correctly calculated
- inappropriate route of administration
- unjustified cessation of treatment
- Failure to prevent cumulative effects of antimalarial drugs
- unnecessary continuation of chemotherapy beyond the recommended length of treatment
- use of unproven and potentially dangerous ancillary treatment
- failure to review antimalarial treatment in a patient whose condition is deteriorating

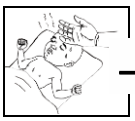
Errors of fluid and electrolyte replacement
- failure to control the rate of intravenous infusion

Failure to elicit a history of recent chemotherapy
Failure to identify or treat metabolic acidosis
Unnecessary endotracheal intubation
Unduly delayed endotracheal intubation (where this is indicated and possible)
Failure to control convulsions
Failure to recognize minor ("subtle") convulsions
Failure to recognize and treat severe anaemia
Daily in considering obstetrical intervention in late pregnancy
Failure to recognize and manage pulmonary oedema
Undue delay in starting peritoneal dialysis or haemodialysis
Failure to Pass nasogastric tube to prevent aspiration pneumonia
Failure to give antibiotics as a covering procedure if the decision is made to delay lumba puncture

Features of severe illness:
- Patient sleepy, confused, unable to walk or sit up
- Convulsions (fits)
- Persistent vomiting
- Yellow eyes
- 'Coca Cola' urine
- Pallor
- Pregnant women with persistent high-grade fever
- Persistent hyper pyrexia

- Bring down fever by sponging patient and give antibiotic
- Give first dose antimalarial
- Refer to level able to manage case

Annex 12: **malaria treatment algorithm for CHWs (Community level).**



Fever ? Wam body? (by history or feels hot or temperature 37.5°C* or above).

NO

Follow-up 3 days later to check on patient's progress or earlier if condition worsens.

YES

Do RDT

RDT Posit ive

- *Treat with AL*
- *Give one dose of paracetamol for fever*
- Advice mother when to return immediately.
- If fever is present every day for more than 3 days, refer to the next level of care for assessment.

