MALARIA

DIAGNOSIS AND TREATMENT GUIDELINES 2015

Vector-borne Disease Control Programme
Ministry of Health
GOVERNMENT OF VANUATU

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These national guidelines for the diagnosis and treatment of malaria in Vanuatu have been prepared by the National Malaria and Vector borne Diseases Control Programme, Ministry of Health, Vanuatu, with technical support from the World Health Organization.

First draft of these guidelines has been written by Esau Naket and Jean-Olivier Guintran.

Initial draft was reviewed first by working group including following persons:

Esau Naket, Malaria Program/ Case management Unit – Ministry of Health
Apisai Tokon, Reproductive health coordinator – Ministry of Health
Janet Fred, MCH/ EPI Coordinator - Shefa Province Health Office
Agnes Mathias , Acting Principle Pharmacist – Ministry of Health
Rodrick Mera, Medical officer - Vila Central Hospital
Walesi Natuman, Paediatric Registrar – Vila Central Hospital
Mark Parlicki, Volunteer Pharmacist - Northern Province Hospital
Caroline Hilton, Village Health Worker Coordinator – Save the Children Australia
Kistina Mitchell, Health Program Manager – Save the Children Australia
Jean Oliver Guintran, Medical officer - WHO /Vanuatu
Lasse Vestergaard, Medical officer - WHO/ WPRO

These guidelines were then discussed during meeting of the working group on October 29-30th, 2014 and drug protocol and dosing were reviewed critically mid-2015 by the principal pharmacists Agnes Mathias and Amanda Sanburg.

LIST OF CONTENT

LIST OF ABBREVIATIONS

ACT	Artemisinin-based Combination Therapy
ALU	Artemether-Lumefantrine
AS	Artesunate
CNS	Central Nervous System
CQ	Chloroquine
DHA-PPQ	Dihydroartemisinin plus piperaquine
ECA	External competency assessment
ECG	Electrocardiogram
FDC	Fixed-dose combination
G6PD	Glucose-6-phosphate dehydrogenase
h	Hour
Hb	Haemoglobin
HRP2	Histidine-rich protein 2
iCCM	Integrated community case management
i.m.	Intramuscular
IMCI	Integrated management of childhood illnesses
i.v.	Intravenous
LLINs	Long lasting insecticide treated nets
MOH	Ministry of Health
MUAC	Mid-upper arm circumference
NRL	National reference laboratory
ORS	Oral rehydration salts
pLDH	Plasmodium lactate dehydrogenase
P.f	*Plasmodium falciparum*
P.m	*Plasmodium malariae*
P.o	*Plasmodium ovale*
PQ	Primaquine
P.k	*Plasmodium knowlesi*
P.v	*Plasmodium vivax*
p.r.	Per rectum
Pv	Plasmodium vivax
QA	Quality assurance
QN	Quinine
RDT	Rapid Diagnostic Test
SOPs	Standard operating procedures
SP	Sulfadoxine-pyrimethamine
VHW	Village Health Worker
WBCs	White blood cells
WHO	World Health Organization

1. INTRODUCTION

Malaria has historically been one of the leading causes of disease in Vanuatu. The whole population of the country is considered at risk of infection.

During last decade, the Ministry of Health (MOH) and its partners have implemented an intensified program to progressively control malaria through: widespread access to diagnosis; widespread access to highly effective treatment; high coverage with Long Lasting Insecticide treated Nets (LLIN); community engagement; and intensive technical assistance. This has seen the incidence of malaria dramatically reduced to only 9 per 1,000 in 2013, and the virtual disappearance of confirmed malaria-related deaths. Despite all successes, early diagnosis and effective treatment of malaria at all health facility levels remains a key component of the national malaria control strategy.

Before 2009, universal access to diagnosis and effective treatment was challenged by the low diagnosis coverage (microscopy limited to 10% of health facilities) and an increasing level of parasite resistance to the first line treatment using chloroquine (CQ) and sulfadoxine-pyrimethamine (SP). Another important barrier is the burden of *Plasmodium vivax* infections, contributing to approximately half of all confirmed cases of malaria cases in the country, although rarely receiving radical treatment with primaquine due to concerns over side-effects in patients with possible G6PD deficiency.

The last edition of the national guidelines for malaria case management has been published in 2009. It included major changes in policy and recommendations. The use of rapid diagnostic tests (RDT) was recommended for every suspected case where malaria microscopy is not available. It also introduced the newly first-line treatment for uncomplicated malaria using artemisinin-based combination treatments (ACT) for both falciparum and vivax malaria. For the treatment of severe malaria, intravenous treatment with artesunate was introduced in replacement of quinine, while pre-referral treatment with artesunate rectal suppositories was introduced at the periphery.

This new edition of national guidelines for the diagnosis and treatment of malaria includes only minor adjustment and complement to define the process for clinical and parasitological diagnosis and few updated instructions and tables to ensure fully effective and safe treatment for malaria at all levels of the health system in Vanuatu.

2. MALARIA CASE MANAGEMENT POLICY IN VANUATU

Case management policy is a set of recommendations and regulations regarding the rational use of antimalarial medicines in the country. It provides guidelines for early diagnostic testing and prompt and effective treatment adapted to the local context, for all levels of the health care systems.

The following key principles and recommendations should be followed, in the public as well as in the not-for-profit and private health sectors.

