

United Republic of Tanzania



Ministry of Health and Social Welfare

National Guidelines for Diagnosis and Treatment of Malaria

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National Guidelines for Malaria Diagnosis and Treatment 2005

Foreword

The National Guidelines for Malaria Diagnosis and Treatment are a revised and updated version of similar Guidelines that were issued in the year 2000. The year 2000 version was revised following a major change in drug policy whereby the former first line drug Chloroquine was replaced with Sulfadoxine-Pyrimethamine (SP). The change was also accompanied with the reintroduction of Amodiaquine as second line drug and Quinine retained its position as the drug of choice for treatment of severe malaria. This shift was necessary following research results, which indicated very high malaria parasite resistance to chloroquine that averaged 60%. By then the parasite resistance to Amodiaquine and SP averaged 6% and 10% respectively. The World Health Organization recommends changing a drug when parasite resistance against it reaches 25%. The lesson learnt was that we would have to establish a system to monitor the performance of the drugs as we implement the new policy in order to ensure effective malaria treatment over time.

In a period of five years since the change of policy, monitoring has indicated that malaria parasite resistance to SP has gone up to an average of 25.5% in the sentinel sites (from 7.8 to 60.5%). For Amodiaquine the resistance went up to an average of 11.5% (from 6.3 to 18.2%). A decision for another change was therefore unavoidable.

The Ministry therefore, had to look for a suitable, highly efficacious replacement drug to SP. Currently, new developments in malaria treatment recommend the use of a combination of drugs that contain one of the Artemisinin compounds (ACTs). The Artemisinin class of compounds have exhibited very high cure rates for malaria and so far no parasite resistance against them has been reported. Having them combined with other suitable antimalarial drugs offers new prospects for achieving high cure rates, delay of development of parasite resistance and achieving a much longer therapeutic life.

The Ministry after several drug efficacy studies and other important considerations has come up with these updated Malaria Treatment Guidelines. From now on, Artemether/Lumefantrine (ALu) is the first line drug for treatment of uncomplicated malaria for all age groups with the exception of pregnant women during the first trimester and children weighing below five kilograms whom Quinine would still be the drug of choice. Quinine is second line drug as well as drug of choice for treatment of severe malaria. Sulfadoxine/Pyrimethamine (SP) remains the drug of choice for Intermittent Preventive Treatment (IPT) of malaria in pregnancy. The aim of IPT is to prevent the worst effects of malaria infection in pregnancy rather than to ensure clinical cure and since no suitable alternative to SP is currently available, a drug with lower efficacy is acceptable.

It is expected that adherence to these new guidelines both in the public and private health sectors will eventually lead to much reduced malaria mortality and morbidity. It has to be emphasized that although proper malaria case management is the cornerstone for malaria control, prevention of malaria by mass usage of insecticide treated nets, environmental management and other proven measures has to be undertaken. Therefore, public education is quite important and has to be undertaken.

The Ministry would like to thank all those who participated in the preparations of these guidelines.

Hon. Prof. David Mwakyusa (MP)
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Acknowledgement

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Hilda Gondwe
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List of abbreviations

ACPR	Adequate Clinical Parasitological Response
ACT	Artemisinin Combination Therapy
ADDO	Accredited Drug Dispensing Outlet
ADR	Adverse Drug Reaction
AIDS	Acquired Immunodeficiency Syndrome
ALP	Alkaline Phosphatase
ALT	Alanine aminotransferase
ALu	Artemether-lumefantrine
AO	Acridine Orange
AQ	Amodiaquine
AST	Aspartate aminotransferase
ASU	Artesunate
A-V block	Atrial-Ventricular block
BP	Blood Pressure
BS	Blood Slide
BUN	Blood Urea Nitrogen
BW	Body weight
CEEMI	Centre for Enhancement of Effective Malaria Intervention
CHMT	Council Health management Team
CNS	Central Nervous System
CORP	Community Owned Resource Persons
CSF	Cerebro Spinal Fluid
CT	Combination Therapy
CT scan	Computerised Tomography Scan
DIC	Disseminated Intra-vascular Coagulation
DOT	Direct Observed Treatment
ETF	Early Treatment Failure
FBP	Full Blood Picture
FEFO	First Expiry First Out
G6PD	Glucose 6 Phosphate Dehydrogenase
Hb	Haemoglobin
HIV	Human Immunodeficiency Virus
IHRDC	Ifakara Health Research Development Centre
IM (I.M. or i.m.)	Intra-muscular

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IMCI	Integrated Management of Childhood Illness
IPT	Intermittent Preventive Treatment
ITN	Insecticide Treated Net
IV (I.V. or i.v.)	Intra-venous
JVP	Jugular Venous Pressure
LPF	Late Parasitological Failure
LTF	Late Treatment Failure
MCH	Maternal and Child Health
MCHA	Maternal and Child Health Aide
MTCT	Mother to Child Transmission
NADH	Nicotinamide Adenine Dinucleotide
NIMR	National Institute for Medical Research
OP	Out Patient
ORS	Oral Rehydration Salts
PR	Pulse Rate
Q-T Interval	Interval on the electrocardiogram between the Q and T waves
RBC	Red Blood Cell
RBG	Random Blood Glucose
RDT	Rapid Diagnostic Tests
RNA	Ribonucleic Acid
RR	Respiratory Rate
SP	Sulfadoxine/Pyrimethamine
SPR	Slide Positive Rate
S-T interval	Interval on the electrocardiogram between the S and T waves
TB	Tuberculosis
TFDA	Tanzania Food and Drug Authority
WBC	White Blood Cell Count
WHO	World Health Organization

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Chapter 1

Introduction

CHAPTER 1: INTRODUCTION

1.1 Background

Malaria remains the most common public health problem in Tanzania. It is the number one cause of morbidity and mortality especially in children below five years of age¹. In 2004 malaria diagnosis in children under five years of age accounted for 43% of all OPD attendances and 40% of deaths recorded in health facilities.

The goal of appropriate malaria diagnosis and treatment is to reduce morbidity, mortality and socio-economic losses. The use of **National Guidelines for Diagnosis and Treatment of Malaria** is key to achieving this goal. In addition, the aim is to attain uniform malaria case management in the country. The guiding principle of antimalarial drug policy is to promote safe, effective, good quality, affordable, accessible and acceptable malaria treatment. At the same time it should encourage rational drug use in order to minimise the development of drug resistance.

Tanzania changed its malaria treatment policy from Chloroquine to Sulfadoxine/Pyrimethamine (SP) monotherapy as the first line drug for the treatment of acute malaria episodes in August 2001. However, over the last 4 years resistance to SP has already been reported to be on the increase. Recent studies (2004) in Tanzania indicate that the mean SP treatment failure is now 25.5%². In addition, molecular markers of SP resistance have recorded high levels of mutation³. The mean treatment failure of Amodiaquine, the second line antimalarial, is 12%. These findings indicate that a change in the treatment guidelines is necessary.

Due to the risk of increasing parasite resistance to existing monotherapies, there is now a global move towards use of combination therapy (CT). Combination therapy with antimalarial drugs is the simultaneous use of two or more blood schizonticidal drugs with independent modes of action and different biochemical targets in the parasite. Combination therapy can be either fixed-combination medicinal products, in which the components are co-formulated in the same tablet or capsule, or multiple-drug therapy, in which the components are co-administered in separate tablets or capsules. Artemisinin based combination therapy (ACT) is antimalarial combination therapy with artemisinin derivatives as one component of the combination⁴. Artemisinin based combinations are highly efficacious and have the potential to delay the spread of drug resistance.

Based on these principles combination therapy is recommended. Specifically, a combination of **Artemether-lumefantrine** (ALu) is recommended as first line therapy for uncomplicated malaria while **Quinine** is recommended as the second line drug in case of treatment failure or the presence of a contraindication to the first

¹ NMCP, Annual Report 2004

² East Africa Network for Monitoring Antimalarial Therapy, 2004

³ Kefas Mugittu et al. Therapeutic efficacy of SP and prevalence of resistance markers in Tanzania. *Am.J.Trop.Med.Hyg* 71(6) pp 696-702 (2004)

⁴ Combination therapy in Malaria, WHO 2004

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line drug for treatment of uncomplicated malaria. Quinine also remains the drug of choice for the treatment of severe malaria.

Unlike in the past whereby the efficacy of antimalarial treatments lasted for many years, current rates in development of resistance along with the arrival of more effective antimalarials, means that malaria chemotherapy may change in the years to come. In keeping with this new and evolving process these guidelines will have to be revised accordingly.

1.2 Broad objective

The broad objective of these Guidelines for Malaria Diagnosis and Treatment in Tanzania is to provide standard management reference for the care of patients with malaria. They form part of the National Drug Policy. These recommendations represent the minimum level of care that patients should expect at different levels of health care in the public and private sectors.

1.3 Specific objectives

- To stipulate at what level of health care delivery specific antimalarial drugs should be made available at all times
- To promote prompt and accurate malaria diagnosis
- To promote rational antimalarial drug management
- To promote intermittent preventive treatment for malaria in pregnancy
- To provide consistent guidance to prescribers and users on the appropriate use of chemoprophylaxis for specific at risk groups
- To provide information to health care managers and service providers on the detection of antimalarial drug resistance

1.4 Rationale

Due to increased resistance of the malaria parasites to antimalarial monotherapies, in order to preserve the efficacy and effectiveness of the existing drugs and to ensure an optimal cure, the Ministry of Health and Social Welfare started a consultative process in mid 2003. The aim was to select alternative options to the interim antimalarial drug regimen that became operational in 2001 (SP 1st line, Amodiaquine 2nd line and Quinine 3rd line).

In January 2004 the MoH appointed a task force to explore suitable alternatives. The task force suggested that Artemisinin based Combination Therapy (ACT) was the most appropriate option for malaria treatment. The ACTs recommended by WHO for the African Region were limited: SP-Artesunate (SP-AS), Amodiaquine-Artesunate (AQ-AS) and Artemether-Lumefantrine (ALu). Since the efficacy of ACT is related to the good efficacy of the individual single components, the first option (SP-AS) was considered as unsuitable due to the documented increased resistance of SP. The two remaining options (AQ-AS and ALu) were thoroughly tested for their therapeutic efficacy. Since the efficacy profile of the two ACTs was found equivalent in term of adequate clinical and parasitological response, (89.9% and 92.8% at day 14 respectively for AQ-AS and ALu), other factors were considered in the selection.

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These were: a) potential for creation of parasite resistance, b) pharmacological safety profile and c) compliance.

- Amodiaquine, one of the component of AQ-AS combination, had already shown some degree of parasite resistance in the country; there were also some concerns on possible cross resistance with Chloroquine
- The safety profile of Amodiaquine generates concerns among the health care providers and the public in Tanzania. The risk of potential side effects and the negative perception of the drug among the users were also considered
- Fixed formulations were found to have a better compliance

Therefore, the task force recommended ALu as the drug of choice for treatment of uncomplicated malaria for Tanzania Mainland.

1.5 Choice of antimalarial drugs

The following antimalarial drugs are recommended for treatment of malaria in Tanzania.

- The first line drug is **Artemether-Lumefantrine**
- The second line drug, where Artemether-Lumefantrine has failed or is contraindicated, is **Quinine**
- The drug of choice for treatment of severe malaria is **Quinine**
- The drug of choice for pregnant women during the first trimester and children weighting below 5 Kg is **Quinine**

Chapter 2

Management of Malaria and health care delivery in Tanzania

CHAPTER 2: MANAGEMENT OF MALARIA AND HEALTH CARE DELIVERY IN TANZANIA

2.1 Introduction

In Tanzania, the levels of health care delivery are divided into four categories:

Category I: Home, Village/Community Primary Health Care Post, Pharmacy, Drug stores including Accredited Drug Dispensing Outlet (*Duka la Dawa Muhimu*)

Category II: Dispensary

Category III: Health Centre

Category IV: Hospital

The categories mentioned above should not be looked at as a rigid sequence of referral from category I - II - III - IV. Instead, a well-trained health worker should be able to recognize the severity of malaria and refer the patient directly to the most appropriate category of care consistent with that condition.

2.2 Home

Staffing

- Parents/guardians
- Community Health Workers (CHW) and other Community Owned Resource Persons (CORPs)
- Dispensing staff of drug store (*duka la dawa muhimu*)

Diagnosis

The diagnosis of malaria should be based on:

- Symptoms such as fever, headache, malaise, joint pains, etc.
- A few basic clinical observations including feeling for body hotness and taking armpit temperature
- Presence of palmar and/or mucosal pallor for early detection of anaemia
- Recent history of convulsion in children

Type of services provided

- Health education and treatment of uncomplicated malaria cases
- Identification of patients with severe disease and non-responsive malaria cases
- Initial supportive treatment and referral to the appropriate level of care
- Where referral is made (e.g. ADDO, CHW), a referral note should be written

Types of treatment available

- Antimalarials: Artemether-Lumefantrine (ALu) tablets
- Analgesics/antipyretics: Paracetamol, Aspirin (not for children below 12 years of age)
- Oral fluids
- Exposure and fanning (*kupepea*)

2.3 Dispensary

At the dispensary a more detailed history should be taken and a more extensive clinical examination should be performed. It is recommended to have laboratory services for malaria parasites.

Staffing

- Clinical Officers
- Assistant Clinical Officers
- Trained Nurses/Public Health Nurses
- MCH Aides, Pharmaceutical Assistants and Medical attendants (Nurse Assistants/Auxiliaries, Laboratory Assistants)

All staff, with the exception of Laboratory and Pharmaceutical Assistants, are trained to administer antimalarial drugs intramuscularly when indicated

Diagnosis is based on

- Clinical history and physical examination
- Blood smear for malaria parasites, Rapid Diagnostic Test (where available)

Type of services provided

- Treatment of uncomplicated malaria cases
- Pre-referral treatment of severe malaria cases with intra-muscular quinine
- Treatment of severe malaria cases where referral is not possible
- Patient education
- Identification of patients with anaemia for the purpose of treatment and/or referral
- Identification of patients with severe disease and treatment failures for referral with the case summary
- Detection of hypoglycaemia (where available)
- Estimation of haemoglobin (where available)

Type of treatment provided

- Antimalarials:
 - *Artemether-lumefantrine* (ALu) tablets
 - *Quinine* (tablets and injectable)
 - *SP* tablets for Intermittent Preventive Treatment
- Analgesics/antipyretics: Paracetamol and Aspirin
- Anticonvulsant drugs: Diazepam (injectable) and Phenobarbitone (injectable/tablets)
- Oral Rehydration Therapy (ORT)
- Exposure and Fanning (*kupepea*)
- Correction of hypoglycaemia: Sugar solution, Dextrose 10% or 25% or 50% solution (where available)

2.4 Health centre

At the health centre, better resources for differential diagnosis and patient monitoring are available. Therefore, a more detailed history should be taken, more extensive

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clinical examination should be performed and a blood smear for malaria parasites should be done.

Staffing

- Assistant Medical Officer
- Clinical Officer
- Assistant Clinical Officer
- Public Health Nurse
- Nurse Midwives
- Medical Attendants (Nurse Assistants/auxiliaries)
- Laboratory Technicians/Assistants
- Pharmaceutical Technicians/Assistants

All staff, with the exception of Laboratory/Pharmaceutical Assistants and Technicians, are trained to administer antimalarial drugs intramuscularly and/or intravenously, when indicated.

Diagnosis is based on:

- Clinical history and physical examination
- Blood smear for malaria parasites, Rapid Diagnostic Test (where available)

Type of services provided

- Treatment of uncomplicated and severe malaria cases
- Patient monitoring
- Patient education
- Identification of patients with severe disease and treatment failures for referral with case summary
- Identification of patients with anaemia for the purpose of treatment and/or referral
- Identification of hypoglycaemia
- Pre-referral treatment
- Detection of hypoglycaemia
- Estimation of haemoglobin (Hb)

Type of treatment available

- Antimalarials:
 - *Artemether-lumefantrine* (ALu) tablets
 - *Quinine* (tablets and injectable)
 - *SP* tablets for Intermittent Preventive Treatment
- Analgesics/anti-pyretics: Paracetamol, Aspirin (not for children under 12 years of age)
- Anticonvulsants: Diazepam (Injectable) and Phenobarbitone (Injectable/tablet)
- Oral Rehydration Salts (ORS)
- Intravenous fluids: Dextrose 5%, Sodium Chloride 0.9% (Normal Saline), Sodium Lactate Compound (Ringer Lactate/Hartmann's solution) and Dextrose Saline
- Correction of hypoglycaemia: dextrose 10%, 25% and 50% solutions
- Exposure and fanning (*kupepea*)

Blood transfusion services are not usually available at the health centre

2.5 Hospital

Staffing:

- Specialists
- Medical Officers
- Assistant Medical Officers
- Clinical officers
- Nursing Officers
- Public Health Nurse A and B
- Nurse Midwives
- Medical Attendants (Nursing Assistant/Auxiliaries)
- Laboratory Technicians/Assistants
- Pharmacists and/or Pharmaceutical Technicians/Assistant
- Other Medical Cadres

Diagnosis

At this level there is sufficient clinical expertise for diagnosis of severe malaria and its complications and adequate differential diagnosis. There should also be greater efficiency and accuracy in microscopic diagnosis of malaria including identification of species, sexual and asexual forms and performance of quantitative parasite counts.

Diagnosis is based on:

- Clinical history, physical examination,
- Laboratory tests, radiology and other tests

Laboratory tests available include:

- Blood smear for malaria parasites
- Blood glucose
- Lumbar puncture for CSF examination
- Full blood picture including Hb
- Urinalysis including haemoglobinuria
- Basic biochemical tests
 - Liver function tests - including bilirubin, ALT, AST and ALP
 - Serum creatinine and blood urea
 - Electrolytes including Sodium, Potassium, Chloride, Bicarbonate and lactate
- Cultures – Blood, urine etc.