YES, fever with DANGER SIGN

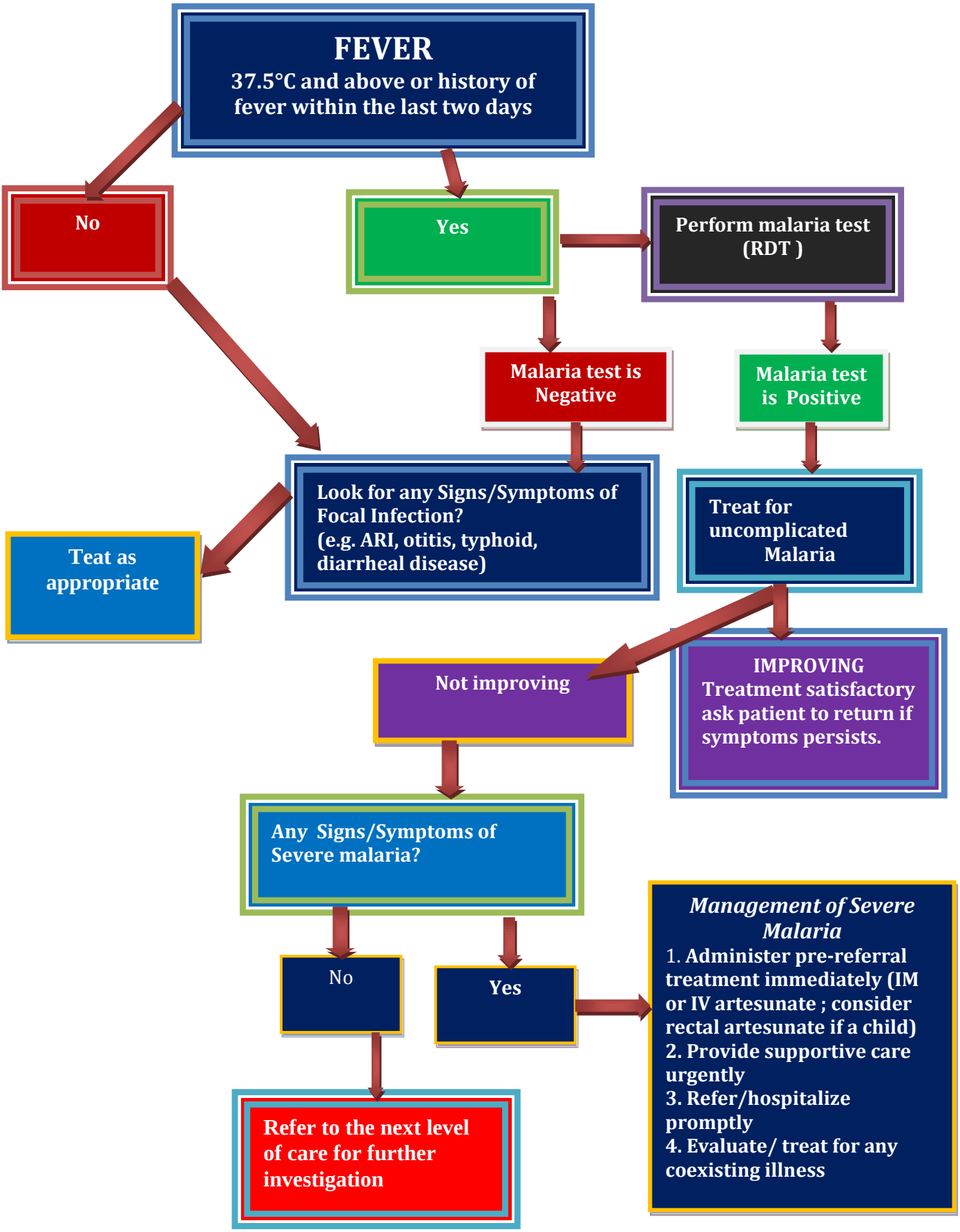
RDT Negative

- Give pre-referral treatment of Artesunate Suppositories (if a child)
- Give mother/caregiver/ patient a referral ticket

- Check the patient for other cause of fever (e.g. diarrhoea, fast breathing) and treat appropriately **OR REFER**
- Give one dose of paracetamol for fever (38.5°C or above).
- Follow-up patient.

Then REFER IMMEDIATELY to nearest next level of care

Annex 13: Flow Chart for Diagnosis and Management of Malaria at the Periphery



Annex 14:Malaria Treatment Flow Chart for Hospitals

The Patient's Journey

If temperature ≥ 38.0°C or history of fever in recent 48 hours: test for malaria

1. The Health Worker completes urgent request form for laboratory tests
2. Test request for MPs sent to the Laboratory
3. Whilst waiting for laboratory results, RDT test could be done where applicable
4. For outpatients: tests are done in main laboratory (MPS)
5. Test done: laboratory technician gives report to caregiver and record
6. Health Worker records results in inpatient chart or on outpatient card

Test Positive

Check for signs of severe malaria:

- Prostration (unable to walk/sit without support or drink/breastfeed)
- ≥ 2 convulsions in 24 hours
- Altered consciousness
- Blood sugar ≤ 2.5 mmo/L
- Hb ≤ 5.0 g/dL (or PCV ≤ 15%)
- Shock (compensated or decompensated)
- Increased work of breathing where pneumonia is unlikely

One or more Signs present

Signs absent

Uncomplicated Malaria: Treat with ACT

1. Use dosage chart
2. Treat any co-infections
3. Tell caregiver to return if symptoms persist after 3 days

Test Negative

Antimalarial not required. Look for another cause of illness. Repeat test if concern remains.

Severe Malaria: Treat with Artesunate IV/IO (alternatively, Artemether IM or Quinine IV/IO)

1. Use dosage chart
2. Doctors to determine frequency of monitoring
3. Treat hypoglycaemia – use hypoglycaemia guideline
4. Check for malnutrition: record Z-score. Caution with fluids in malnutrition
5. Doctors to determine maintenance fluids/feeds
6. Do not give bolus iv fluids for shock unless the cause is gastroenteritis
7. If Hb ≤ 5 g/dl transfuse 20ml/kg whole blood urgently (note: if malnutrition or heart failure see anaemia guideline)
8. Treat co-infection – see guideline
9. If unconscious – use coma guideline

This Malaria Treatment flow chart for hospitals is based on the Malaria Case Management Guideline and is approved by the National Malaria Control Programme of the Ministry of Health and Sanitation

Drug Treatment

Uncomplicated Malaria

First-line drug for children above 3kg is oral Artemether plus Lumefantrine twice daily for three days. Prescribe as in the table below. Nurse to supervise the first treatment. If child vomits tablets, admit & treat with iv/im artesunate or artemether i.m.

Weight (Kg)	Age	20/120mg					
		Day 1		Day 2		Day 3	
		Morning	Evening	Morning	Evening	Morning	Evening
5 – 14	>3yrs	1 tab/dose	1 tab/dose	1 tab/dose	1 tab/dose	1 tab/dose	1 tab/dose
15-24	4-8yrs	2 Tabs/dose	2 Tabs/dose	2 Tabs/dose	2 Tabs/dose	2 Tabs/dose	2 Tabs/dose
25-34	9-14yrs	3 tabs/dose	3 tabs/dose	3 tabs/dose	3 tabs/dose	3 tabs/dose	3 tabs/dose
>35	(>14yrs	4 tab/dose	4 tab/dose	4 tab/dose	4 tab/dose	4 tab/dose	4 tab/dose
>35	1 tablet AL 80/480mg fixed dose, twice per day						

AL 80/480mg fixed dose. A higher strength of AL that has 6 tablets instead of 24 for a complete dosing regimen

Severe Malaria

First-line drug: artesunate i.v./i.o. Alternative drugs: artemether i.m. or quinine i.v./i.o.

	Artesunate: Dose 2.4mg/kg at time 0 hr, 12 hr, 24 hr, then daily		Artesunate: Dose 3.0mg/kg at time 0 hr, 12 hr, 24 hr, then daily		Artemether: Loading 3.2 mg/kg Maintenance dose 1.6 mg/kg (once daily)		Quinine: Loading dose 20 mg/kg Maintenance dose 10 mg/kg (8 hrly)		
	i.v./i.o.		i.v		i.m. in thigh		Infusion i.v./i.o. over 4 hours		
Weight (kg)	Dose (mg)	Dose (ml) of 60mg in 6mls	Dose (mg)	Dose (ml) of 60mg in 6mls	Loading dose (mg)	Maintain dose (mg) 24 hrly	Loading dose (mg)	Maintain dose (mg) 8 hrly	Volume (ml) 5% dextrose
3.0 - 3.9	7.5	0.75	10	1	10	5	60	30	30
4.0 - 4.9	10	1	12	1.2	13	6	80	40	40
5.0 - 5.9	12	1.2	15	1.5	16	8	100	50	50
6.0 - 6.9	14	1.5	18	1.8	19	10	120	60	60
7.0 - 7.9	17	1.7	20	2	22	11	140	70	70
8.0 - 8.9	19	1.9	24	2.4	26	13	160	80	80
9.0 - 9.9	22	2.2	27	2.7	29	14	180	90	90
10.0 - 10.9	24	2.4	30	3	32	16	200	100	100
11.0 - 11.9	26	2.6	33	3.3	35	18	220	110	110
12.0 - 12.9	29	2.9	36	3.6	38	19	240	120	120
13.0 - 13.9	31	3.1	40	4	42	21	260	130	130
14.0 - 14.9	34	3.4	42	4.2	45	22	280	140	140
15.0 -15.9	36	3.6	45	4.5	48	24	300	150	150
16.0 - 16.9	38	3.8	48	4.8	51	26	320	160	160
17.0 - 17.9	41	4.1	50	5	54	27	340	170	170
18.0 - 18.9	43	4.3	54	5.4	58	29	360	180	180
19.0 - 19.9	46	4.6	57	5.7	61	30	380	190	190
20.0 - 20.9	48	4.8	60	6	64	32	400	200	200

Follow injection drugs with 3 days oral ACT (Artemether/Lumefantrine or ASAQ). If the child is unable to tolerate oral medication continue injection drugs for 6 days.

Artesunate i.v./i.o.: Give every 12 hours for the first three doses (time 0, 12 hrs. and 24 hrs.). Use a minimum of 3 doses before switching to oral AL

Artesunate i.m: (less than 20kg body weight) Concentration: 20mg/ml. Example: $\frac{3.0 \text{ mg} \times \text{body weight (kg)}}{\text{IM artesunate solution concentration of } \mathbf{20mg/ml}}$

Artesunate typically comes as a powder together with a 1ml vial of 5% bicarbonate that then needs to be further diluted with either normal saline or 5%.

- ***DO NOT*** use water for injection to prepare artesunate for injection
- ***DO NOT*** give artesunate if the solution in the syringe is cloudy
- ***DO NOT*** give artesunate as a slow iv drip (infusion)
- ***YOU MUST*** use artesunate ***within 1 hour*** after it is prepared for injection

Preparing i.v. artesunate	**IV**	**IM**
Artesunate powder (mg)	60 mg	60 mg
Sodium Bicarbonate (mls, 5%)	1 ml	1 ml
Normal Saline or 5% Dextrose (mls)	5 mls	2 mls
Total volume	**6 mls**	**3 mls**
Artesunate concentration mg/ml	10 mg/ml	20 mg/ml

Artemether i.m.: Use a minimum of loading and one maintenance dose before switching to oral ACT.