Type of services provided

- Treatment of uncomplicated and severe malaria cases
- Health education
- Identification of patients with complicated conditions that cannot be managed at district/regional hospitals (e.g. renal failure, uncontrollable convulsions, etc.) for treatment at consultant hospitals
- Identification of patients with anaemia for the purpose of treatment
- Patient monitoring
- Blood transfusion services
- Intensive care

Type of treatment available

- Antimalarials
 - *Artemether-lumefantrine* (ALu) tablets
 - *Quinine* (tablets and injectable)
 - *Artemether* injectable
 - *SP* tablets for Intermittent Preventive Treatment
 - Other antimalarial drugs may be available
- Analgesics/antipyretics: Paracetamol, Aspirin (not for children under 12 years of age)
- Anticonvulsant drugs: Diazepam Injectable and Phenobarbitone (injectable /tablet)
- Oral Rehydration Salts (ORS)
- Intravenous fluids: Dextrose 5%, Sodium Chloride 0.9% (Normal Saline), Sodium Lactate Compound (Ringer Lactate/Hartmann's solution), Dextrose saline, etc.
- Blood transfusion services
- Correction of hypoglycaemia: Dextrose 10%, 25% and 50% solution
- Exposure and fanning (*kupepea*)

Chapter 3

Diagnosis of malaria

CHAPTER 3: DIAGNOSIS OF MALARIA

3.1 Introduction

In high transmission areas a significant proportion of individuals have parasitaemia but do not necessarily suffer from malaria disease. An individual with malaria infection may be completely asymptomatic. It should be noted that the **aim of diagnosis** is to assist in the treatment of the disease and not the asymptomatic infection.

In order to minimize the irrational use of antimalarials, reduce the potential for developing parasite resistance and provide quality services, it is important to improve the accuracy of malaria diagnosis.

3.2 Clinical features of malaria

Malaria is an acute disease. Patients usually present with fever, chills and profuse sweating. The clinical features of malaria vary from mild to severe, according to the species of the parasite present, the patient's state of immunity, the intensity of the infection and the presence of accompanying conditions such as malnutrition, anaemia and other diseases.

Fever is the most common feature of malaria. It may persist for several days, accompanied by headache, aching joints and general discomfort. The classic presentation of malaria with high fever chills, shivering and sweating however may not occur. The onset of malaria symptoms may resemble a flu-like illness. In infants the early symptoms of malaria may be quite variable and difficult to recognize. They may be limited to poor appetite, restlessness and loss of normal interest in the surroundings. Some patients, especially children, may present with a cough and/or vomiting and diarrhoea.

In *P. falciparum* infections (which constitutes more than 90% of the cases in Tanzania), the headache, nausea and vomiting are usually more severe than in other malarial infections and there is a greater tendency towards the development of delirium, haemolytic jaundice and anaemia. The mortality is much greater than in other forms of malaria. Those who survive but who have continuing infection as a result of inadequate or no treatment may suffer several weeks or months of poor health. Anaemia, weakness and febrile episodes are characteristic of these cases.

The above signs and symptoms are not specific for malaria and can be found in other disease conditions. Therefore, it is always necessary to find out other causes of illness.

3.3 Assessment of the patient

3.3.1 Clinical assessment

A detailed history should be taken and a thorough physical examination made in order to diagnose diseases other than malaria. A careful assessment of a patient

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with suspected malaria is essential in order to differentiate between uncomplicated and severe disease. Laboratory investigations are done to complement clinical diagnosis. In health care facilities without laboratory services, diagnosis is based only on signs and symptoms.

Table 1 Distinguishing features of uncomplicated malaria in relation to age groups

Features	Less than five years	Older children and adults
<i>Fever</i>	+++	+
<i>Headache</i>	+	++
<i>Joint pains</i>	+	++
<i>Malaise</i>	+	++
<i>Vomiting/diarrhoea</i>	+++	+
<i>Body ache</i>	+	++
<i>Poor appetite</i>	++	++
<i>Body weakness</i>	++	++
<i>Pallor</i>	+++	+
<i>Enlarged spleen</i>	++	+

Note: + = less common, ++ = common, +++ = Very common

Table 2 Clinical and laboratory features of severe malaria⁵

Clinical Manifestations of severe malaria	Less than five years	Older children and adults
Behavioural Changes	+	+++
Prostration/Extreme weakness	+++	+++
Coma	+++	++
Respiratory distress	+++	++
Convulsions	+++	+
Vomiting everything	++	+
Inability to drink or breast feed	++	+
Circulatory collapse/Shock	+	++
Pulmonary oedema	+	+
Bleeding tendency /DIC	+	++
Jaundice	+	+++
Acute Renal Failure	+	++
Haemoglobinuria	+	++
Features and Laboratory Indices severe malaria	Less than five years	Older children and adults
Severe malarial anaemia (Hb <7g/dl or haematocrit <21%)	+++	+
Hypoglycaemia (< 2.5 mmol/L)	+++	++
Metabolic Acidosis (Arterial pH <7.3, Bicarbonate <15 mmol/L)	+++	++
Hyponatraemia (<130 mmol/L)	+	+
Hyperparasitaemia >5000 asexual parasites per 200 WBC (>200,000 asexual parasites per µL)	++	+
Uraemia (BUN >6.7 mmol/L)	+	+++

Note: + = less common, ++ = common, +++ = Very common

⁵ Modified from WHO, Severe falciparum malaria. Transaction of the Royal Society of Tropical Medicine and Hygiene, 2000,94 (Suppl. 1)

3.4 Laboratory investigations

Investigations may be done depending on the capacity of the laboratory and the clinical indications. Laboratory tests should be interpreted in conjunction with clinical findings.

The role of laboratory tests for malaria management

- As we move towards more expensive antimalarial drugs and in order to preserve their efficacy, there is an urgent need for improved laboratory services to confirm clinical diagnosis and support patient care.
- Where microscopy is possible this service should be strengthened through an efficient quality assurance system, availability of equipment, consumables and skilled staff.
- Urgent laboratory investigations should be made available for all patients admitted with severe malaria
- Since parasite-based diagnosis is important, rapid diagnostic tests (RDTs) may be an alternative or complement to microscopy

Urgent laboratory investigations

- Thick and thin blood smears for malaria parasites (for reporting of results see [Appendix 1](#))
- Blood glucose estimation in patients with altered consciousness
- Haematocrit and/or haemoglobin estimation
- Lumbar puncture to exclude meningitis at hospital and health center levels (if facilities for LP are available)

Other laboratory investigations

The following investigations, if available, are also helpful in the management of severe malaria:

- Serum creatinine or urea. There is no need to measure both, as creatinine is more useful
- Electrolytes. These may occasionally reveal a correctable abnormality such as hyponatraemia. Both creatinine and electrolytes are most valuable when acute renal failure threatens or develops
- Full blood cell count and differential white cell count. Sometimes these may indicate the possibility of an additional diagnosis
- Blood gases, pH and anion gap. Acidaemia is an indicator of severe disease in both conscious and unconscious patients
- Chest X-ray. May identify pulmonary oedema or lobar consolidation. It may be of value in assessing respiratory distress syndrome
- Plasma and cerebrospinal fluid lactate concentrations. These are raised in lactic acidosis. High levels are associated with a poor prognosis
- Improvements to conventional microscopic techniques for identifying malaria parasites may be available. These techniques include the **Quantitative Buffy Coat** (QBC) and the **Acridine Orange** (AO) methods.

Rapid Diagnostic Tests

Rapid diagnostic tests (RDTs) are qualitative techniques based on the detection of malaria parasite antigens⁶. The tests can be done by minimally trained personnel and are rapid (can be performed in about 15 minutes) and highly sensitive and specific with a high diagnostic reliability⁷. The test may remain positive for up to one month after treatment even though the patient has been cured. Quantification of parasites is not possible hence the tests cannot be used for evaluation of clinical outcome.

Rapid diagnostic tests can be used at all levels; however, it will be preferable to deploy at levels where microscopy is not possible (e.g. dispensary, health centre).

⁶ The tests detect: *P. falciparum* histidine rich protein II (HRP-II) produced by trophozoites and young gametocytes; and parasite lactate dehydrogenase (pLDH) produced by live trophozoites and gametocytes.

⁷ Mboera et al. Comparison of the Paracheck-Pf® test to microscopy for confirmation of *Plasmodium falciparum* malaria in epidemic prone districts of Tanzania, 2005

Chapter 4

Management of uncomplicated malaria

CHAPTER 4: MANAGEMENT OF UNCOMPLICATED MALARIA

4.1 Introduction

The management of a patient with malaria will be determined by the clinical presentation and the diagnosis of either uncomplicated or severe disease.

The objectives of treatment of uncomplicated malaria are:

- ***To provide rapid and long lasting clinical and parasitological cure***
- ***To reduce morbidity including malaria related anaemia***
- ***To halt the progression of simple disease into severe and potentially fatal disease***

In order to achieve these objectives, uncomplicated malaria must be diagnosed early and the correct treatment administered without delay. Since the progression towards severe and fatal disease is rapid, especially in children under five years of age, it is recommended that diagnosis and treatment of uncomplicated malaria should be done within 24 hours from the onset of symptoms.

4.2 Clinical features of uncomplicated malaria

All health care providers should be able to recognize the following features of uncomplicated malaria:

- Fever
- Headache
- Joint pains
- Malaise
- Body weakness
- Vomiting
- Diarrhoea
- Chest pains
- Poor appetite
- Anaemia (mild to moderate)
- Hepato-splenomegaly especially in children

The flow charts in [Figure 1 and 2](#) illustrate the actions for the management of a patient with suspected malaria (see also [appendix 2 and 4](#) for algorithms).

Figure 1 Management of a patient with suspected malaria in health facilities without laboratory services

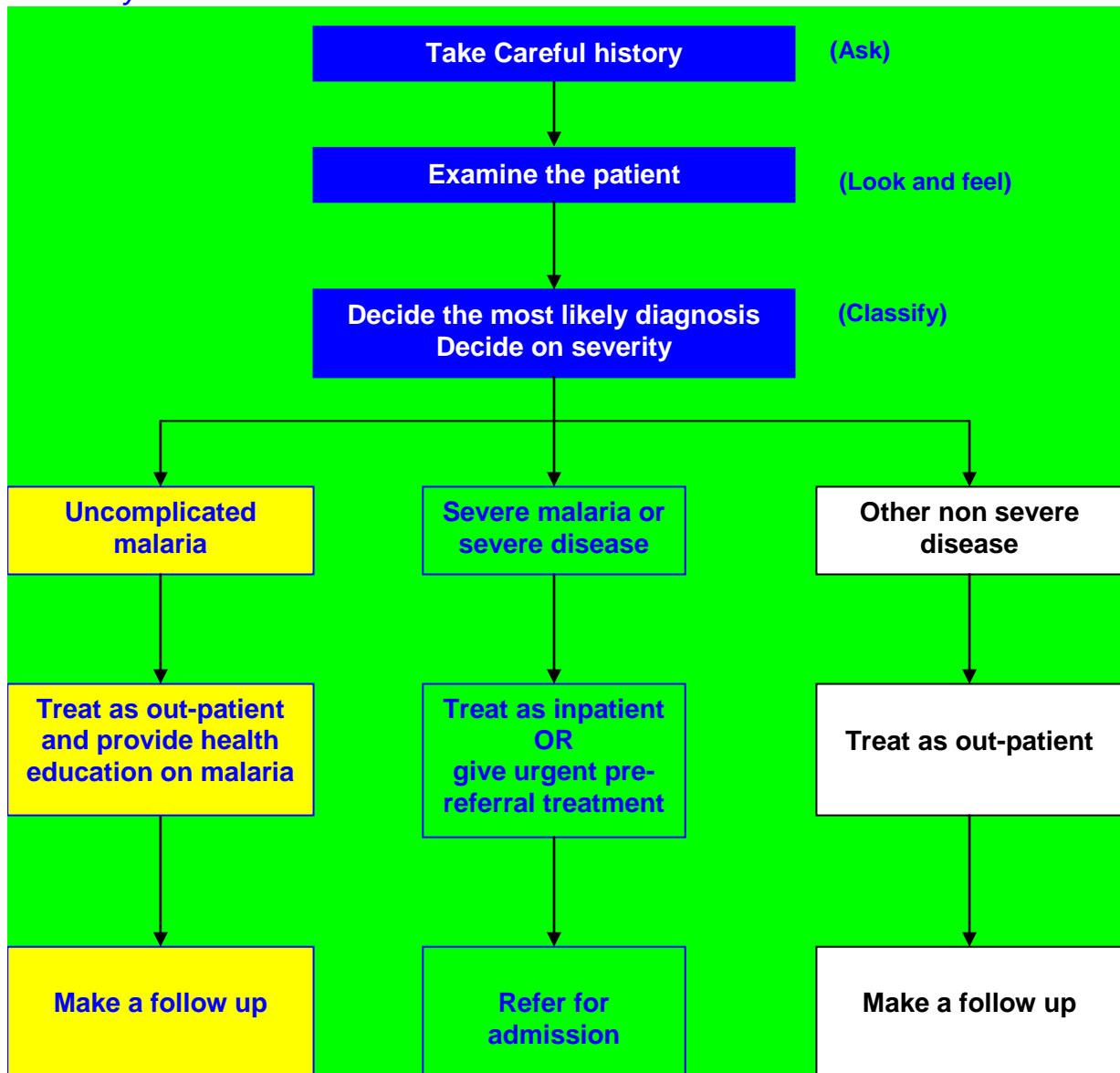
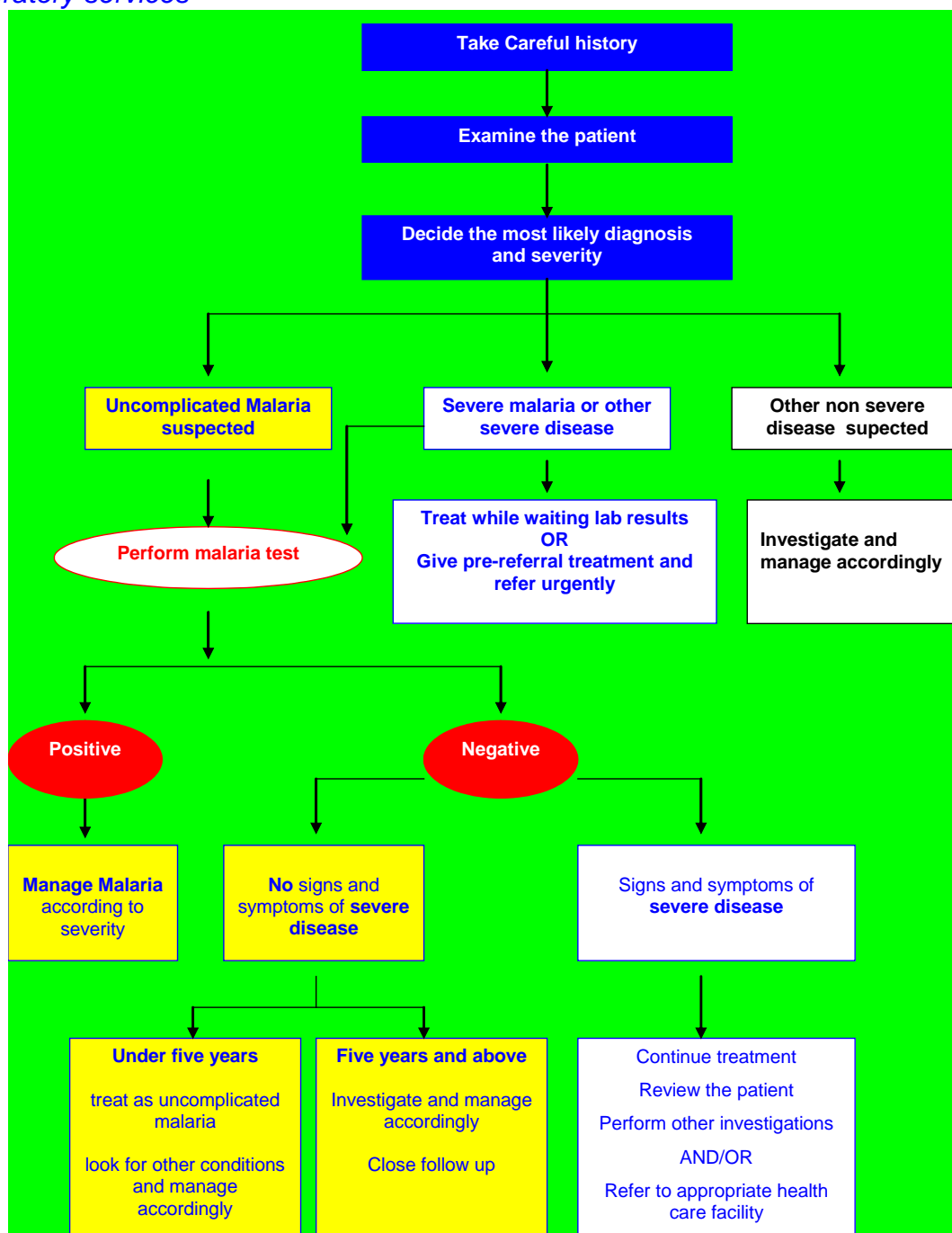


Figure 2 Management of a patient with suspected malaria in health facilities with laboratory services



Negative blood slide/RDT in a patient **without** signs and symptoms of severe disease

- If under five years of age and still malaria is suspected treat as uncomplicated malaria; also look for other causes and manage accordingly
- If above five years of age, look for other causes and manage accordingly; close follow up and ask to come back if condition does not improve

A negative blood slide/RDT in a patient **with** signs and symptoms of severe disease

- Treat as severe malaria and add broad spectrum antibiotic(s)
- Review the patient and manage accordingly
- Repeat the blood slide after 4-6 hours and perform other investigations (e.g. lumbar puncture, blood culture and sensitivity, etc.)
- Eventually, refer to appropriate health care facility

4.3 Treatment of uncomplicated malaria using combination therapy

Combination therapy refers to the use of two or more antimalarial drugs with independent mode of action and different biochemical targets in the parasite, which are synergistic or additive, or complementary in their effect.

Combination therapy can be either:

- fixed combination therapy, where all components are co-formulated in a single tablet/capsule like Artemether-Lumefantrine (ALu)
- co-administered therapy, where the components are simultaneously administered in separate tablets/capsules

The aim of combination therapy is to improve treatment efficacy and also delay the development of drug resistance.

Artemisinin-based combination therapy (ACT) refers to combinations comprising of an artemisinin derivative and another antimalarial drug. Examples of artemisinin derivatives are artemether, artesunate and dihydroartemisinin. Artemisinin derivatives are efficacious, short acting and generally safe. The partner drug should be as well efficacious, safe and compatible. Some examples of partner drugs are Lumefantrine, Amodiaquine, Chlorproguanil-Dapsone and Mefloquine.

4.4 Treatment of uncomplicated malaria with first line drug: Artemether-Lumefantrine

The first line drug for the treatment of uncomplicated malaria is **Artemether - Lumefantrine** (ALu).

Drug description

Artemether-lumefantrine (ALu) is an oral fixed combination tablet of 20mg Artemether – a derivative of artemisinin, and 120mg Lumefantrine. Artemether is effective against all human malaria parasites species. It has a rapid schizonticidal action against *Plasmodium falciparum*. Recrudescence is therefore frequent when it is used as a monotherapy. Lumefantrine is an aryl amino alcohol. It has a longer elimination half-life of up to 10 days and is associated with a low recrudescence rate, but has a slower onset of action. ALu therefore combines the benefits of the fast onset of action of Artemether with the long duration of action and high cure rate of Lumefantrine in a single oral formulation. It is highly efficacious even against multi drug resistant malaria parasites with clearance of the parasites from the blood within 2 days.

Available formulations

Tablets: Fixed formulation Artemether 20 mg, Lumefantrine 120mg

Indications:

- First line treatment of uncomplicated malaria

Contraindications

- Hypersensitivity to either Artemether or Lumefantrine

Not recommended

- Children below 5kg body weight
- First trimester of pregnancy
- Lactating mothers with child below 5kg of body weight

Use of Artemether-lumefantrine (ALu) in Pregnancy and Lactation

Pregnancy

Presently, Artemisinin compounds cannot be recommended for treatment of malaria in the first trimester of pregnancy. However, they should not be withheld if treatment is considered to be life saving for the mother and other anti malarial are considered to be unsuitable. In the first trimester of pregnancy quinine should be used as first line treatment. During the first trimester (12 weeks of pregnancy) it is not recommended to take ALu at all. After the first trimester ALu tablets is first line medicine.

Lactation

No data is available on the excretion of either of the two compounds in breast milk. Due to the long elimination half-life of Lumefantrine (up to 10 days), it is not recommended in mothers breast-feeding children below 5kgs. In this case quinine should be used. ALu can be used as first line treatment in lactating mothers if no suitable alternative is available.

Adverse effects of Artemether-lumefantrine (ALu)

While the overall incidence of side effects to ALu is low, the common adverse effects reported include sleep disorders, headache, dizziness, nausea, anorexia, abdominal pain, pruritus, rash, cough, palpitation, arthralgia and myalgia. Lumefantrine does not cause prolongation of QT interval and therefore it is safe in patients with cardiac illness.

Artemether-lumefantrine administration

- The first dose of Artemether-lumefantrine should preferably be administered at the health facility as direct observed treatment (DOT)
- When administering Artemether-lumefantrine, if the drug is vomited or spat out within 30 minutes, the dose should be repeated
- ALu should be taken with meals to enhance its absorption

Dosage regimen

The dose of artemether-lumefantrine (ALu) is **1.5/12 mg/kg** bodyweight twice a day for three days. For convenience purposes, the dosing schedule for ALu (strength 20/120 mg) is reported in [table 3](#).

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Table 3: Dosage schedule of Artemether 20mg & Lumefantrine 120 mg (ALu) (number of tablets recommended at approximate timing of dosing)

Kg	Dose Hours Age	Day 1		Day 2		Day 3		Colour Code Coartem®
		1 st	2 nd	3 rd	4 th	5 th	6 th	
		0 (*) tablets	8 tablets	24 tablets	36 tablets	48 tablets	60 tablets	
5 up to 15	3 months up to 3 years	1	1	1	1	1	1	Yellow
15 up to 25	3 years up to 8 years	2	2	2	2	2	2	Blue
25 up to 35	8 years up to 12 years	3	3	3	3	3	3	Red
35 and above	12 years and above	4	4	4	4	4	4	Green

(*) 0 hours means the time of starting medication (see appendix 5 for time schedule for 1st and 2nd dose)

For practical purposes, a simpler dosage regimen is recommended in order to improve compliance: the first dose should be given as DOT; the second dose should strictly be given after 8 hours; subsequent doses could be given twice daily (morning-evening) in the second and third day of treatment until completion of 6 doses (see illustration below).

WEIGHT	AGE	Day 1		Day 2		Day 3	
		Start Dose	After 8 hrs*	Mornin Night	Morning Night		
5 - 15 kg	3 months up to 3 years						
15 - 25 kg	3 years up to 8 years						
25 - 35 kg	8 years up to 12 years						
35 kg and above	12 years and above						

*Strictly after 8 hours

Non response to ALu may be due to:

- Vomiting the drug
- Poor quality of the drug
- Inadequate dosage
- Fever/symptoms from a cause other than malaria
- Parasite resistance to the drug (rare)

Management of non-response to malaria treatment with ALu

Where a patient returns between 4 to 14 days after treatment with ALu complaining of continued symptoms of malaria, non-response should be considered and the following recommendations followed after a full history and examination:

- Where laboratory facilities are not available and malaria is still suspected, treatment with Quinine should be started immediately with strict follow up
- Where laboratory facilities are available, a blood smear (and not RDT) should be examined. If parasites are found treatment with Quinine should be started and treatment failure recorded. If parasites are not found other causes for the symptoms should be sought and treated accordingly

As far as possible malaria cases should be followed up on the third day if symptoms persist or immediately if the condition worsens. Health workers should know where they could refer cases that fail to respond to the recommended drug regimen for further investigations and appropriate management

4.5 Management of fever.

Patients with high fever (38.5⁰C and above) should be given an anti-pyretic drug like paracetamol or aspirin every 4 to 6 hours (maximum 4 doses in 24 hours) until symptoms resolve, usually after two days. Children below 12 yrs should not be given aspirin because of the risk of developing Reye's syndrome.

*Table 4. Treatment schedule for paracetamol (500mg) tablets
Dosage for children: 10 mg/Kg bw*

Age (years)	Weight (Kg)	Dose
2 months up to 3 yr	4 up to 14	1/4
3 up to 5	14 up to 19	1/2
5 up to 12	19 up to 35	1
12 up to 14	35 up to 45	1 1/2
14 and above	45 and above	2

4.6 Treatment of uncomplicated malaria with second line drug: Quinine

Available formulation

- Tablets 300 mg
- Injection 600 mg in 2 mls
- Quinine hydrochloride syrup 100 mg/5ml

Indications

- Treatment of uncomplicated malaria where ALu is contraindicated
- Treatment of uncomplicated malaria where ALu has failed
- Drug of choice for treatment of uncomplicated malaria
 - in first trimester of pregnancy,
 - in lactating mothers with children below 5 kg
 - in children under weighing below 5 Kg
- Drug of choice for treatment of severe malaria

Contraindications

- Hypersensitivity to quinine
- Optic neuritis
- Myasthenia gravis

Use in pregnancy and lactation

Quinine is safe in pregnancy. In therapeutic doses it does not induce 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
- Hypoglycaemia, through stimulation of secretion of insulin from pancreatic 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
- Injection sterile abscess

Dosage regimen

Treatment with **Quinine tablets** (salt) should be given **for 7-10 days** at a dose of **10 mg/kg every 8 hours**. Refer to chapter 5 for details on Quinine use. Preferably the dose to be given should be calculated for each single patient according to the weight (not exceeding a maximum dose of 600mg). The [table 5](#) below is given for guidance when it is impossible to weigh patients.

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Table 5: Dosage schedule for malaria treatment using oral Quinine (salt, 300mg tablet) for different age groups

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

Age (years)	Weight (Kg)	Number of tablets
Up to 11 months	5 up to 11	$\frac{1}{4}$
1 up to 5	11 up to 19	$\frac{1}{2}$
5 up to 8	19 up to 25	$\frac{3}{4}$
8 up to 12	25 up to 35	1
12 up to 14	35 up to 50	1 $\frac{1}{2}$
14 up to 16	50 up to 60	1 $\frac{3}{4}$
16 and above	60 and above	2

Non-response to Quinine treatment

Refer the patient for thorough investigations and management.

4.7 Health education for uncomplicated malaria patient/caretakers

Focus health education messages on the following:

- Importance of compliance
- Doses and dose schedules
- When to return immediately (worsening conditions especially when fever remains high, excessive vomiting etc.)
- Continue with feeding and fluid intake
- When to return for follow up to health facility (to ensure good progress)
- Personal protection measures especially use of Insecticide Treated Nets
- Environmental sanitation

Chapter 5

Management of severe malaria

CHAPTER 5: MANAGEMENT OF SEVERE MALARIA

5.1 Introduction

Severe *Plasmodium falciparum* malaria is a medical emergency. Delay in diagnosis and provision of appropriate treatment may lead to serious complications and even death. In Tanzania the commonest presentations of severe malaria are severe anaemia and cerebral malaria.

5.2 Features of severe malaria

One or more of the following features indicate severe malaria

Table 6: Features of severe malaria

Clinical features	Description/criteria
Prostration/extreme weakness	Unable to stand or sit up without support
Impaired consciousness	Altered level of consciousness Acute confusional state, coma
Change of behaviour	Hallucinations, delusions, agitation
Convulsions	Repetitive abnormal muscular movements
Respiratory distress (due to lactic acidosis and/or pulmonary oedema)	<i>Acidotic breathing</i> : deep and laboured breathing <i>Pulmonary oedema</i> : laboured breathing, restlessness, blood stained frothy sputum especially in adults
Bleeding tendency/DIC	Easy/prolonged bleeding
Jaundice	Yellow colouration of mucus membranes
Circulatory collapse/shock*	Low systolic BP ** and fast pulse rate ***
Vomiting everything	Throwing up after every feed/drink
Inability to drink or breast feed	Not able to swallow
Condition	Corresponding Indices
Severe malarial anaemia	Hb <7g/dl or haematocrit < 21%
Haemoglobinuria	Dark brown or Positive Hb on dipstick urine
Pulmonary oedema	Chest X-ray
Hyperparasitaemia	>5000 asexual parasites per 200 WBC (>200,000 asexual parasites per μ L)
Metabolic acidosis	Arterial pH <7.3, Bicarbonate <15 mmol/L
Acute renal failure	Oliguria urine output <0.3 ml/kg/hr in children and <17ml/hr in adults Raised serum creatinine >130 mmol/L and BUN >6.7 mmol/L
Hypoglycaemia	Glucose <2.5 mmol/L

* Shock: cold extremities, capillary refill delayed for ≥ 3 seconds (when a nail of the thumb is pressed); weak and fast pulse;

** Low systolic BP <50 mmHg in children and <90 mmHg in adults;

*** Fast pulse rate ≥ 150 per minute in children and ≥ 100 beats per minute in adults;

Table 7: Clinical features and laboratory indices of severe malaria in adults and children and their prognostic values⁸

Features	Prognostic values	
	Children	Adults
Clinical Manifestations		
Behavioural changes	+	+
Prostration	+	+
Coma	+++	+++
Respiratory distress	+++	+++
Repeated convulsions	+++	++
Circulatory collapse/Shock	+++	+++
Pulmonary oedema	+++	+++
Bleeding tendency /DIC	+++	+++
Jaundice	++	+
Acute renal failure	+++	+++
Haemoglobinuria	+	+
Vomiting everything	++	++
Inability to drink or breast feed	+++	++
Condition and Laboratory Indices		
Severe malarial anaemia (Hb <7 g/dl or haematocrit <21%)	++	++
Hypoglycaemia (<2.5 mmol/L)	+++	+++
Metabolic Acidosis (Arterial pH <7.3, Bicarbonate <15 mmol/L)	+++	+++
Hyperparasitaemia >5000 asexual parasites per 200 WBCs (> 200,000 asexual parasites per µL)	+	++
Uraemia (BUN >6.7 mmol/L)	++	++

Prognosis: + poor, ++ very poor, +++ = worse

5.3 Treatment of severe malaria

The drug of choice for treatment of severe malaria is parenteral **Quinine** preferably given by intravenous infusion. Refer to chapter 4 for the pharmacological profile of Quinine.

5.4 Management of severe malaria at home, shopkeeper and village health post

Management should include

Early recognition of symptoms and signs defining severe malaria with appropriate early health care seeking behaviour

- Control of fever by the use of anti-pyretics and fanning (*kupepea*)
- Administration of oral artemether-lumefantrine (ALu)
- Continued feeding and fluid intake
- Immediate referral to the nearest health care facility

⁸ Modified from WHO, Severe falciparum malaria. Transaction of the Royal Society of Tropical Medicine and Hygiene, 2000,94 (Suppl. 1):1-90

5.5 Management of severe malaria at dispensary level

Management should include

- Early diagnosis of severe malaria based upon a complete history, physical examination and, where possible, blood smear/RDT examination for malaria parasites. Taking and reporting of blood smear must not be allowed to delay treatment unduly
- Provision of pre-referral treatment with intra-muscular quinine and
- Immediate referral with clinical summary, to the nearest health care facility where resources for the continuing care of patients with severe malaria are available

General management

Assessment and resuscitation

- Airway – ensure airway is open with no foreign objects,
- Put the patient in semi prone position
- Breathing – ensure there is adequate respiratory movement
- Circulation – measure pulse rate and blood pressure
- Blood slide for malaria parasites (do not wait for results)
- Blood glucose estimation by glucose strips
- Hb estimation

Pre-referral treatment

- Administration of intra-muscular quinine (refer to [table 8](#))
- In suspected severe malaria where meningitis and septicaemia cannot be ruled out, a broad-spectrum antibiotic (e.g. Chloramphenicol) should be administered
- Correction of hypoglycaemia by using oral sugar-water
- Control fever with anti-pyretics and fanning (*kupepea*)
- Control convulsion with diazepam (refer to 5.11)

Dilution of quinine for intra-muscular use

- Quinine Dihydrochloride injection (300 mg/ml) for intra-muscular use
- Dose of 10 mg of salt/kg bodyweight (not exceeding a maximum dose of 600mg)
- Dilution: diluted four times in water for injection to a concentration of 60 mg/ml. This dilution will minimize the risk of sterile abscess formation.
- Preferably the dose should be calculated for each single patient according to the body weight. [Table 8](#) below is given for guidance

*Table 8: Dilution schedule for intra-muscular Quinine administration
(Dose = 10 mg/kg of body weight)*

Age (years)	Weight (Kg)	Volume of undiluted Quinine (300 mg/ml)	Volume of diluent (to add to each dose)	Total volume of diluted Quinine (60 mg/ml)
2 up to 4 months	4 up to 6	0.2 ml	0.8 ml	1.0 ml
4 up to 9 months	6 up to 8	0.3 ml	1.2 ml	1.5 ml
9 up to 12 months	8 up to 10	0.4 ml	1.6 ml	2.0 ml
12 months up to 3yrs	10 up to 14	0.5 ml	2.0 ml	2.5 ml
3 up to 5	15 up to 19	0.6 ml	2.4 ml	3.0 ml
5 up to 8	19 up to 25	0.7 ml	2.8 ml	3.5 ml
8 up to 12	25 up to 35	1.0 ml	4.0 ml	5.0 ml
12 up to 14	35 up to 50	1.4 ml	5.6 ml	7.0 ml
14 up to 16	50 up to 60	1.8 ml	7.2 ml	9.0 ml
16 and above	60 and above	2.0 ml	8.0 ml	10.0 ml

The calculated dose should be divided into two halves and then administered by deep intra-muscular injection preferably into the mid anterolateral aspect of the thigh (one injection on each side)

5.6 Management of severe malaria at health centre level

Management should include

- Early diagnosis of severe malaria based upon a complete history, physical examination and blood smear/RDT for malaria parasites. Taking and reporting of blood smear must not be allowed to delay treatment unduly
- Provision of appropriate treatment with intra-venous Quinine
- Treatment of hypoglycaemia. Hypoglycaemia remains a major problem in the management of severe malaria especially in young children and pregnant women. It should be deliberately looked for and treated accordingly.
- Referral with clinical summary to the nearest hospital when clinical need dictates (e.g. blood transfusion or intensive care)

General management

Assessment and resuscitation

- Airway – ensure airway is open with no foreign objects
- Put the patient in semi prone position
- Breathing – ensure there is adequate respiratory movement
- Circulation – measure Pulse rate and Blood pressure
- Blood slide for malaria parasites (do not wait for results)
- Blood glucose estimation by glucose strips/glucometer
- Hb estimation

Where facilities for intravenous therapy are available

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- Management should follow the guidelines presented for hospital level (see 5.7)

Where facilities for intravenous administration of Quinine are not available:

- Injectable Quinine should be given by the intra-muscular route at a dose of 10 mg/kg bodyweight of salt every 8 hours (refer to [table 8](#) for dilution and dosage), until the patient is able to take oral medication
- Once oral treatment can be tolerated Quinine tablets should be continued to complete a 7 days treatment course

OR

- A full course of ALu may be administered to complete treatment (except in pregnant women during first trimester and children below 5 kg body weight)

5.7 Management of severe malaria at hospital level

Management should include:

Early diagnosis of severe malaria based upon a complete history, physical examination and blood smear/RDT for malaria parasites. Taking and reporting of blood smear and other investigations must not be allowed to delay treatment unduly