Quinine i.v./i.o.: Use a minimum of loading and three maintenance doses before switching to oral ACT.

Please note: If a patient is deteriorating on treatment please discuss immediately with resident or consultant

Co-infection in Severe malaria for a child

There is high risk of a bacterial co-infection (~10%)

When no focal sign of bacterial infection consider
Ampicillin 50 mg/kg/dose four times per day. Change to amoxicillin syrup when changing to oral artmether+lumefantrine. Treat for 5 days.

Sign of pneumonia or septicaemia
Ampicillin 50 mg/kg/dose four times per day PLUS gentamicin 7.5 mg/kg/dose once per day for 5 days.

Sign of coma or meningitis
Ceftriaxone 100 mg/kg/dose once per day (inject slowly over 5 minutes) or
Chloramphenicol 25 mg/kg/dose four times per day PLUS ampicillin 50 mg/kg four times per day

Annex 15: Notes on antimalarial drugs

AMODIAQUINE
Amodiaquine is a 4-aminoquinoline anti-malarial drug similar in structure and activity to chloroquine. Like chloroquine, it possesses anti-pyretic and anti-inflammatory qualities.

Available Formulation
Tablets: Amodiaquine base 200mg

Indications
Combined with artesunate as 1st line treatment of uncomplicated malaria

Contraindications
Hypersensitivity to Amodiaquine
Hepatic disorders
Amodiaquine is not recommended for use as chemoprophylaxis

Use in pregnancy and lactation
Amodiaquine can be used in pregnancy and lactation as at present there is no evidence that Amodiaquine is contraindicated in these situations

Adverse effects
The most common adverse effects are nausea, vomiting, abdominal pain, diarrhea and itching. Rarely Amodiaquine may cause agranulocytosis, hepatic dysfunction and hypotension.

Dosage regimen
Treatment with Amodiaquine in Sierra Leone should be given at a dose of 10**mg/base per kg body weight daily for three days in combination with artesunate at 4mg/kg daily for 3 days.**

QUININE
Quinine is an alkaloid derived from the bark of the cinchona tree. It is a blood schizontocidal. Quinine is rapidly absorbed when taken orally and peak plasma concentrations are attained after 1-3 hours and has a plasma half-life of 10 hours.

Formulations
Tablets: 200 and 300 mg salt
Injectable: 300 mg/ml

Indications
Drug of choice for treatment of severe *P. falciparum* malaria
Treatment of multi-drug resistant malaria

Contraindications
Known hypersensitivity to quinine
Haemoglobinuria
Optic neuritis
Tinnitus
Myasthenia gravis
Use with caution in patients with a trial fibrillation or severe heart disease

Use in Pregnancy and Lactation
Quinine is safe in pregnancy in therapeutic doses it does not labour. Uterine contractions and fetal distress associated with the use of quinine may be attributable to fever and effects of malaria disease. The risk of quinine induced hypoglycaemia is however greater in pregnant women than in non-pregnant women.

Adverse effects
Cinchonism (tinnitus, muffled hearing, sometimes vertigo or dizziness)
Hypotension especially if injected rapidly by the intravenous route
Use with caution in patients on beta-blockers, digoxin and calcium channel blockers (e.g nifedipine) because hypotension, conduction disturbances and anginal symptoms may/occur

Hypoglycaemia, through stimulation of secretion of insulin from pancreatice beta cells. Hypoglycaemia is particularly likely to develop after intravenous infusion in pregnancy since beta cells are more susceptible to a variety of stimuli at that time
Dosage schedule for malaria treatment (The dose for intravenous use is given in page 39 – 40)

Oral Quinine (salt, 300mg tablets) for different age groups.

Dose: 10mg/kg body weight given every 8 hours for 7 days

WEIGHT KG	AGE IN MONTHS/YEARS	DAILY DOSAGE FOR SEVEN DAYS
3.3-7.4	0 – 3 months	**75mg ¼ tablet every 12 hours**
7.5 – 9.8	4 – 11 months	**75mg ¼ tablet every 12 hours**
10.0 – 14.4	1 – 3 years	**225mg ¾ tablet every 12 hours**
18.5 – 34.9	7 – 11 years	**300mg 1 tablet every 12 hours**
35.0 -59.9	**12 – 14 years**	**450mg 1½tablets every 8 hours**

32.