- Provision of appropriate treatment with intra-venous Quinine
- General management, nursing care and monitoring
- Treatment of complications e.g. blood transfusion where appropriate
- Treatment of hypoglycaemia. Hypoglycaemia remains a major problem in the management of severe malaria especially in young children and pregnant women. It should be deliberately looked for and treated accordingly.
- Laboratory investigations for other complications where indicated

General management

Assessment and resuscitation

- Airway – ensure airway is open with no foreign objects
- Put the patient semi prone position
- Breathing – ensure there is adequate respiratory movement
- Circulation – measure Pulse rate and Blood pressure
- Blood slide for malaria parasites (do not wait for results)
- Blood glucose estimation by glucose strips/glucometer
- Hb estimation

Insert intravenous cannula

- Blood samples for random blood glucose (RBG), full blood picture (FBP), serum creatinine, liver function tests (bilirubin, AST, ALT, ALP) and serum electrolytes
- Start dextrose-saline or dextrose 5% infusion

Insert naso-gastric tube (if indicated)

- For feeding and medication

Insert urethral catheter (if indicated)

- Urine for dipstick
- Urinary output measurement

Nursing care and monitoring

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- Fluid input and output chart
- Level of consciousness
- Temperature, PR, RR and BP
- Investigations: Hb, Glucose, Creatinine, electrolytes if indicated

Table 9: Investigations

Essential	If indicated
Blood glucose estimation	Blood culture and sensitivity
Blood film for malaria parasites/RDT	Chest radiograph
Full blood picture	Cerebrospinal Fluid analysis
Urinalysis (including detection of Hb)	Urine culture and sensitivity
	Biochemical tests: serum creatinine, liver function tests (bilirubin, AST, ALT, ALP) arterial pH and serum electrolytes

Administration of intravenous quinine

Dose

- Quinine 10 mg/kg body weight of salt
- Diluted in 5-10 ml/kg body weight of 5% Dextrose or dextrose-saline
- Infused over 4 hours and repeated every 8 hours.
- The total volume given will depend on the patient's overall fluid balance

The **drop rate** is calculated as follows:

$$\text{Drop rate per minute} = \frac{\text{amount of fluid to be infused (in ml)} \times 20 \text{ (drop factor)}}{\text{time period to be infused (in minutes)}}$$

The [table 10](#) below is given for easier calculation:

Table 10: Dilution schedule and drop rate for intravenous Quinine administration

Age (years)	Weight(kg)	Quinine dose	Volume of undiluted quinine solution (300mg/ml)	Amount of fluid to be infused (in 4 hours)	Drop rate per minute
2 up to 4 months	4 up to 6	60 mg	0.2 ml	50 ml	4 drops
4 up to 9 months	6 up to 8	90 mg	0.3 ml	100 ml	8 drops
9 up to 12months	8 up to 10	120 mg	0.4 ml	100 ml	8 drops
12 up to 3yrs	10 up to 14	150 mg	0.5 ml	100 ml	8 drops
3 up to 5	15 up to 19	180 mg	0.6 ml	150 ml	13 drops
5 up to 8	19 up to 25	210 mg	0.7 ml	200 ml	17 drops
8 up to 12	25 up to 36	300 mg	1.0 ml	250 ml	21 drops
12 up to 14	36 up to 50	420 mg	1.4 ml	350 ml	30 drops
14 up to 16	50 up to 60	540 mg	1.8 ml	500 ml	42 drops
16 and above	60 and above	600 mg	2.0 ml	500 ml	42 drops

Infusions should be discontinued as soon as the patient is able to take oral medication. Patients should be properly instructed to complete the 7-day treatment. Alternatively, a full course of ALu may be administered to complete treatment

Oral Quinine maintenance doses should be 7 mg/kg body weight in patients with impaired renal function

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5.8 Monitoring of patients with severe malaria

All patients with severe malaria should be closely monitored as described in [table 11](#) below.

Table 11: Important observations and their implications during treatment of severe malaria

Regularly observe	Possible observation	Appropriate action
A. Clinical		
Breathing	Increased respiratory rate: <ul style="list-style-type: none"> • < 2 months: 60 or more per minute • 2 up to 12 months: 50 or more per min • 1 yr up to 5 yrs: 40 or more per min • 5 yrs and above: 20 or more per min Or difficulty in breathing	<ul style="list-style-type: none"> - Check position of the patient - Put the patient in semi-prone (Fowler's) position - Give oxygen if there is respiratory distress - Review urine output - Examine lung, heart and size of the liver - Chest X ray if available - If pulmonary oedema is demonstrated, or seems likely treat appropriately.
Axillary temperature	$\geq 38.5^{\circ}C$ If temperature remains high or rises despite 24 hours of quinine therapy	<ul style="list-style-type: none"> - Give paracetamol if not given within the past 4 hours - Fanning (<i>kupepea</i>) - Reassess and investigate for other possible causes while continuing treatment
Blood pressure	BP Falls: <ul style="list-style-type: none"> • <90 mmHg systolic in an adult • < 50 mmHg in infants and children (using paediatric cuff) 	<ul style="list-style-type: none"> - Review fluid balance, urine output, quinine infusion rate and haematocrit. - If hypovolaemic give saline infusion where indicated. - Look for hemorrhage - Take blood for bacteriological culture and sensitivity if facilities are available - Give broad spectrum antibiotic (for possible bacteraemia)
Urine output	Oliguria: <ul style="list-style-type: none"> • <17 ml/hr in an adult or • <0.3 ml/kg/hr in infants and children 	<ul style="list-style-type: none"> - Review fluid input and status of hydration - Correct fluid deficit if necessary - Prevent or manage acute renal failure if suspected - Catheterize if acute renal failure
Coma score	Deterioration See appendix 6 for Glasgow and Blantyre coma scale	<ul style="list-style-type: none"> - Reassess and investigate for other possible causes while continuing treatment - Immediately check blood glucose (correct hypoglycemia if suspected) - Lumbar puncture

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Convulsions	These can recur, or develop for the first time during treatment and may be due to hyperpyrexia, abnormal blood glucose or electrolyte imbalance or other causes	<ul style="list-style-type: none"> - Check axillary temperature if $\geq 38.5^{\circ}\text{C}$, treat as above - Check blood glucose (correct hypoglycemia if suspected) - Check fluid balance - Check electrolytes if possible (to detect hyponatraemia) - Give anticonvulsant drugs
Bleeding from venepuncture sites or spontaneous haemorrhage	Prolonged bleeding time suggesting <i>Disseminated intravascular coagulopathy</i> (DIC)	<ul style="list-style-type: none"> - Check bleeding time - Grouping and cross matching blood - Give whole fresh blood as needed to correct blood loss and bleeding tendency (20 ml/kg for children, 2 units in adults)
B. Laboratory		
Blood glucose	Falls below 2.5 mmol/L (<45 mg/dl) OR <3.0 mmol/L (54mg/dl) in malnourished children	<ul style="list-style-type: none"> - Ask when last fed. A child will become hypoglycaemic if deprived of glucose for more than 12 hours - Give IV 10 or 25% glucose bolus - Review infusion - Maintain feeding
Haematocrit	Falls to 12% or below	<ul style="list-style-type: none"> - Grouping and cross-matching blood - Give blood transfusion 10 mls/kg body weight of packed cells - Repeat haemoglobin and haematocrit at regular intervals - Consider transfusion if in cardiac failure even if Hb is >4g/dl
Haemoglobin	Falls to 4g/dl or below	
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	<ul style="list-style-type: none"> - Take BS for malaria parasites daily until the results are negative - Review adequacy of antimalarial dosage - Consider alternative

5.9 Non-response to quinine therapy

Non-response to quinine therapy should be suspected if there is:

- Persistence of clinical features of severe malaria
- Failure of clearance of parasites after 5 days of treatment
- Other possible causes of illness which have not been investigated

Patients with malaria who have not responded to quinine therapy should be given **parenteral Artemether**.

Dose:

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

5.10 Emergency management of severe malaria

5.10.1 Convulsions

Convulsions are common in children with severe *P. falciparum* malaria but are relatively rare in adults. The general principles for the care of patients with convulsions should be as follows:

- Maintenance of a clear airway
- Monitoring of vital signs: temperature, pulse rate, respiratory rate and blood pressure
- Nurse the patient in a semi-prone position
- Check blood glucose where possible, or give IV dextrose

Anticonvulsant drug

- Diazepam 0.15 mg/ kg (maximum 10 mg for adults.) slow bolus IV injection In children diazepam rectal route should be used. Give a dose of 0.5-1.0 mg/ kg. Draw the IV preparation into a small syringe and remove the needle. Insert 5 cm of a nasogastric tube into the rectum. Inject the diazepam into the nasogastric tube and flush it with 5 ml of water. If a nasogastric tube is not available, use a syringe without a needle. Hold buttocks together for few minutes to ensure retention and absorption of the drug.

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 phenobarbitone 20 mg/ kg IM or IV after another 10 minutes

Diazepam should not be used in infants below 1 month of age. Instead use phenobarbitone 20mg/kg IM or IV. If convulsions persist, repeat phenobarbitone 10 mg/ kg after 30 minutes

5.10.2 Hypoglycaemia

- Check blood glucose 4 hourly. If blood glucose falls < 2.5 mmol/l or level of consciousness deteriorates
- In children
 - Give 5 mls/kg of 10% dextrose OR 2.5 mls/kg of 25% dextrose as bolus

- If 50% dextrose solution is available, it should be diluted to make 25% by adding an equal volume of water for injection or normal saline
- In adults
 - Give 125 mls of 10% dextrose OR 50 mls of 25% dextrose dextrose as bolus

Where dextrose is not available, sugar water should be prepared by mixing 20 gm of sugar (4-level tea spoons) with 200 ml of clean water. 50 ml of this solution is given ORALLY or by naso-gastric tube if unconscious

5.10.3 Hypotension

Give colloid fluids (plasma expander) or blood if haemoglobin is less than 5g/dl

5.10.4 Pulmonary oedema

Check for

- Restlessness
- Frothy sputum
- Basal crepitations
- Low oxygen saturation (< 95%)

Give

- Oxygen
- IV frusemide
- Mechanical ventilation may be needed.

5.10.5 Metabolic Acidosis

In malaria patients metabolic acidosis is attributed to **lactic acidosis**.

Check for

- Respiratory distress, deep and laboured breathing

Give

- Oxygen
- Correct hypovolaemia

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Chapter 6

Anaemia and malaria

CHAPTER 6: ANAEMIA AND MALARIA

6.1 Introduction

Etiology of anaemia in malaria endemic areas is often multi-factorial, with different causes interacting in a vicious cycle of nutritional deficiencies, infections and inherited red blood cell disorders. However, malaria remains one of the main contributors.

Anaemia is a major cause of the high morbidity and mortality associated with malaria. It is especially serious in young children and pregnant women. In the IMCI evaluation in Kilombero, Ulanga, Rufiji and Morogoro rural ⁹ it was found that 87% of children <5 years had an Hb <11 g/dl, 39% had an Hb <8 g/dl and 3% had an Hb <5 g/dl. About 60% of anaemia in infants is due to malaria and 30% is due to iron deficiency¹⁰.

6.2 Definition

Anaemia is defined as reduction of red blood cells or haemoglobin (Hb) concentration or both below the normal range for the age and sex of the individual (see [table 12](#)).

Anaemia due to malaria is usually normocytic and normochromic in nature. During the course of malaria infection, red blood cells are destroyed. Anaemia can result from repeated or persistent malaria infections, which may result from inadequate treatment, parasite resistance or no treatment at all. Anaemia due to malaria may develop rapidly following an acute malaria attack or insidiously over a period of time.

Table 12: Normal Haemoglobin concentration levels by ages and sex

Category	Hb g/dl
Newborn	13.5 - 20
Children less than 6 years	11 - 13
Adult females, not pregnant	12 - 16
Adult females, pregnant	11 - 15
Adult males	13 - 17

The various mechanisms by which malaria may cause anaemia include:

- Haemolysis of parasitised and nonparasitised red blood cells (RBC)
- Enhanced splenic uptake of RBC
- Dyserythropoiesis or impaired red blood cell production
- Unexplained massive intravascular haemolysis (blackwater fever) may complicate some infections

⁹ Schellenberg D, Armstrong Schellenberg JA, Mushi A, de Savigny D, Mgalula L, Mbuya C, Victora C. *The Silent Burden of Anaemia in Tanzanian Children: a Community-based Study. Bull WHO 2003;81(8):581-590*

¹⁰ Menendez C, Kahigwa E, Hirt R, Vounatsou P, Aponte J, Font F, Acosta C, Galindo C, Kimario J, Urassa H, Brabin B, Smith T, Kitua A, Tanner A, Alonso P. *Randomised placebo-controlled trial of iron supplementation and malaria chemoprophylaxis for prevention of severe anaemia and malaria in Tanzanian infants. The Lancet 1997; 350: 844-850.*

For this reason, an understanding of the association between malaria and anaemia is essential. Effective treatment of both conditions is important in reducing the burden of morbidity and mortality due to malaria and anaemia.

6.3 Clinical presentation of anaemia

In areas of high malaria endemicity the association between malaria and anaemia is strong. However, patients presenting with anaemia and malaria are frequently not treated correctly because their symptoms and signs are often missed. All patients, especially pregnant women and young children, presenting to health facilities with malaria should be checked carefully for anaemia.

Ask for (symptoms):

- Easy fatigue/easy tiring
- Inability to feed and drink (Infants and children)
- Dizziness and breathlessness on exertion in pregnant women
- History of eating soil (especially in children or pregnant women)

Look for (signs):

- Pallor (palms, soles, nails beds, conjunctivae and tongue)
- Signs of respiratory distress (nasal flaring, chest indrawing and deep breathing or grunting)
- Signs of congestive heart failure (dyspnoea, tachycardia, gallop rhythm, basal crepitations, oedema, puffy eyes, raised jugular venous pressure and enlarged tender liver)

6.4 Classification of anaemia according to severity

Mild/moderate anaemia, Hb 7-11 g/dl

- Some pallor

Severe anaemia, Hb <7 g/dl

- Severe palmar pallor
- Excessive tiring
- Dyspnoea or breathlessness
- Warm hands
- Peripheral oedema: Pedal pitting
- Tachycardia, collapsing pulse, wide pulse pressure and gallop rhythm.
- Ejection systolic murmur ('flow' murmur)

Life threatening anaemia, Hb<5g/dl

- Respiratory distress
 - Nasal flaring
 - Chest indrawing
 - Deep breathing or grunting
- Congestive heart failure
 - Pulmonary oedema: basal crepitations

- Peripheral oedema: pedal, periorbital, sacral.
- Circulatory congestion: raised jugular venous pressure and enlarged tender liver
- Tachycardia
- Gallop rhythm

6.5 Management of life threatening anaemia (Hb < 5g/dl) associated with malaria

Features

- Respiratory distress
- Congestive heart failure

Treatment

This is a medical emergency.

- Admit the patient
- Treat malaria as severe malaria with parenteral anti malarials (see management of severe malaria)
- Prop the patient up with pillows or clothing
- Administer oxygen 2.5 L/min to improve oxygen delivery
- Draw blood for grouping and cross matching

Make an effort to have 24 hours access to laboratory estimation of Hb before transfusing – if not feasible consider rapid tests for Hb estimation (e.g. WHO Haemoglobin colour scale) to guide decisions on transfusion

Indications for urgent blood transfusion

- Hb equal or less than 4 g/dl and/or
- Signs of heart failure
- Signs of respiratory distress

Administration of blood

- Use packed cell (10 ml/kg in children) or whole blood 20 ml/kg body weight
- Transfuse slowly (4-6 hours per unit)

$$\text{Drip: drops/min} = \frac{\text{volume to be transfused in ml} \times 20(\text{or } 15) \text{ drop factor}}{\text{time of transfusion in hours (4-6 hours)} \times 60 \text{ minutes}}$$

1ml whole blood= 20 drops

1ml packed cell= 15 drops

- Where blood is not available, give pre-referral treatment and refer urgently to a health facility with blood transfusion services.
- Diuretics: Frusemide (IV/IM) for an adult 40 mg or 1 mg/kg bodyweight for children

Children with malarial anaemia are hypovolaemic

Follow-up after discharge

- Start folic acid and ferrous sulphate (do not give ferrous to sickle cell patients)

- Review after 14 days to check on haemoglobin or haematocrit level.
- Continue treatment for at least three months
- Encourage patients to protect themselves from being bitten by mosquitoes by sleeping under an Insecticide Treated Net (ITN)

6.6 Management of severe anaemia (Hb 5 up to 7g/dl) associated with malaria

Features

- Severe palmar pallor, excessive tiring, dyspnoea or breathlessness, warm hands, peripheral oedema, pedal pitting, tachycardia, collapsing pulse, wide pulse pressure and gallop rhythm, ejection systolic murmur ('flow' murmur)

Management

This condition can be managed as an outpatient with close monitoring OR can be admitted depending on the severity of the above features

- Treat malaria
- Perform full blood count to investigate morphological type
- Do other investigations to identify other underlying causes of anaemia e.g. stool sample for hookworm and treat accordingly
- Give oral haematenics for at least three months
- Advise to return immediately if condition worsens
- Follow up after 15 days

6.7 Management of mild/moderate anaemia (7 up to 11 g/dl) associated with malaria

Features

- Some pallor, body weakness

Management

Patients with some pallor or moderate anaemia (Hb >7g/dl) need to be treated for malaria, as persistent parasitaemia is a cause of anaemia by dyserythropoiesis and haemolysis. Iron and folic acid speed up haematological recovery after malaria and should be given at least for three months. It is also important to treat hookworm infestation in children, as this is a common cause of iron deficiency anaemia.