SULFADOXINE(500mg) PYRIMETHAMINE(25mg) (FANSIDAR)

A synergistic combination of antifolate drugs
.

Available formulation:
Tablets: Sulfadoxine 500 mg with pyrimethamine 25 mg

Indications:
Intermittent Preventive Treatment in pregnancy (IPT)

Contraindications
History of sulfonamide hypersensitivity

Adverse effects of Sulfadoxine/pyrimethamine (SP)
These may include skin reactions which in some cases may be severe in the form of Steven-Johnson Syndrome (erythema multiforme or toxic epidermal necrolysis). This is quite rare but can be fatal particular in patients who are immuno compromised. Very rarely bone marrow suppression can occur and haemolysis in G6PD-deficient individuals may be seen.

Steven-Johnson Syndrome:
The clinical features of Steven-Johnson Syndrome are mucosal lesions at two or more sites and skin lesions consisting of small blisters on dusky purpuric maculae or atypical targets. Frequent signs and symptoms (in 10-30% of cases) involve fever, arthalgia, myalgia and lesions of the respiratory and gastrointestinal tracts.

The illness is severe for the first 10 days and usually takes about 30 days to resolve.

Treatment of Steven-Johnson Syndrome:
- Stop giving sulfa drugs immediately
- Hospitalize the patient
- Give appropriate I.V. fluids
- Give antibiotic containing steroid eye drops
- Give broad spectrum antibiotics
- Protect patient day and night under a mosquito net
- Maintain hygiene and take all measure to prevent infection
- Give a highly nutritious diet

Caution
Sulfa containing drugs carry a theoretical risk of causing kernicterus in the neonate when administered to the mother just before delivery.

HALOFANTRINE
It is active against multi-drug – resistanct *falciparum* malaria. There is no parenteral preparation. Oral bioavailability (including absorption) of the drug is poor, it is therefore not suitable for use in patients with severe malaria especially those with persistent vomiting or altered consciousness. It should be used as a last resort when the above drugs have failed. Side effects include abdominal pain, diarrhoea and pruritus. Halofantrine is not recommended for use in pregnancy.

MEFLOQUINE (Lariam)
This drug is structurally similar to quinine. It is a potent long acting blood schizontocide effective against all malaria parasites including *P. falciparum* parasites resistant to 4 aminoquinolines (chloroquine and amodiaquine), SP and quinine. However, resistance to mefloquine develops very fast.

Indications
Treatment of all forms of malaria
Prophylaxis against malaria

Contraindications
History of allergy to mefloquine
Pre-existing neurological or psychiatric disease including epilepsy
Concomitant use of halofantrine, SP, quining, anti-convulsants and beta blockers e.g. propranolol
Treatment with mefloquine in the previous 4 weeks
Pregnancy during the first trimester
Persons undertaking fine co-ordination and spatial discrimination e/g/ drivers, pilots, machine operators

Use in Pregnancy and Lactation
Mefloquine should be used in pregnancy only if there are compelling medical reasons
Pregnancy should be during and for three months after completing prophylaxis
Prophylactic use during pregnancy should be avoided as a matter of principle
Nursing mothers should be advised not to breast feed while taking mefloquine

Adverse effects
Dizziness, sinus bradycardia, sinus arrhythmia, neuropsychiatric disorders

Dose
It is given as a single or spilt dose:
- Single – one dose of 15mg base/kg
- Split – one dose of 15mg base/kg followed 6 to 24 hours later by one dose of 10 mg base/kg (total dose 25 mg base/kg).

ARTEMISIN AND ITS DERIVATIVES
These are potent and rapidly acting blood schizontocides and reduces gametocyte carriage rate. They are effective against malaria parasites including multi-resistant strains of *P.falciparum*. They are generally very safe drugs and are well tolerated.

Indications
All forms of malaria including severe *P.falciparum* malaria resistant to quinine
Malaria due to multi-resistant strains of *P.falciparum*

Contraindications
They are generally very safe drugs and are well tolerated
They should not be with drugs which cause QT interval prolongation such as quinidine
They should not be used with neuroleptics, astemizole and erythromycin.
Use in pregnancy and lactation.

Adverse effects
They are generally well tolerated but there have been documented cases of nausea, vomiting, itching and fever. In addition abnormal bleeding and dark urine have occasionally been domented as well as minor cardiac changes (non specific **S-T** changes and first degree **A-V** block). These return to normal after improvement of malaria symptoms.