Folic acid tablets administration

- Start a 3 months treatment course (5 mg daily)

Ferrous sulphate tablets administration

- Start a three months course at dose of 6 mg/kg of elemental iron daily
- Adults need 200mg ferrous sulphate (one tablet) three times daily

6.8 Management of anaemia associated with malaria in pregnancy

- In anaemic pregnant women, even if there are no signs or symptoms of malaria, give an effective antimalarial appropriate for the gestational age. (see chapter 7)

Chapter 7

Management of malaria in pregnancy

CHAPTER 7: MANAGEMENT OF MALARIA IN PREGNANCY

7.1 Introduction

Pregnant women have a high risk of peripheral parasitaemia and placental malaria. In sub-Saharan Africa close to 45% of pregnant women have malaria infection during pregnancy¹¹ and almost half of women who are pregnant for the first time (primigravidae) will be parasitaemic on their first antenatal visit¹². They also suffer from a higher number of clinical malaria attacks than non-pregnant women. Malaria infection during pregnancy is often asymptomatic. However, in primigravidae malaria tends to be more frequent and the attacks are more severe. Infection with *P. falciparum* during pregnancy results in a wide range of adverse consequences for the pregnant woman, developing foetus and the newborn. Pregnant women, especially primigravidae, are more susceptible to malarial infection than non-pregnant women.

7.2 Effects of pregnancy on malaria

During pregnancy the naturally acquired partial immunity to malaria declines. The decline in immunity is most pronounced during the first and second pregnancy. The reasons for the decline in immunity is yet undetermined.

7.3 Effects of malaria on pregnancy

Malaria is an important cause of morbidity and mortality for the pregnant woman, the foetus and the newborn. The effects of malaria in pregnancy are related to the malaria endemicity, with abortion more common in areas of low endemicity and intrauterine growth retardation more common in areas of high endemicity.

Table 13: Effects of malaria on morbidity and mortality among pregnant woman, foetus and newborn

	Pregnant Woman	Foetus	Newborn
Morbidity	Severe malaria (*)	Intrauterine growth retardation	Low birth weight
	Anaemia Premature labour	Congenital Infection	Prematurity Congenital /neonatal malaria
	Hypoglycaemia		
Mortality	Severe malaria (*)	Abortion	Low birth weight
	Severe anaemia	Stillbirth	Prematurity
		Congenital malaria	Congenital /neonatal malaria

(*) especially cerebral malaria and pulmonary oedema

¹¹ Steketee (1996), *Malaria treatment and prevention in rural Malawi, American Journal of Tropical Medicine and Hygiene*, 55 (1 Suppl):8-16

¹² Menendez C. (1995), *Malaria during Pregnancy, Parasitology Today* 11(5): 178-183

7.4 Management of malaria in pregnancy

Early diagnosis and effective case management of malaria illness in pregnant women is crucial in preventing the progression of uncomplicated malaria to severe disease and death.

7.5 Uncomplicated malaria in pregnancy

7.5.1 Clinical features of uncomplicated malaria

The clinical presentation of malaria during pregnancy is often hidden. Some pregnant women will present with the typical features of uncomplicated and/or severe malaria (see chapters 4 and 5). However in others, anaemia may be the only recognizable clinical feature.

7.5.2 Management of uncomplicated malaria

During history taking and physical examination, it is particularly important to elicit signs and symptoms of severe malaria. Whenever malaria is suspected, laboratory confirmation of malaria parasites should be performed if possible. If laboratory facilities are not available, treatment should be started on the basis of clinical presentation. If a laboratory is present, a negative result does not rule out malaria. RDTs have an added value, as they can be positive even if parasites are hidden in the placenta.

Quinine is safe in pregnancy. In therapeutic doses it does not induce labour. Uterine contractions and foetal distress with the use of quinine may be attributable to fever and effects of malaria disease.

Presently, Artemisinin derivatives cannot be recommended for treatment of malaria in the first trimester of pregnancy. However, they should not be withheld if treatment is considered to be life saving for the mother and other antimalarial are considered to be unsuitable. Artemether-lumefantrine (ALu) is not recommended during pregnancy in the first trimester.

During the first trimester of pregnancy quinine should be used as drug of choice for treatment of uncomplicated malaria.

During the second and third trimesters of pregnancy Artemether-Lumefantrine should be used as drug of choice for treatment of uncomplicated malaria

7.6 Severe malaria in pregnancy

7.6.1 Clinical features of severe malaria in pregnancy

Pregnant women infected with malaria are more susceptible to develop severe malaria. They commonly present with the following features:

- high fever
- hyperparasitemia
- low blood sugar
- severe haemolytic anaemia
- cerebral malaria
- pulmonary oedema

7.6.2 Management of severe malaria in pregnancy

The management of severe malaria in pregnant women does not differ from the management of severe malaria in other adult patients (see chapter 5).

The drug of choice for treatment of severe malaria is intravenous quinine. The dose is 10mg quinine dihydrochloride salt/kg body weight given by infusion in 5% dextrose over four hours, repeated every eight hours

Infusion should be discontinued as soon as the patient is able to take medication orally. Give **quinine** tablets 10mg/kg body weight every 8 hours to complete treatment up to seven days. N.B. Do not exceed 600mg per dose.

Blood smear for malaria parasites should be taken daily until negative. Review adequacy of antimalarial dosage. Consider alternative or give additional drug if parasitaemia and/or clinical signs persist (see chapter 5).

The risk of quinine induced hypoglycaemia is greater in pregnant than non-pregnant women. Blood sugar should be monitored regularly and if falls below 2.5 mmol/L (< 45 mg/dl) give IV 10% or 25% dextrose.

While the patient is on IV Quinine treatment, pay particular attention to the feeding of the patient.

7.7 Anaemia associated with malaria in pregnancy

Pregnant woman with haemoglobin level (Hb) <11 g/dl (or haematocrit <33%) is considered anaemic. In Tanzania, prevalence of anaemia in pregnant women ranges from 23% in malaria low transmission areas¹³ to 82% in malaria high transmission areas¹⁴. The etiology of anaemia in pregnancy is multifactorial. In primigravidae, malaria is the major contributor to anaemia. Malaria infection in pregnancy worsens the pre existing anaemia. Anaemia increases the risks of maternal mortality, especially in the face of complications such as abortion and haemorrhage and can be a direct cause of mortality due to cardiac failure. Anaemia can also contribute to stillbirth and low birth weight.

In Tanzania **the major** causes of anaemia in pregnancy are:

¹³ Hinderaker SG et al.: Anaemia in pregnancy in the highlands of Tanzania. Acta Obstet Gynecol Scand 2001, 80:18-26

¹⁴ Marchant T et al.: Socially marketed insecticide-treated nets improve malaria and anaemia in pregnancy in southern Tanzania. Trop Med Int Health 2002, 7:149-158

- Malaria
- Hookworm and schistosomiasis infection (due to increased blood loss).
- Iron and folate deficiency (due to poor dietary intake and increased demand due to pregnancy)
- Chronic infection including TB, HIV/AIDS
- Deliveries at short intervals (less than 3 years)

There are three approaches for addressing the maternal anaemia problem:

- Early diagnosis
- Treatment
- Prevention

7.7.1 Management of mild/moderate anaemia (Hb 7 up to 11 g/dl) in pregnancy

- Perform appropriate investigations (BS, peripheral blood film, stool examination, RBC indices, urinalysis)
- Treat the cause of anaemia if determined
- Give the following drugs
 - Full course of oral quinine in the first trimester or ALu in second and third trimesters
 - Iron: Give orally 200mg ferrous sulphate three times a day
 - Folic Acid 5 mg daily
 - Anthelmintics (e.g. mebendazole from second trimester)
 - Treat schistosomiasis if the patient lives in areas with high schistosomiasis transmission (after delivery)
- Monitor response to treatment
 - Clinical response
 - Hb measurement is recommended every 2 weeks until Hb reaches 11 g/dl
 - Reticulocyte count

For non-responding patients other investigations should be considered e.g. bone marrow aspiration.

7.7.2 Management of severe anaemia (Hb < 7g/dl) in pregnancy

Severe anaemia has to be aggressively treated before the woman goes into labour. During labour a patient may go into cardiac failure because of the increased work of the heart. Likewise, the shunting of the blood to the circulation from the placental bed after delivery, may overload the circulation and precipitate cardiac failure.

Aims of treatment

- Correct anaemia and improve Hb concentration to a safe level (> 7 g/dl) before the patient goes into labour
- Avert congestive cardiac failure by increasing the oxygen carrying capacity

Management of severe anaemia

Gestational age should determine the appropriate approach for the management of severe anaemia in pregnancy. Before 36 weeks of gestational age if the patient is not in cardiac failure the treatment should be as for the moderate anaemia (see section 7.7.1). If in failure and after 36 weeks of gestational age with or without failure:

- Treat the cause if determined
- Give blood transfusion (preferably packed cells)
- Continue with iron and folic acid up to 3 months after delivery
- Follow up the patient every 2 weeks until Hb reaches 11 gr/dl

7.7.3 Prevention of anaemia

Antenatal Clinic

- Combined ferrous sulphate 200mg + folic acid 0.25mg (*FeFo*) once or twice daily
- Intermittent Preventive Treatment in the second and third trimester
- Early detection of anaemia
 - Hb screening
 - Symptom sign surveillance
- De-worming as indicated in the focused antenatal care (FANC)
- Treat any underlying infection

All women should be advised on appropriate diet during pregnancy and on personal malaria protection using insecticide treated nets (ITN).

7.8 Prevention of malaria during pregnancy

Controlling the effects of malaria infection on the pregnant woman and the foetus requires a balanced programme of effective case management of malaria illness and prevention of the consequences of asymptomatic infection. Evidence based effective preventive interventions are required. These interventions consist of intermittent preventive treatment and use of insecticide treated nets.

7.8.1 Intermittent preventive treatment (IPT)

Intermittent preventive treatment is the administration of drug therapy in full therapeutic doses at predetermined intervals during pregnancy even if individuals have no signs of malaria. IPT should not be considered as chemoprophylaxis; the woman is not protected from infection and still could be infected after taking SP for IPT.

The drug of choice for IPT is Sulfadoxine/Pyrimethamine (SP).

SP remains the drug of choice for IPT even though it is no longer the first line drug for malaria treatment. This is because the aim of IPT is to prevent the worst effects of malaria infection in pregnancy¹⁵ rather than to cure a potentially life-threatening illness. As such, a

¹⁵ placental parasitaemia, severe anaemia for the mother and low birth weight for the newborn

lower efficacy antimalarial is acceptable for IPT than for curative purposes. It is particularly important that drugs used in pregnancy are known to be safe. It is also likely that drugs with a long half-life are the most effective when used as IPT.

The first IPT dose is administered between 20-24 weeks of gestational age. The second IPT dose should be administered at 28-32 weeks.

IPT should be administered as direct observed treatment (DOT) during an antenatal care visit

If malaria is diagnosed after administration of IPT with SP a full treatment with antimalarials should be given according to the guidelines (see section 7.5.2).

IPT is not a contraindication to tetanus toxoid injection and the two can be administered simultaneously.

Pregnant women who are known to have hypersensitivity to sulfonamides (most commonly skin rashes) should not receive SP for IPT. Neither Quinine, nor Artemether-lumefantrine (ALu) should be used for IPT. Currently there is no other recommended alternative drugs for IPT apart from SP.

7.8.2 Insecticide Treated Net

- Pregnant women should be advised to sleep under Insecticide Treated Nets (ITNs) at night and to take other personal protective measures to reduce contact with mosquitoes
- Mothers should be encouraged to protect their newborn infants with Insecticide Treated Nets (ITNs)

Chapter 8

Management of malaria in the neonate and infants below 5 kg

CHAPTER 8: MANAGEMENT OF MALARIA IN THE NEONATE AND INFANTS BELOW 5 KG

8.1 Introduction

Malaria in the neonate (first four weeks of life) is very rare: in Muhimbili Neonatal Unit the incidence of congenital malaria in hospitalised newborn is 3/100,000¹⁶. Congenital or acquired malaria in this age group is life threatening and requires immediate treatment. The signs and symptoms resemble those seen in the newborn with septicaemia. Quinine remains the drug of choice for treatment.

8.2 Clinical features

The clinical features of malaria in the newborn include:

- Fever
- Lethargy
- Unable to breastfeed
- Vomiting
- Irritability
- Respiratory distress
- Seizures
- Jaundice
- Pallor
- Hepatosplenomegaly

Laboratory findings will include the presence of malaria parasites, hyperbilirubinaemia, anaemia (Hb<13.5 g/dl), hypoglycaemia and acidosis.

8.3 Management of neonatal malaria

- Neonates with suspected malaria should be admitted to the hospital immediately as they can deteriorate quickly and die at home.
- Symptoms and signs of neonatal malaria mimic serious bacterial infection. Therefore, thorough investigation should be done.

Assessment and resuscitation

- Airway: ensure airway is open
- Breathing: ensure there is adequate respiratory movements, give oxygen if there is cyanosis
- Circulation: measure pulse rate

¹⁶ A.Masawe, personal communication

Investigations

The following investigations should be done:

FBP, blood sugar, blood culture and sensitivity, blood slide for malaria parasite, serum electrolytes.

Treatment

- Broad spectrum antibiotic as provided in the Standard Treatment Guidelines (STG)
- Parenteral quinine 10mg/kg 8 – 12hourly till the baby is able to breast-feed, then oral quinine is given to complete 7days treatment
- If a neonate is not able to breast feed, give 10% glucose IV 60ml/kg/24hours
- Give blood transfusion if HB is <10g/dl

Nursing care and monitoring

- Monitor vital signs (PR, RR & Temperature)
- Monitor input/output
- Check BS for malaria parasite daily
- Ensure feeding
- Advise on use of ITNs

8.4 Management of malaria in infants below two months and below five Kg

Malaria is quite uncommon in infants below 2 months of age. Since Artemether-Lumefantrine is currently not recommended for infants below 5 Kg, quinine is the drug of choice in this category.

Chapter 9

Malaria and HIV co- infection

CHAPTER 9: MALARIA AND HIV CO-INFECTION

9.1 Introduction

Malaria and HIV infections are both endemic in Tanzania and co-infection is common. The two diseases are the most important health problems in the country, being the leading causes of morbidity and mortality.

HIV infection/AIDS reduces immunity to malaria resulting in more frequent and severe infections. On the other hand, malaria enhances progression of HIV infection to AIDS and increases its severity. Acute malaria episodes temporarily increase viral replication and hence viral load. The concentrations of HIV-1 RNA in the blood tend to be higher in HIV-infected individuals with acute malaria illness than in HIV-infected individuals with no malaria parasites.

9.2 Clinical features of malaria in HIV/AIDS

HIV infection/AIDS increases the risk and severity of malaria. People with HIV/AIDS are more likely to have symptoms of malaria and higher parasite densities than those without HIV infection. Symptoms of malaria may be more severe, persistent and even modified in the presence of HIV infection/AIDS.

9.2.1 Clinical features of uncomplicated malaria in HIV/AIDS

Fever

Fever is a major symptom of both AIDS and malaria. Patients with AIDS often present with fever, which may be intermittent or continuous. The acute fever due to malaria could be masked with the prolonged fever of HIV/AIDS. One should always consider a possibility of malaria in AIDS patients presenting with fever.

Anaemia

Anaemia may be a feature of both AIDS and malaria.

Headache

Headache may be a feature of both AIDS and malaria. However, the other causes of headache in AIDS patients such as cerebral toxoplasmosis, meningitis and intracranial tumours should be ruled out.

Other constitutional symptoms

Diarrhoea, joint aches and general body weakness are found in both, AIDS and malaria. The symptoms tend to be chronic in AIDS and acute in malaria, hence masked in the background of AIDS.

9.2.2 Clinical features of severe malaria in HIV / AIDS

Severe malaria in HIV/AIDS patients frequently presents as cerebral malaria or severe anaemia.

Cerebral malaria

AIDS patients with cerebral malaria may present with central nervous system manifestations (CNS) such as altered level of consciousness, prostration and convulsions.

It is important to note that the manifestation of cerebral malaria resembles the CNS manifestation of HIV/AIDS e.g. convulsions, prostration and coma

Severe malarial anaemia

A patient with severe anaemia due to malaria may present with severe pallor with or without heart failure.

The presence of severe anaemia in HIV/AIDS patients may reflect an advanced disease or co-morbidity with malaria

9.3 Diagnosis

Diagnosis should follow the general principles of diagnosis of malaria based on accurate history taking, complete physical examination and appropriate laboratory tests as in any other malaria patient.

Consider the possibility of malaria in HIV/AIDS patients presenting with fever, pallor, headache and the other constitutional symptoms. More extensive work up should be performed to exclude other infective causes of fever.

In suspected cerebral malaria in a HIV/AIDS patient, emphasis should be put on cerebrospinal fluid (CSF) examination to rule out other life threatening conditions such as bacterial and cryptococcal meningitis. When available, a CT scan should be performed to rule out cerebral toxoplasmosis.

9.4 Treatment of uncomplicated and severe malaria in HIV /AIDS

Treatment of uncomplicated and severe malaria in HIV/AIDS should follow the same principles of treating uncomplicated and severe malaria. However it should be noted that, clearance of parasitaemia may not necessarily be accompanied by clearance of symptoms (fever) due to the presence of other underlying infections. HIV/AIDS infected adults with low CD4 cell counts may be more susceptible to treatment failure of anti malaria drugs.

9.5 Malaria and HIV/AIDS in pregnancy

HIV infected pregnant women have an increased risk of infection with malaria parasites and are more likely to develop clinical malaria. Their malaria parasite density is increased

compared to non-HIV infected pregnant women and have reduced response to antimalarial treatment. HIV and malaria co-infected pregnant women are at very high risk of anaemia and placental malaria. Pregnant women with dual infection have poorer birth outcomes (foetal loss, pre-term delivery, low birth weight). A considerable proportion of children born to women with HIV and malaria has low birth weight and are more likely to die during infancy. Malaria infection during pregnancy may be associated with increased risk of *mother to child transmission* (MTCT) of HIV.

9.6 Effect of malaria on HIV infected children

The effects of malaria on HIV infected children include increased risk of illness and anaemia.

9.7 Prevention

As people living with HIV/AIDS in areas of high transmission are particularly vulnerable to malaria, their protection by ITN should be of high priority.

HIV positive pregnant women at risk of malaria should always be protected by ITNs. They should be referred to PMTCT services. According to the stage of HIV infection, pregnant women at risk of malaria should also receive either IPT with SP (at least 3 doses), or daily co-trimoxazole prophylaxis¹⁷

HIV infected individuals with advanced immunosuppression (CD4 T-cell count $\leq 200\mu\text{l}$) should receive co-trimoxazole prophylaxis until their CD4 count is above 200 μl to prevent them from infections like respiratory tract infections but also malaria

¹⁷ Those women on co-trimoxazole prophylaxis should not be taking SP for IPT at the same time, as this would increase the effects of sulphonamide side effects.

Chapter 10:

*Therapeutic
efficacy of
antimalarial
drugs*

CHAPTER 10: THERAPEUTIC EFFICACY OF ANTI MALARIAL DRUGS

10.1 Introduction

The aim of the national malaria treatment guidelines is to offer antimalarials that are highly effective. The main determinant of policy change is the therapeutic efficacy and the consequent effectiveness of the antimalarials in use. The primary objective of monitoring the therapeutic efficacy is to evaluate the sensitivity of the recommended antimalarial drugs. One way of monitoring the efficacy of currently used drugs for the treatment of malaria is a close follow-up of treated cases in the health care facilities. This is a recommended good routine clinical practice in order to timely detect and manage treatment failures. The second way to monitor the therapeutic efficacy of antimalarial drugs is *in vivo* drug sensitivity tests using elaborated scientific protocols¹⁸.

10.2 Non response to an antimalarial treatment

Where a patient returns between 4 to 14 days after treatment with recommended antimalarial drug after ruling out other cause of disease complaining of continued symptoms of malaria, non-response should be considered.

Causes of non-response to antimalarial treatment include:

- *Vomiting the drug*
- *Inadequate dosage*
- *Fever/symptoms from a cause other than malaria*
- *Poor quality of the drug*
- *Parasite resistance to the drug*

The clinician can give an indication of treatment failure if the patient has taken the antimalarial drug appropriately i.e. according to the correct dosage and duration. The clinician should change the antimalarial drug to the second line treatment according to national guidelines. If the clinician observes frequent occurrence of suspected non response to first line antimalarial therapy, he/she should alert relevant authorities.

¹⁸ Assessment and Monitoring of antimalarial drug efficacy for the treatment of uncomplicated falciparum malaria, WHO 2003

10.3 Parasite Resistance to Antimalarial Drugs (*in vivo* drug sensitivity tests)

Drug resistance in malaria is defined as the ability of parasite strain to survive and/or multiply despite the administration and absorption of a drug given in doses equal to or higher than those usually recommended, but within the limit of tolerance of the subject.

A methodology has been developed by WHO where the therapeutic efficacy of antimalarial drugs can systematically be monitored. However, prescribers in their routine clinical practice are not expected to engage themselves in this elaborate protocol. In Tanzania about 10 sentinel sites in different epidemiological settings are regularly performing drug sensitivity tests using modified WHO protocol. See [Table 14](#).

Table 14: Classification of treatment failures

Test Days	Danger Signs ¹⁹	Temperature (≥ 37.5 °C)	Parasitaemia	Outcome
0 – 3	Present	Yes/No	Any positivity	ETF
2	Absent	Yes/No	Positive > D0	ETF
3	Absent	Yes	Any positivity	ETF
3	Absent	No	$\geq 25\%$ of D0	EPF
4 -14	Present	Yes/No	Any positivity	LTF
4 -14	Absent	Yes	Any positivity	LTF
4 -14	Absent	No	Any positivity	LPF
4 -14	Absent	Yes/No	No	ACPR

ETF: Early Treatment Failure

EPF: Early Parasitological Failure

LTF: Late Treatment Failure

LPF: Late Parasitological Failure

ACPR: Adequate Clinical and Parasitological Response

D0: Day 0

¹⁹ General Danger signs in children include: Vomiting everything, Inability to drink or breast feed, Recent history and/or observed convulsions, Lethargy/impaired consciousness. General danger signs in adults: Prostration, Change in behaviour (agitation, violence, hallucination, etc), Impaired consciousness, Jaundice

Chapter 11

Malaria chemo prophylaxis

CHAPTER 11: MALARIA CHEMOPROPHYLAXIS

11.1 Introduction

Chemoprophylaxis is the regular use of antimalarial drugs to prevent development of malaria parasites following any possible inoculation.

11.2 Indication for malaria chemoprophylaxis

Chemoprophylaxis is recommended for use in the following special groups:

- Patients with sickle cell anaemia
- Non-immune travellers
- Non-immune pregnant women
- Hyper Reactive Malaria Splenomegaly (Tropical Splenomegaly Syndrome)

11.3 Common antimalarial used as prophylactic agents

11.3.1 Chemoprophylaxis in patients with sickle cell anaemia

Chloroquine is still recommended until other alternative drugs are available.

Dose

Adult 300 mg base weekly
Children 5 mg base/kg weekly

11.3.2 Chemoprophylaxis for non-immune travelers

Table 15 Drugs indicated for chemoprophylaxis

	Indications	Adult	Children	Pregnancy	Start	Finish
Proguanil <i>Paludrine</i> ®	Non-Immune Stay >3 months	200 mg daily	3mg/kg daily	Yes	1 week before	4 weeks after
Mefloquine <i>Lariam</i> ®	Non-Immune Stay <3 months	250 mg weekly	5 mg/kg weekly	Avoid	4 weeks before	4weeks after
Proguanil/ Atovaquone <i>Malarone</i> ®	Up to 28 days	1 tab daily	See table 15	Avoid	1 day before	1week after
Doxycycline	Up to 6 months	100 mg daily	>12 years	Avoid	1week before	4weeks after

Refer to [chapter 14](#) of these Guidelines for drug information.

Table 16 Atovaquone/Proguanil paediatric dosage

Weight (kg)	Atovaquone/ Proguanil (<i>Malarone</i> ®) Total Daily Dose	Dosage Regimen for Prevention of Malaria in Paediatric Patients
11 up to 20	62.5 mg/25 mg	1 Atovaquone/Proguanil (<i>Malarone</i> ®) Paediatric (¼ Adult strength) tablet as a single dose daily
20 up to 30	125 mg/50 mg	2 Atovaquone/Proguanil (<i>Malarone</i> ®) Paediatric (½ Adult strength) tablet(s) as a single dose daily
30 up to 40	187.5 mg/75 mg	3 Atovaquone/Proguanil (<i>Malarone</i> ®) Paediatric (¾ Adult strength) tablet(s) as a single dose daily
40 and above	250 mg/100 mg	4 Atovaquone/Proguanil (<i>Malarone</i> ®) Paediatric (1 adult strength) tablet(s) as a single dose daily

11.3.3 Chemoprophylaxis for non-immune pregnant women

Non-immune pregnant women should ideally not travel to malarious areas unless absolutely necessary. Proguanil prophylaxis should be taken during the first three months (first trimester) of pregnancy; mefloquine prophylaxis may be taken from the fourth month of pregnancy onwards.

Chemoprophylaxis is currently not recommended for pregnant women living in malaria endemic areas. Instead, intermittent preventive treatment (IPT) is recommended ([see chapter 7](#)).

11.3.4 Chemoprophylaxis for Hyper Reactive Malaria Splenomegaly

Refer the patient to appropriate level of health care in order to exclude other conditions and for further management.

Chapter 12

Malaria epidemics

CHAPTER 12: MALARIA EPIDEMICS

12.1 Introduction

A malaria epidemic is defined as the occurrence of new cases of malaria clearly exceeding the number expected at that particular time and place

Generally there is an inverse relationship between the usual intensity of malaria transmission and the risk of epidemics. Unstable malaria transmission areas, such as fringe highlands and semi arid zones, are prone to malaria epidemics. Factors associated with unexpected increases in malaria transmission may be man-made (environmental modification) or natural (climatic). Furthermore, movements of non-immune population to areas with sustained malaria transmission (refugees, seasonal labourers) and failure of malaria control measures (impaired antimalarial drug efficacy) may contribute to the occurrence of outbreaks. According to the above criteria, in Tanzania about 20% of the districts are classified as malaria epidemic prone and more than 8 million people are living in those areas. The epidemic prone district in Tanzania are: Mpwawa, Dodoma, Kongwa (central zone), Muleba, Karagwe (Kagera), Ngorongoro, Karatu, Lushoto, Babati, Hanang, Hai, Same (northern highlands), Njombe, Iringa, Kilolo, Mufindi, Makete, Sumbawanga, Nkasi, Mbozi, Ileje, Rungwe, Ludewa, Mbinga (southern highlands). The last major epidemics have been reported in Muleba district following the *el nino* rains in 1997-1998.

High morbidity and mortality usually occurs during an epidemic. In Tanzania the number of admissions, blood transfusions and deaths during malaria outbreaks have been found to be 4-5 times higher in epidemic than in non-epidemics years respectively.

12.2 Measures to be considered during malaria epidemics

- Improved malaria case management
- Indoor residual house spraying
- Community mobilization and participation
- Community health education about malaria control in the epidemic area
- Enhance use of ITNs

12.3 Malaria diagnosis in the event of malaria epidemics

General principles

Early diagnosis and treatment is key to reducing malaria morbidity and mortality. However, in epidemic and complex emergency situations, facilities for laboratory diagnosis may be either unavailable or so overwhelmed with the case-load that parasite-based diagnosis is impossible. In such circumstances, it is impractical and unnecessary to demonstrate parasites before treatment in all cases of fever. Once malaria has been confirmed, and if

case numbers are high, treatment based solely on the clinical history is appropriate in most cases, using a full treatment course.

However, parasite-based diagnosis is essential to:

- diagnose and confirm the cause of an epidemic of febrile illness
- confirm the end of an epidemic and
- follow progress in high-risk cases, e.g. severe malaria.

It would also be useful to diagnose a proportion of cases parasitologically during the epidemic, to monitor the Slide Positivity Rate (SPR). As the epidemic wanes, the proportion of fever cases investigated for parasites can be increased. It is important to monitor the clinical response to treatment wherever possible; bearing in mind that other causes of fever may be involved.

Use of rapid diagnostic tests in epidemic situations

Rapid diagnostic tests (RDTs) offer the advantage of simplicity and speed in epidemic situations. Current experience with RDTs indicates that:

- they are useful for confirming the cause and end-point of malaria epidemics;
- they should not be relied on as the sole basis for treatment;
- they should be backed up with adequate quality assurance, including temperature stability and testing
- negative test results should not preclude treatment.

If RDTs are used, transport and storage should be based on the following principles:

- Avoid heat exposure, e.g. at airports and in vehicles.
- Ensure that stockpiles are stored in central locations that are kept as cool as possible (e.g. air conditioned areas) in readiness for an outbreak, with quality testing every few months to ensure that RDTs remain in good condition. Proper storage extends the shelf-life.
- Seek to maximize the length of time for which RDTs are kept under such conditions before rapidly deploying them to the field for short-term use.
- Consider simple methods to reduce the temperature at outlying sites (e.g. evaporative cooling, thatched roofs).

12.4 Disease management in the event of malaria epidemics

12.4.1 Managing uncomplicated malaria cases

Malaria epidemics are emergencies in which populations at risk in epidemic-prone areas are mainly non-immune or only partially immune. The blood schizonticidal drug to be used in epidemics (and complex emergencies) must therefore be highly efficacious (> 95% cure), be safe and offer good patient compliance. Therefore uncomplicated malaria should be managed with Artemether-lumefantrine (see chapter 4). Complete treatment doses should always be given in all circumstances.

12.4.2 Managing severe malaria

Management of severe malaria in epidemic situations will often take place in temporary clinics or situations in which staff shortages and high workloads make intensive care monitoring difficult.

Drug treatment should therefore be as safe as possible, with simple dosing schedules and a minimum need for monitoring.

The efficacy of intravenous (IV) quinine and intramuscular (IM) artemether are similar under hospital conditions. However, due to the complicated dosing regimen of IV Quinine, then IM Artemether is the drug of choice for severe malaria in most epidemic situations.

Dosing schedule for IM Artemether

3.2 mg/kg bodyweight (loading dose) IM followed by 1.6 mg/kg bodyweight IM daily for 6 days

12.5 Preparedness

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12.5.1 Monitoring drug resistance

In epidemics and complex emergencies there is no opportunity to monitor drug efficacy. Drug resistance monitoring must be an integral part of preparedness plans and actions.

12.5.2 Central stocks of supplies and equipment

It is essential to ensure that adequate supplies of diagnostics and antimalarial drugs are available by establishing and maintaining stocks at National and District level to deal with the eventuality of an epidemic. These stocks will need to be continuously rotated to ensure that commodity shelf-lives do not expire. Replenishment assumes prompt release, transport and customs clearance of commodities (if required).

12.5.3 Prevention of malaria during epidemics

During malaria epidemics there is an increased risk of malaria infection for the whole population. Therefore, all the population should be protected by ITNs and other personal protection measures.

Chapter 13

Public health education on malaria case management

CHAPTER 13: PUBLIC HEALTH EDUCATION ON MALARIA CASE MANAGEMENT

13.1 Introduction

Health education is the part of health care that is concerned with creating awareness and promoting appropriate health behaviour. Health education should encourage behaviours that promote health, prevent illness, cure disease and facilitate rehabilitation. Through health education, people should gain a better understanding of how their own behaviour may affect their health.

Health education has an important role to play in bringing about the desired changes in human behaviour, especially early diagnosis and treatment for children under five years of age²⁰, because:

- What individuals do when they have fever or other symptoms suggestive of malaria will largely determine the progression of the disease
- What parents/caretakers do to their children when they have features of severe malaria (e.g. convulsions or anaemia) will largely determine the eventual outcome
- What individuals, families and communities do to protect themselves against mosquito bites, (e.g. use of ITN and reduction of mosquitoes breeding sites), will influence the risk of infection

13.2 Health education for malaria diagnosis and treatment

Health education is important to ensure a correct malaria case management. Therefore, all stakeholders should consider the following:

- Education on early recognition of symptoms and signs of malaria
- Education for demand of better services at health facility level
- Education on signs and symptoms of severe malaria
- Promotion of early and appropriate health care seeking behaviour
- Promotion of prompt and effective action for treatment and care of suspected cases of malaria
- Promotion of appropriate referral system for severe cases of malaria and treatment failures

²⁰ Since the progression towards severe and fatal disease is rapid, especially in children under five years of age, it is recommended that diagnosis and treatment of uncomplicated malaria should be done within 24 hours from the onset of symptoms.

13.3 The role of health service providers in promoting appropriate malaria case management and preventive measures

Health workers at all levels of care should ensure that health education is given to all patients/caretakers using the following measures:

- Education on continued feeding and fluid intake during illness, especially in children under five years old
- Education on compliance with medical treatment
- Education on side effects of the drugs if any
- Education on when the patient should return for follow-up
- Education on when the patient should return immediately
- Promotion of personal protective measures such as the use of insecticide treated nets, repellants and environmental manipulation and management.

Chapter 14

Other antimalarial drugs available in Tanzania

CHAPTER 14: OTHER ANTIMALARIAL DRUGS AVAILABLE IN TANZANIA

14.1 Introduction

The Ministry of Health, public and private health care providers and the community have a collective responsibility to apply standardized treatment protocols to maximize the usefulness of the few antimalarial drugs that are available and retard the development of parasite drug resistance. Therefore, this chapter provides information on antimalarial drugs already registered in Tanzania as of 2005.

It is necessary that health care providers should make themselves aware of the range, rational use and safety of the antimalarial drugs registered and available and limit their use accordingly.

Some of the drug formulations described in this chapter are monotherapies. Their use is discouraged to minimize the risk of developing parasite resistance. However they have been retained during the transition period from mono to combination therapy. They will be withdrawn from use when the supply of combination drugs will be optimal.

14.2 Antimalarial mono-therapies or single component of combination therapies

14.2.1 Artemisinin and its derivatives

These are potent and rapidly acting blood schizonticides and gametocides. 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-drug resistant strains of *P.falciparum*

Contraindications

- They should not be used with drugs which cause QT interval prolongation e.g. quinidine, halofantrin etc
- They should not be used with neuroleptics, and erythromycin

Use in pregnancy and lactation

Artemisinin and its derivatives can be used during the second and third trimester of pregnancy in areas of multi-drug resistance if there is no other effective treatment available. Their use in the first trimester of pregnancy is not recommended.

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 documented 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

- **Dihydroartemisinin:** available as tablets of 50 mg and 60 mg and powder for suspension 160 mg/80 mls. Dose: 4 mg/kg divided in two doses administered on the first day followed by 2 mg/kg once a day for 5 days
- **Artesunate:** available as tablets/capsules (50 mg, 100 mg and 200 mg). Dose: 4 mg/kg divided in two doses administered on the first day followed by 2 mg/kg once a day for 5 days
- **Artemether:** available as capsules (40 mg), powder for suspension (300 mg/100 mls) and injectable (80 mg/ml). Oral dose: first day, 4mg/kg bodyweight twice, day 2 to day 5 2mg/kg bodyweight daily. Injectable 3.2 mg/kg bodyweight loading dose IM, 1.6 mg/kg IM daily for 6 days
- **β-Artemether:** available as capsules (20 mg, 40 mg, 50 mg), and injectable (20 mg/ml and 80 mg/ml)

14.2.2 Sulfadoxine/Pyrimethamine,

This is a synergistic combination of antifolate drugs. The combination is a highly active blood schizonticide against *P.falciparum*. It is rapidly absorbed from the gut following oral administration. The plasma half-life of pyrimethamine is about 4 days and that of sulfadoxine is about 8 days.