Available Formulations
Artemisinin: available as tablets, capsules and suppositories. **Dose**: 20mg/kg divided in two doses administered in the first day, followed by 10 mg/kg once a day for 5 days.

Artemisinin suppositories have proved effective even in cerebral and severe falciparum infection:40mg/kg (loading dose) intra-rectally, then 20mg/kg 24, 48 and 74 hrs later, followed by an oral antimalarial drug.

Dihydroartemisinin (Cotexin ®): available as tablets, capsules of 50mg and 60mg. Dose: 4 mg/kg divided in two doses administered on the first day followed by 2mg/kg once a day for 5 days.

Artemether: available as Intra-Musculat injection 80mg/ml), capsules (40mg) and tablets (50mg). Dose: 4mg/kg divided in two doses administered on the first day followed by 2mg/kg once a day for 5 days.
Artemether (Intramuscular): Dose 3.2 mg/kg (loading dose) IM followed by 1.6 mg/kg daily for 6 days.
Artesunate: available as tablets (50mg and 100mg). Dose: 4mg/kg divided in two doses administered on the first day followed by 2mg/kg once a day 5 days.

Sodium artesunate: available as intravenous injection. This is given in a dose 2.4mg/kg followed by 1.2mg/kg at 12 and 24 hrs then 1.2mg/kg daily for six days.

LUMEFANTRINE-ARTEMETHER

Formulations

Tablets containing 20mg of aretemether plus 120mg of lumefantrine (benflumetol)

Indications

Artemether-lumefantrine can be used for the treatment of uncomplicated infection with *P-falciparum*, including strains from multidrug-resistant areas.
It is the recommend 2nd line drug for managing uncomplicated malaria in Sierra Leone.

Recommended treatment

In semi-immune patients, the manufacturer recommends the 4-dose regimen, consisting of 1,2,3 0r 4 tablets taken at 0 h, 8 h, 24 h and 48 h. The total course for an adult is 16 tablets, which gives a total dose of 320 mg of artemether plus 1920 mg of lumefantrine.

In areas with multidrug-resistant *P.falciparum* and in non-immune patients, an intensive 6 –dose course consisting of the doses shown above 0 h and 8 h, and twice daily doses on the next 2 days is recommended, as shown on page 39. Thus, the course for an adult would be 4 tablets at 10 h and 8 h and 4 tablets twice a day on the second and third days.

There is no evidence of increased toxicity with the 6-doses as compared to the 4-dose regimen and, for simplicity of implementation, it is recommended to use the 6-dose regimen in all areas.

Chemoprophylaxis

This drug is not recommended for chemoprophylaxis.

Use in pregnancy

This drug should not be used in pregnant women. Safety of its use in pregnancy has not yet been established.

Adverse effects

The following adverse effects have been reported

- Dizziness and fatigue
- Anorexia, nausea, vomiting,abdominal pain
- Palpitations, myalgeia, sleep disorders, arthralgia, headache and rash.

Contraindications

- **Pregnant and lactating women**
- **Persons with known hypersensitivity to either of the components**
- **Persons with severe malaria that requires parenteral treatment.**

PROGUANIL HYDROCHLORIDE

Proguanil (Paludrine®) is a valuable drug for casual prophylaxis. It kills the pre-erythrocytic tissue (liver) stages of plasmodium. It has slow schizontocidal action on the erythrocyctic forms but is highly effective against the primary exoerythrocytic (hepatic) forms and has sponrontocidal effect on *P.falciparum.* It is less active against *P. virax*

Indications
Proguanil is the recommended drug where chemoprophylaxis is indicate. It is not recommended for the treatment of malaria.

Contraindications
Proguanil should be used with caution in-patients with severe renal impairement

Use in pregnancy and lactation
Proguanil maybe used safely at prophylactic doses during pregnancy.

Adverse effects
At normal dosage levels the side effect most commonly encountered is mild gastric intolerance. This usually subsides as treatment continues. Occasionally mouth ulceration, stomatitis and irreversible hair loss may occur. Overdose may cause haematuria, renal irritation, gastric discomfort and vomiting. The drug should not used in persons with liver or kidney disfunction.

Formulations
Tablets of 100 mg proguanil hydrochloride containing 87 mg proguanil base.

Dose
For prophylaxis the dose is 3 mg/kg daily. The adult dose is 200 mg daily.

Proguanil is currently not recommended for treatment of malaria either alone or in combination with other antimalarial drugs.