Available formulations

- Tablets: Sulfadoxine 500 mg with pyrimethamine 25 mg.
- Injectable Sulfadoxine/Pyrimethamine (There are no clear therapeutic benefits of using parenteral over oral formulations of SP)

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 major) or toxic epidermal necrolysis. This is quite rare but can be fatal. 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 macules or atypical targets. Frequent signs and symptoms (in 10-30% of cases) involve fever, arthralgia, 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
- Apply 0.25% gentian violet in mouth ulcers

14.2.3 Sulfalene/Pyrimethamine (Metakelfin®)

Is an alternative SP formulation. With the same indication and dosage as Sulfadoxine + pyrimethamine.

Available formulation

Tablets Sulfalene (500mg) + Pyrimethamine (25mg).

Contraindications

History of sulfonamide hypersensitivity.

Use in pregnancy

It is not contraindicated in 2nd and 3rd trimester of pregnancy.

14.2.4 Amodiaquine

Amodiaquine is a 4-aminoquinoline antimalarial 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

- Treatment of uncomplicated malaria, where no better drug is available
- A combination of amodiaquine and artesunate has been found to be more efficacious than amodiaquine alone (see [paragraph 14.2.1](#))

Contraindications

- Hypersensitivity to Amodiaquine

- Hepatic disorders
- Should not be used for chemoprophylaxis because of its toxicity profile

Use in pregnancy and lactation

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

Adverse effects

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

Dosage regimen

Treatment with Amodiaquine should be given at total dose of 25mg base per kg body weight over three days.

Table 17: Dosage schedules for treatment of uncomplicated malaria using Amodiaquine tablets 200 mg base

Age (years)	Weight (Kg)	Number of tablets of 200 mg base				Total tablets
		Day 1 10 mg/kg	Day 2 10 mg/kg	Day 3 5 mg/kg		
Up to 4 months	5 up to 7	1/4	1/4	1/4	3/4	
4 up to 12 months	7 up to 11	1/2	1/2	1/4	1 1/4	
1 up to 3	11 up to 15	3/4	3/4	1/4	1 3/4	
3 up to 5	15 up to 19	1	1	1/4	2 1/4	
5 up to 8	19 up to 25	1 1/4	1 1/4	1/2	3	
8 up to 12	25 up to 35	1 1/2	1 1/2	1 1/4	4 1/4	
12 up to 14	35 up to 50	2 1/2	2 1/2	1 1/4	6 1/4	
14 up to 16	50 up to 60	3	3	1 1/2	7 1/2	
16 and above	60 and above	3	3	2	8	

Syrup

Is only indicated where a child is unable to take tablet formulations

14.2.5 Mefloquine

This drug is structurally similar to quinine. It is a potent long acting blood schizonticide 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.

Available formulation

Tablet 250mg mefloquine base

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, quinine, 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 avoided during and for three months after completing prophylaxis
- Prophylactic use during pregnancy should be avoided in the first three months
- 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 split dose:

- Single – one dose of 15 mg base/kg bodyweight
- Split – one dose of 15 mg base/kg bodyweight stat followed by another dose of 10 mg/kg bodyweight 6 to 24 hours later (total dose 25 mg base/kg).

14.2.6 Halofantrine

Halofantrine is a blood schizonticide active against all malaria parasites. It is active against *P. falciparum* infections resistant to chloroquine and SP. Halofantrine does not have activity against gametocytes or the hepatic stages of malaria parasites.

Indications

Its use should be restricted only to acute multi-drug resistant falciparum infections in hospitals following parasitological or careful clinical diagnosis.

Contraindications

- History of allergy to halofantrine
- Pre-existing cardiac disease

- Family history of sudden death
- Treatment with mefloquine in the previous three weeks
- Pregnant women and children under 10 kg body weight
- Breast feeding should be discontinued while taking halofantrine
- Do not use for prophylaxis

Use in pregnancy and lactation

- Should not be used in pregnancy
- Should not be used by lactating mothers
- Caution: Avoid concomitant use with chloroquine, quinine, tricyclic anti-depressants, anti-psychotics and some anti histamines such as terfenadine and astemizole

Adverse effects

Halofantrine has been shown to produce a dose-related prolongation of the QT interval. This effect has been associated with serious arrhythmias, occasionally with a fatal outcome even at the recommended therapeutic dose.

Available formulations

Tablets containing 250 mg halofantrine hydrochloride (223 mg halofantrine base). Paediatric suspension containing 100 mg halofantrine hydrochloride (93.2 mg halofantrine base) in 5 ml.

Dose

The standard dose for both adults and children is 8 mg base/kg 6 hourly for three doses given on an empty stomach. The total maximum dose is 24 mg base/kg equivalent in adults to 1500 mg base. A second course of therapy is recommended one week after the initial treatment in non-immune patients to prevent relapse.

14.2.7 Proguanil Hydrochloride

Proguanil (Paludrine®) is a valuable drug for causal prophylaxis. It kills the pre-erythrocytic (liver) stages of Plasmodium species. It has slow schizonticidal action on the erythrocytic forms but is highly effective against *Plasmodium falciparum*. It is less active against *P. Vivax*.

For those staying longer than three months in an endemic area Proguanil is recommended.

Dose

Adult	200 mg daily
Children	3 mg/kg body weight daily

The drug can normally be used continuously for a period of up to five years. Proguanil should be taken one week before traveling to an endemic area. It should be continued through out exposure and 4 weeks after returning from an endemic area.

Indications

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

Precautions

The drug should be used with caution in patients with renal impairment. The drug can delay metabolism of the anticoagulant warfarin. The drug is considered to be safe in pregnancy and lactation at prophylactic doses, but folate supplementation is advised.

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, anorexia, nausea, diarrhoea, and irreversible hair loss may occur; overdose may cause haematuria, renal irritation, gastric discomfort and vomiting. The drug should be used with care in persons with liver or kidney dysfunction.

Available formulation

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

Note

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

14.2.8 Doxycycline

Indications

- Prophylaxis (see chapter 11)
- Treatment of malaria in combination with other antimalarial drugs (e.g. Artesunate or Quinine)

Dose

- For treatment: only in combination with other antimalarial: 3.5 mg/kg bw once a day for 7 days
- For prophylaxis: adult dose is 100 mg daily

Can normally be used continuously for a period of at least 6 months (professional guidance is required).

Consider a trial course before departure; if this regimen is used for the first time, it can be used to detect the likelihood of developing allergic reactions. Doxycycline needs to be started one week before exposure and continued throughout exposure and for 4 weeks after return from malaria endemic area.

When other tetracyclines are being used for acne, this provides protection against malaria so long as an adequate dose is taken.

Contraindications

Doxycycline is contraindicated during pregnancy, breastfeeding, and in those with systemic lupus erythematosus, porphyria and children aged less than 12 years because permanent teeth discolouration can occur.

It should be used with caution in women on oral contraceptive pills as it may reduce the effectiveness of the pills.

Adverse effects

Occasionally the drug causes anorexia, nausea and diarrhoea. Long term use may lead to superinfections such as candida infection and sore tongue (glossitis) and rarely hepatitis, colitis and blood dyscrasias.

Photosensitivity of skin can occur. Use of sunscreens is especially important and if severe, alternative prophylaxis should be used. Heartburn is common, so the capsule should be taken with a full glass of water.

14.3 Other Artemisinin based combination drugs available in Tanzania

14.3.1 Artesunate and Amodiaquine combination

Artesunate plus amodiaquine appears to be a viable option for treatment of uncomplicated malaria. However, continued monitoring of resistance to AQ and the impact of AQ resistance on the effectiveness of the combination would need to be carefully monitored.

The dosage schedule is shown in table 18 below:

Table 18: *Dosage for treatment of uncomplicated malaria using Artesunate + Amodiaquine tablets*

(once a day for three days)

Weight (Kg)	Age (yr)	Daily dosage of Artesunate (4mg/kg)		Daily dosage of Amodiaquine (10mg/kg)
		Number of tablets (50mg/tab)	Number of tablets (200mg/tab)	Number of tablets (153mg/tab)
Below 10	Less than 1	½ tab/day	¼ tab/day	½ tab/day
10 up to 20	1 up to 6	1 tab/day	½ tab/day	1 tab/day
20 up to 35	6 up to 12	2 tabs/day	1 ½ tabs/day	2 tabs/day
35 and above	12 and above	4 tabs/day	3 tabs/day	4 tabs/day

14.3.2 Artesunate and Mefloquine combination

Artesunate and mefloquine is a non-fixed combination, it involves co-administration of separate tablets of each of the two drugs.

Indication

The combination is indicated for the treatment of uncomplicated *Plasmodium falciparum* infection in high transmission area (endemic area). Also treatment of malaria caused by multi-drug resistance strains of plasmodium species

Contraindications

Hypersensitivity to mefloquine, artesunate or to the chemically related compounds like artemisinin derivatives, quinine, quinidine and alike.

This combination is not recommended for epileptics as mefloquine may increase risk of seizure

Use in pregnancy

This drug should be avoided during first trimester of pregnancy and during breast feeding.

Side effects

Abdominal pain, nausea, vomiting, diarrhoea, dizziness, insomnia, asthenia, anorexia, headache, neuropsychiatric disorders, allergic reactions including rash, pruritus.

Precaution / warning

Caution should be exercised when operating machinery and other activities, which require full attention and fine motor coordination.

Dosage and available formulation

Tablets (separate tablets): Artesunate 200 mg + Mefloquine hydrochloride 250 mg. The total recommended treatment is 4 mg/kg bw of artesunate given once a day for 3 days and 25 mg base/kg bw of mefloquine usually split over 2 or 3 days.

Table 19 Dosing schedule for artesunate plus mefloquine

Age (years)	Dose in mg (no. of tablets)					
	Artesunate			Mefloquine		
	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3
5 up to 11 months	25 (½)	25	25	–	125 (½)	–
1 up to 7	50 (1)	50	50	–	250 (1)	–
7 up to 13	100 (2)	100	100	–	500 (2)	250 (1)
13 and above	200 (4)	200	200	–	1000 (4)	500 (2)

14.4 Other combination drugs

14.4.1 Proguanil Hydrochloride/Atovaquone

Indications

- Treatment of uncomplicated falciparum malaria
- Prophylaxis of malaria particularly where resistance toward other antimalarial drugs is suspected.

Contraindications

Renal impairment, diarrhoea or vomiting. Avoid in pregnancy and breastfeeding. Avoid concomitant administration with tetracycline, rifampicin, indinavir and metoclopramide due to reduced plasma concentration of atovaquone.

Side effects

Nausea, vomiting, mouth ulcers, stomatitis, diarrhoea, abdominal pain, anorexia, fever, headache, dizziness, insomnia, cough, visual disturbance, angioedema, blood dyscrasia, and hair loss.

Caution: avoid operating machinery and other activities, which require full attention and fine motor coordination

Formulation and strength available (Malarone®)

Adult strength formulation (tablets)

Proguanil hydrochloride 100 mg

Atovaquone 250 mg

Paediatric formulation (tablets)

Proguanil hydrochloride 25 mg

Atovaquone 62.5 mg

Dose for treatment of falciparum malaria

- Adult and children over 40 kg body weight 4 adult strength tablets once daily for 3 days
- Child 31-40 kg body weight 3 adult strength tablets daily for 3 days
- Child 21-30 kg body weight 2 adult strength tablets daily for 3 days
- Child 11–20 kg body weight 1 adult strength tablet daily for 3 days
- Child 9–10 kg body weight 3 paediatric tablets daily for 3 days
- Child 5–8 kg body weight 2 paediatric tablets daily for 3 days

Dose for prophylaxis of malaria

See [chapter 11](#)

Chapter 15

Management of antimalarial drugs

CHAPTER 15: MANAGEMENT OF ANTIMALARIAL DRUGS

15.1 Introduction

Artemisinin based combination therapy (ACT) is expensive and has limited shelf life (2 years). ACTs are usually available in different blister packages according to age group categories. The right quantities of ACT should be procured to avoid unnecessary wastage and overstocking. ACT should be stored properly to safeguard them against pilferage, theft, deterioration and damage.

The management procedures such as ordering, storage, inventory control, distribution, prescribing, dispensing, use and feedback must be strictly followed to ensure uninterrupted supply of antimalarials. ACTs should be prescribed based on the treatment guidelines to maximise their rational use.

15.2 Ordering

Regional and District pharmacists and In-charges of health facilities should order their requirements according to their respective needs. Prior to initiating orders, the pharmacist or pharmacy In-charge should make sure that there are adequate information on the expected number of patients with malaria to be treated with ACT/other antimalarials in a defined period of time (usually quarterly). He/she, in collaboration with colleagues, must determine what to order, quantities and source of supply. The order should be submitted to the relevant authorities for endorsement and approval. The amount to be ordered must be determined by using quantification procedure.

15.3 Storage and inventory control

The appropriate authority at regional, district and health facility level should receive medicines and related supplies. In case of a hospital, the Hospital Therapeutic Committee should receive drugs. The receiving procedure is accomplished by filling a Goods Received Note (GRN) as an acknowledgement for the receipt of the products in good order and condition. Any discrepancy must be recorded during the receiving.

Medicines and related supplies must be stored appropriately in accordance with Good Storage Practices (GSP) so as to avoid deterioration and/or damage of the products.

Medicines and related supplies should be ordered and issued from a store using approved documents. It is important for the pharmacist or pharmacy in-charge to make sure that orders for medicines and related supplies are genuine and quantities ordered or issued are within the normal consumption pattern. Medicines and related supplies should be issued on the basis of FEFO (First Expiry, First Out).

The health facilities should maintain a rational and accountable distribution system through proper inventory control of medicines and related supplies. Tracking, stock inventory and management should follow the stipulated procedures.

15.4 Supervision of drug management activities

While doing supportive supervision, the RHMT/CHMT or hospital management team should look at all aspects of good pharmaceutical services including ordering, storage, inventory control, distribution, dispensing and usage.

Chapter 16

Pharmaco vigilance

CHAPTER 16: PHARMACOVIGILANCE

16.1 Introduction

Pharmacovigilance is a set of activities related to the detection, assessment, understanding and prevention of adverse drug reaction. The noxious (harmful) and unintended response to a medicine administered at therapeutic doses is known as Adverse Drug Reaction (ADR). Individual factors may play an important role towards development of ADRs.

16.2 Importance of pharmacovigilance

- Tanzania has introduced new drugs for the management of malaria and HIV/AIDS, for which there is insufficient safety data. It is therefore imperative to monitor the safety of these new medicines
- The continuous evaluation of drug safety and efficacy will help to make safer and more effective treatment available to patients
- Information about rare but serious adverse reactions, chronic toxicity, use in special groups (such as children, the elderly or pregnant women) or drug interactions is often incomplete or not available
- Monitoring after effects of accidental use of contraindicated drugs for specific groups (e.g. pregnant women in the first trimester and newborns under 5kg of body weight)
- Data derived from the surveillance should assist the regulatory authorities to make evidence-based decisions
- Early detection of ADR may prevent or reduce ADR related morbidity and mortality.

16.3 Clinical presentation of adverse drug reactions

ADRs may present with non-specific symptoms and signs and they can mimic features of some diseases. Hence, it is difficult to distinguish between ADR and clinical features of the treated condition. However, the following step-wise approach may be helpful in assessing possible drug-related ADRs:

- Ensure that the medicine prescribed is the medicine dispensed and actually used by the patient at the dose advised
- Verify that the onset of the suspected ADR was after taking the drug
- Determine the time interval between the beginning of drug treatment and the onset of the event
- Evaluate the suspected ADR after discontinuing the drugs and monitor the patient's status
- Analyse the alternative causes (other than the drug) that could on their own have caused the reaction

- Use relevant up-to-date literature on drugs and their adverse reactions and verify if there are previous conclusive reports on this reaction
- Fill in the ADR reporting form (yellow form) and submit to the relevant authority as instructed
- Manage the patient accordingly, including referral to appropriate level
- Make all necessary arrangements for patient follow up

16.4 Reporting adverse drug reactions

Who should report?

All health care providers (specialists, medical doctors, clinical officers, pharmacists or nurses) should report ADRs as part of their professional responsibility, even if they are doubtful about the precise relationship with the given medication.

What should be reported?

All suspected adverse drug reactions should be reported, particularly to a new drug or new combination of drugs.

How to report

The Tanzania Food and Drugs Authority (TFDA) has developed ADR reporting forms (yellow forms) as provided in [appendix 7](#). these forms are available at DMO's office. The DMO is responsible for distributing them to all health facilities both public and private. The yellow forms can be filled by any health care provider. These forms which have prepaid stamp once completed should be posted to TFDA.

What happens after reporting?

Upon receipt of the forms, TFDA is responsible for sending an acknowledgement letter to the ADR reporting centre. In addition, TFDA is responsible for assessment of causality of the ADR and taking appropriate actions including product recall if necessary.

Appendices

Appendix 1: 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 (μl) 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 μl of blood by the simple formula given below:

$$\frac{\text{Number of parasites} \times 8000 \text{ WBC}}{\text{Number of leucocytes counted}} = \text{Parasite count per } \mu\text{l}$$

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.

(b) The “plus” system

This is a semi-quantitative method developed for epidemiological purposes rather than disease management. It is less satisfactory and is not recommended.

The [table](#) below shows the correlation between the two systems.

Correlation between methods of blood slide reporting

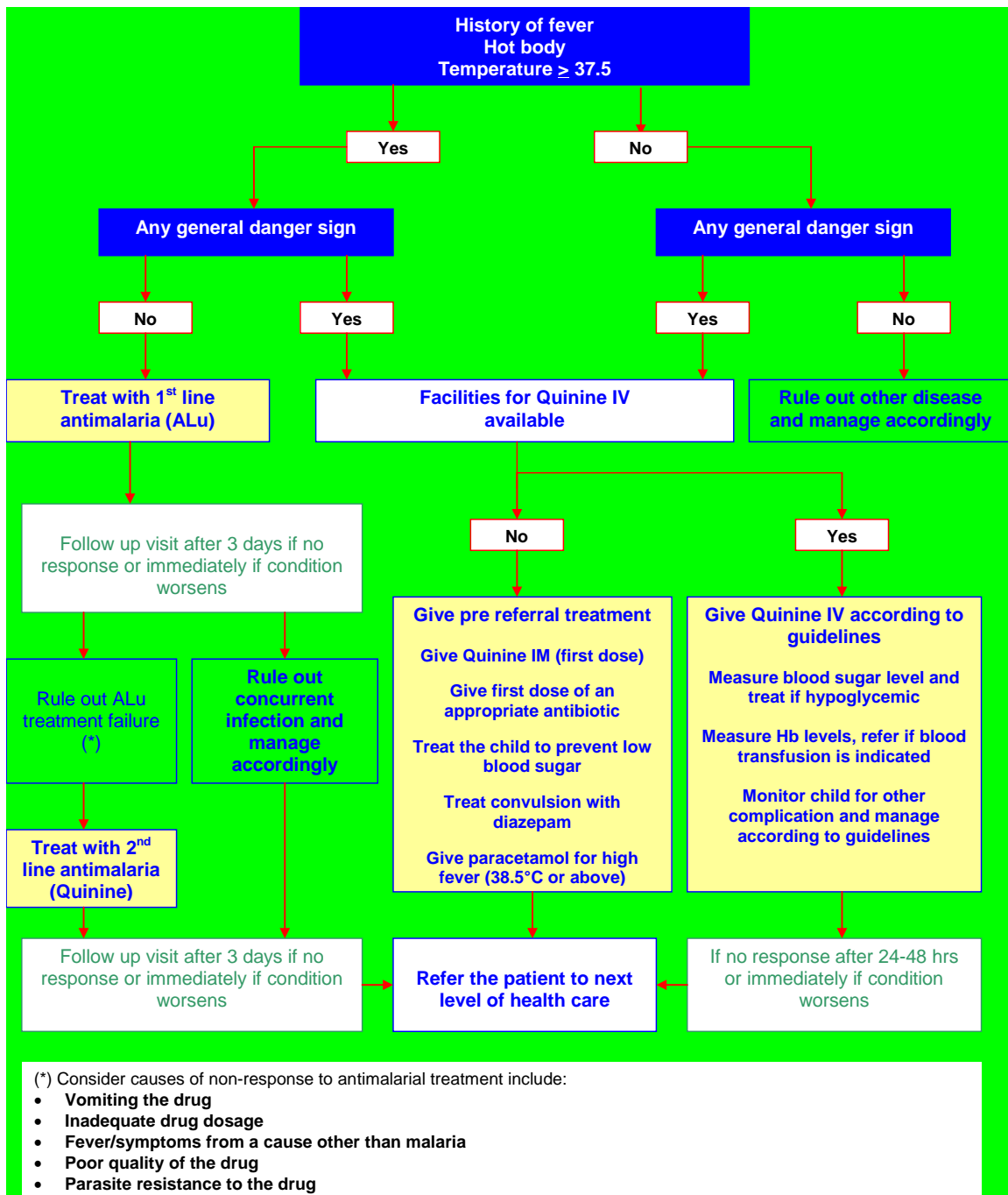
+ 1-10 parasites per 100 field	4-40 parasites per μl
++ 11-100 parasites per 100 field	40-400 parasites per μl
+++ 1-10 parasites per one field	400- 4000 parasites per μl
++++ 11-100 parasites per one field	4000- 40,000 parasites per μl

Appendix 2a: Integrated Management of Childhood Illness algorithm for child with fever

Check For General Danger Sign	
ASK: <ul style="list-style-type: none"> • Is the child able to drink or breastfeed? • Does the child vomit everything? • Has the child had convulsion? 	LOOK: <ul style="list-style-type: none"> • See if the child is lethargic or unconscious • See if the child is convulsing now
If the child is convulsing now, 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?					
<i>If yes, then ask:</i>	<i>Look and feel</i>	<i>Classify</i>	<i>Look and feel</i>	<i>Classify</i>	<i>Identify treatment</i>
<ul style="list-style-type: none"> • For how long? • If more than 7 days, has fever been present every day? 	<ul style="list-style-type: none"> • Look or feel for stiff neck 	<i>FEVER</i>	<ul style="list-style-type: none"> • Any general danger sign • Stiff neck 	<i>VERY SEVERE FEBRILE DISEASE OR SEVERE MALARIA</i>	<ul style="list-style-type: none"> ➤ Give Quinine for severe malaria (first dose) ➤ Give first dose of an appropriate antibiotic ➤ Treat the child to prevent low blood sugar ➤ Give one dose of paracetamol in the clinic for high fever (38.5°C or above) ➤ Refer URGENTLY to hospital
			<ul style="list-style-type: none"> • Fever (by history or feels hot or temperature 37.5°C or above) 	<i>MALARIA</i>	<ul style="list-style-type: none"> ➤ Treat with first line oral antimalarial treatment (ALu) ➤ Give one dose of paracetamol for high fever (38.5°C or above) ➤ Advise mother when to return ➤ Follow up in 3 days if fever persist ➤ If fever is present every day for more than 7 days, refer for assessment ➤ Advise mother on the use of ITN

Appendix 2b: Algorithm for child with fever (modified from Integrated Management of Childhood Illness)

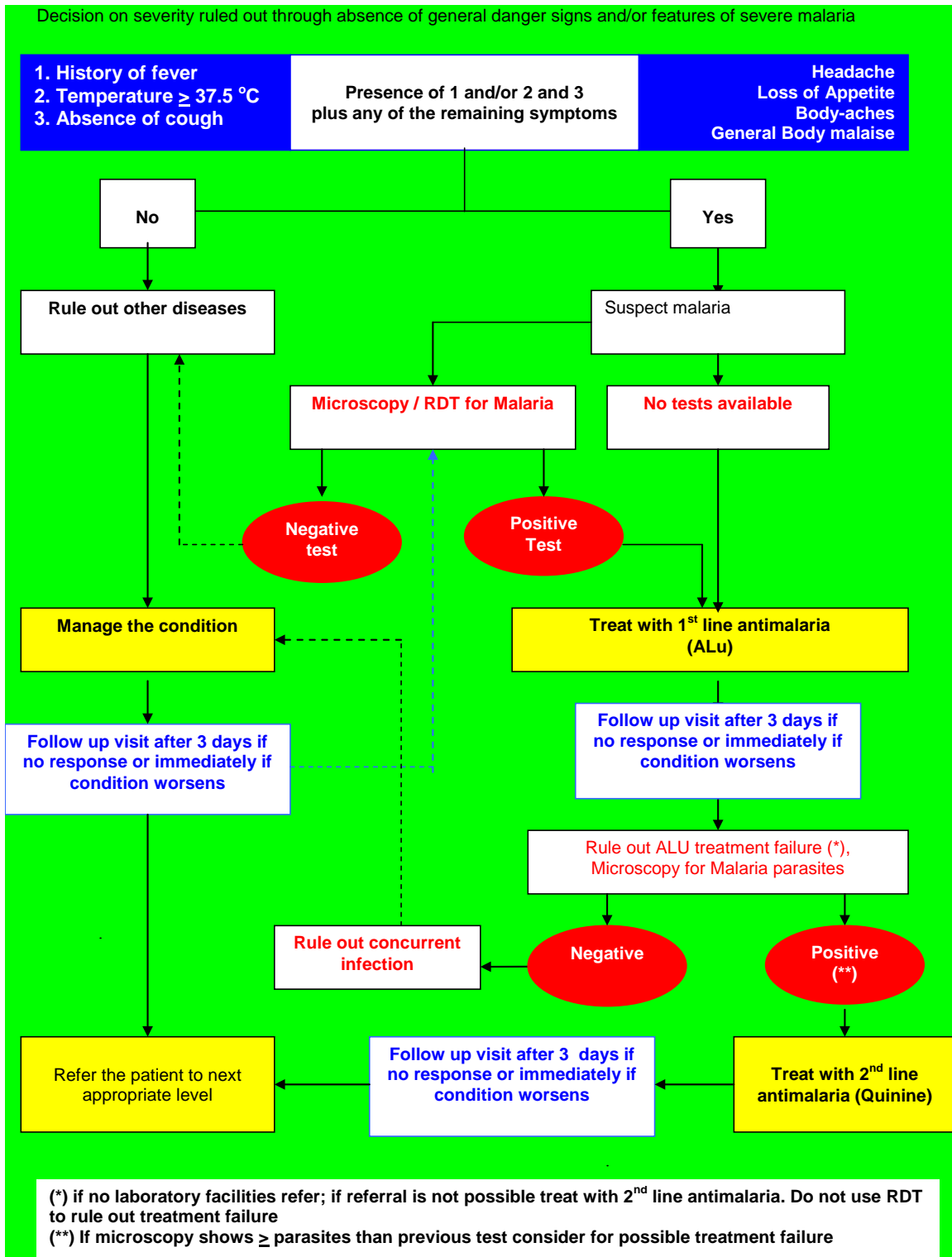


Appendix 3: Classification and management of anaemia by severity in children one week up to 5 years of age according to IMCI²¹

Signs	Classification	Action
<ul style="list-style-type: none"> • Severe palmar pallor • Signs of heart failure - Dyspnoea - Tachycardia - Gallop rhythm - Basal crepitations - Enlarged tender liver 	SEVERE ANAEMIA	<ul style="list-style-type: none"> • Give Quinine i/m first dose • Refer <u>urgently</u> to health facilities where blood transfusion services are available
Some palmar pallor	ANAEMIA	<ul style="list-style-type: none"> • Give first line antimalarial treatment (ALu) • Give folic acid and iron for three months • Advise when to return immediately • Advise that patient must be reassessed if fever persists after 3 days • Give mebendazole to a child aged 1 year and above if has not received it in the previous 6 months • Follow up in 14 days to check for severity of anaemia; if no deterioration continue with iron and folic acid for three months • Assess feeding and give advise appropriately • Advise on home care • Advise on personal protection with ITN
No palmar pallor	NO ANAEMIA	<ul style="list-style-type: none"> • Advise on feeding • Advise on personal protection with ITN

²¹ Modified from the IMCI protocol for district health workers

Appendix 4: Management of uncomplicated malaria in patients aged 5 years and above



Appendix 5: Time schedule for 1st and 2nd dose of Artemether-lumefantrine

<i>1st dose</i>	<i>2nd dose</i>
1:00 AM	9:00 AM
2:00 AM	10:00 AM
3:00 AM	11:00 AM
4:00 AM	12:00 PM
5:00 AM	1:00 PM
6:00 AM	2:00 PM
7:00 AM	3:00 PM
8:00 AM	4:00 PM
9:00 AM	5:00 PM
10:00 AM	6:00 PM
11:00 AM	7:00 PM
12:00 PM	8:00 PM
1:00 PM	9:00 PM
2:00 PM	10:00 PM
3:00 PM	11:00 PM
4:00 PM	12:00 AM
5:00 PM	1:00 AM
6:00 PM	2:00 AM
7:00 PM	3:00 AM
8:00 PM	4:00 AM
9:00 PM	5:00 AM
10:00 PM	6:00 AM
11:00 PM	7:00 AM
12:00 AM	8:00 AM

<i>Dozi ya kwanza</i>	<i>Dozi ya pili</i>
7:00 Usiku	3:00 asubuhi
8:00 Usiku	4:00 asubuhi
9:00 Usiku	5:00 asubuhi
10:00 alfajiri	6:00 mchana
11:00 alfajiri	7:00 mchana
12:00 alfajiri	8:00 mchana
1:00 asubuhi	9:00 mchana
2:00 asubuhi	10:00 jioni
3:00 asubuhi	11:00 jioni
4:00 asubuhi	12:00 jioni
5:00 asubuhi	1:00 usiku
6:00 mchana	2:00 usiku
7:00 mchana	3:00 usiku
8:00 mchana	4:00 usiku
9:00 mchana	5:00 usiku
10:00 jioni	6:00 usiku
11:00 jioni	7:00 usiku
12:00 jioni	8:00 usiku
1:00 usiku	9:00 usiku
2:00 usiku	10:00 alfajiri
3:00 usiku	11:00 alfajiri
4:00 usiku	12:00 alfajiri
5:00 usiku	1:00 asubuhi
6:00 usiku	2:00 asubuhi

Appendix 6: The Glasgow coma scale

		Score
Eyes open:	Spontaneously	4
	To speech	3
	To pain	2
	Never	1
Best verbal response:	Oriented	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	None	1
Best motor response:	Obeys command	5
	Localises pain	4
	Flexion to pain	3
	Extension to pain	2
	None	1
Total		3-14

A state of unrousable coma is reached at a score of <10.
 This scale can be used repeatedly to assess improvement or deterioration.

The Blantyre coma scale

The BLANTYRE COMA SCALE is applicable to children, including those who have not learned to speak

		Score
Best motor response:	Localises painful stimulus ^(a)	2
	Withdraws limb from pain ^(b)	1
	Non-specific or absent response	0
Verbal response:	Appropriate cry	2
	Moan or inappropriate cry	1
	None	0
Eyes movements:	Directed (e.g. Follow mother's face)	1
	Not directed	0
Total		0-5

A state of unrousable coma is reached at a score of <3
 This scale can be used repeatedly to assess improvement or deterioration

^a rub knuckles on patient's sternum

^b firm pressure on thumbnail bed with horizontal pencil

AVPU scale

A	Alertness (is the patient alert?)	0
V	Response to voice command (does the patient respond to his name?)	1
P	Response to pain (does the patient feel pain?)	2
U	Unresponsive (patient does not respond at all)	3

The level of consciousness worsen as you move down in the scale

Appendix 7: Report of suspected adverse drug reaction including birth defects

TANZANIA FOOD AND DRUGS AUTHORITY

Note: Identities of reporter, patient and institution will remain confidential

I. PARTICULARS OF PATIENT

Patient Initials or Record No.: _____ Sex: _____

Date of Birth (DD-MM- YYYY) or age:- _____ Weight in kg:- _____

II. DETAIL OF ADVERSE DRUG REACTION

<input type="checkbox"/> Headache	<input type="checkbox"/> Shock / anaphylaxis	<input type="checkbox"/> Skin rash	Date Reaction Started → ____/____/____ Date Reaction Stopped (if known) → ____/____/____
<input type="checkbox"/> Diarrhoea	<input type="checkbox"/> Nausea or vomiting	<input type="checkbox"/> Others	
Description of reaction (if possible).....			

Other relevant information: e.g. medical history, allergies, pregnancy, smoking, alcohol use, etc. **Please enclose any relevant laboratory results including dates (if done)**

III. DETAILS OF SUSPECTED DRUG (S) AND ALL OTHER DRUGS USED

Name of suspected drug(s) (Please specify brand name if known)	Dosage	Frequency	Route	Therapy Date		Batch. No & Expiry date (If known)	Reason for use
				Start	Stop		
1.							
2.							
3.							

Other drugs (including herbal medicines consumed at the same time and or 1 month before)

1.							
2.							
3.							

IV. MANAGEMENT OF ADVERSE REACTION

Reaction subsided after stopping the suspected drug/reducing the dose: Yes No nknown

Reaction reappeared after reintroducing drug: Yes No Not applicable

Do you consider the reaction to be serious? Yes No

If yes, please indicate why the reaction is considered to be serious **(please tick all that apply)**:

Patient Died due to reaction Required or prolonged hospitalization

Is life threatening Causes irreversible disability or incapacity

Causes a congenital anomaly Others, please give details.....

Treatment of adverse reaction Yes No **(if yes please specify)**.....

Outcome of the reaction Not yet recovered Recovered Fatal (Date of death): ____/____/____

V. PARTICULARS OF REPORTER (HEALTH CARE PROVIDER)

Name: _____ Profession: _____ Name and Address of the health _____

C

Contact phone No: _____ E-mail: _____ facility: _____
Signature: _____ Date of this report: ____/____/____

Please tick if you wish to receive information about other local reports associated with the suspected drug(s)

Thank you for your cooperation

Submission of an ADR case report does not discredit the competence of the reporter.

Ref No. (for official use)

--	--	--	--	--	--	--	--	--	--

Guide to filling the form

How to report?

- Dully fill in the form as required
- Use a separate form for each patient
- Report direct to TFDA through the following addresses:-



Mail : Tanzania Food and Drugs Authority,
P. O. Box 77150, Dar es Salaam



Fax: 22- 2450793



Phone: 22-2450512 / 2450751



Internet; <http://www.tfda.or.tz>
E-mail: adr@tfda.or.tz

The ADR reporting form and the guidelines are also available for downloading at <http://www.tfda.or.tz>

An Adverse Drug Reaction (ADR) is defined as a reaction which is noxious and unintended, and which occurs at doses normally used in human for prophylaxis, diagnosis, or therapy of a disease, or for the modification of physiological function.

What to report?

Please report all undesirable patient effect suspected to be associated with drugs, cosmetics or medical devices use.

Report even if:

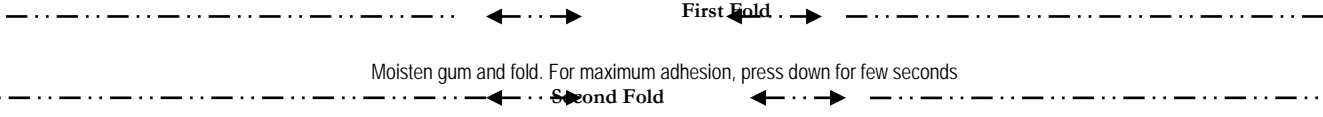
- You're not sure that the product caused the event
- You don't have all the details

When to report?

As soon as possible

Submission of follow-up reports:

Any follow-up information for an ADR that has already been reported can be sent on another ADR form or it can be communicated directly to TFDA by telephone, fax or e-mail. Please indicate that it is a follow-up report.. It is very important that follow-up reports are



POSTAGE WILL BE PAID BY LICENCEE

BUSINESS REPLY SERVICE LICENCE No. BRS 01

TO: THE DIRECTOR GENERAL
TANZANIA FOOD AND DRUGS AUTHORITY
P. O. BOX 77150
DAR ES SALAAM

No postage stamp required If posted in Tanzania.