Early diagnosis and treatment to prevent transmission
Early diagnosis and treatment of malaria is essential for two main reasons: 1) to minimize malaria morbidity and prevent deterioration and development of severe and life-threatening complications e.g. cerebral malaria, and 2) to prevent malaria transmission. Therefore, early diagnosis and treatment is beneficial both for the individual patient and for his/her community.

Universal access to quality assured diagnosis
Targeted treatment is achieved by examining every suspected case of malaria with either high quality microscopy or with a malaria rapid diagnosis test (RDT). Diagnostic based on microscopy is now only available in hospitals but RDTs have been introduced in all health facilities, to be used where and when microscopy is not available. Quality of microscopy must be controlled by a national reference laboratory. Procurement of RDTs must comply with criteria based on results of the WHO/FIND product evaluation.

Parasitological diagnosis for every fever
Every patient with fever should be tested for malaria. As a result, unnecessary treatments will thus largely be avoided, while alternative causes of illness and other required treatment should be looked for. Increasing diagnostic coverage also means that reporting of malaria will improve, which will enable more accurate planning and procurement of drugs. Presumptive treatment of malaria should be avoided to any extent possible.

Uncomplicated cases of *P.falciparum* and *P.vivax* treated by ACTs
Due to increasing rates of parasite resistance to previously used first-line antimalarials, Vanuatu has adopted a standard 3 days treatment with artemether- lumefantrine (ALU) for both species. Products to be procured must be user-friendly fixed-dose combination and pre-qualified by WHO for internationally recommended standards of manufacturing and quality. Chloroquine and sulfadoxine-pyrimethamine should no longer be used for the treatment of malaria.

Radical treatment with primaquine for vivax-malaria
Plasmodium vivax remains responsible for a significant burden of malaria in Vanuatu. Radical treatment with primaquine is therefore highly recommended for cases of confirmed vivax-malaria. However, important exceptions to the use of primaquine for vivax-malaria still include the following groups: 1) Pregnant and lactating women, 2) children below 1 year, and 3) patients with G6PD deficiency.

Artesunate suppositories for pre-referral treatment in Dispensaries and Aid posts
Patients, who have already developed signs of severe illness when arriving at a peripheral health facility, should be given pre-referral treatment in the form of artesunate suppositories, and thereafter immediately be referred for parenteral treatment at a higher-level health facility.

Artesunate injections for the treatment of severe malaria cases
Due to its superior efficacy compared to quinine for parenteral treatment of severe malaria, artesunate injections is now the recommended first-line treatment for severe malaria for both children and adults, including pregnant women in 2nd and 3rd trimester.

Integrated community case management in Dispensaries and Aid posts
Community case management of malaria should be implemented in the context of the integrated community case management (iCCM) strategy. In addition to diagnostics and medicines for malaria, the iCCM strategy package includes diagnostic tools for pneumonia, and medicines for pneumonia and diarrhoea (respiratory rate timers, antibiotics, ORS and zinc).

Patient counselling to ensure compliance and correct timing of treatments
To ensure effective treatment and to prevent development of drug resistance, health workers will be trained to counsel patients to adhere to correct duration and time intervals of treatments.

Integrated supervision and quality assurance and for diagnosis and treatment
Substantial resources are invested to assure health workers apply standard clinical practices. Monitoring is already in place using specially designed malaria information system with line-listing allowing longitudinal measures of case management indicators. Regular supervision of peripheral health facilities by zone nurses from Health Centres will be reinforced as well as access to job-aids, technical documents, updates and refresher trainings.

Sales regulation of antimalarial medicines
The list of drugs to be sold in “Sale of Medicine Regulation order” has been amended to ban supply of oral artemisinin-based monotherapy medicines.

Selection of safe, effective and quality antimalarial
Protocols should be in line with WHO guidelines and products prequalified by WHO to be eligible for procurement. Fixed-dose combination (FDC) formulations are preferred over blistered co-packaged or loose tablet combinations to promote adherence to treatment and to reduce the potential selective use of the medicines as monotherapy.

Access of drugs in private sector
Private and not-for-profit sectors are very limited. They will be supplied with drugs and RDTs by provincial pharmacies to limit the risk of importation and marketing of inadequate products.

Management of drug resistance

A change of an antimalarial medicine should be initiated if the total treatment failure proportion is ≥ 10%, as assessed through in vivo monitoring of therapeutic efficacy. A new antimalarial medicine should only be selected when the medicine has an average cure rate of >95% as assessed in therapeutic efficacy studies.

3. DIAGNOSIS OF MALARIA

3.2 Assessment of patient with fever in Aid-Posts

The approach of integrated Community Case Management (iCCM) of childhood illness is recommended.

In addition to **malaria, pneumonia, diarrhoea and malnutrition** are among the leading causes of death among children aged 2 to 59 months. It is common for a child to have two or more of these conditions at the same time and the child needs treatment for each of them. Furthermore, there is often a significant overlap in the clinical manifestation of pneumonia and malaria.

Caregivers (parents and guardians) or patients themselves should be informed to seek care **within 24 hours** of onset of fever. They should immediately contact the designated Village Health Worker (VHW) to access prompt malaria diagnostic testing.

The VHW should assess the condition of the patient and look for danger signs and symptoms of severe disease as in Box 1 below.

Box 1: List of iCCM danger signs

- cough for 21 days or more
- diarrhoea for 2 weeks or more
- diarrhoea with blood in the stool
- fever for 7 days or more
- convulsions
- not able to drink or breastfeed
- repeated vomiting
- chest in-drawing
- lethargic or unconscious
- stiff neck
- red on the Mid-Upper Arm Circumference (MUAC) strap
- swelling of both feet

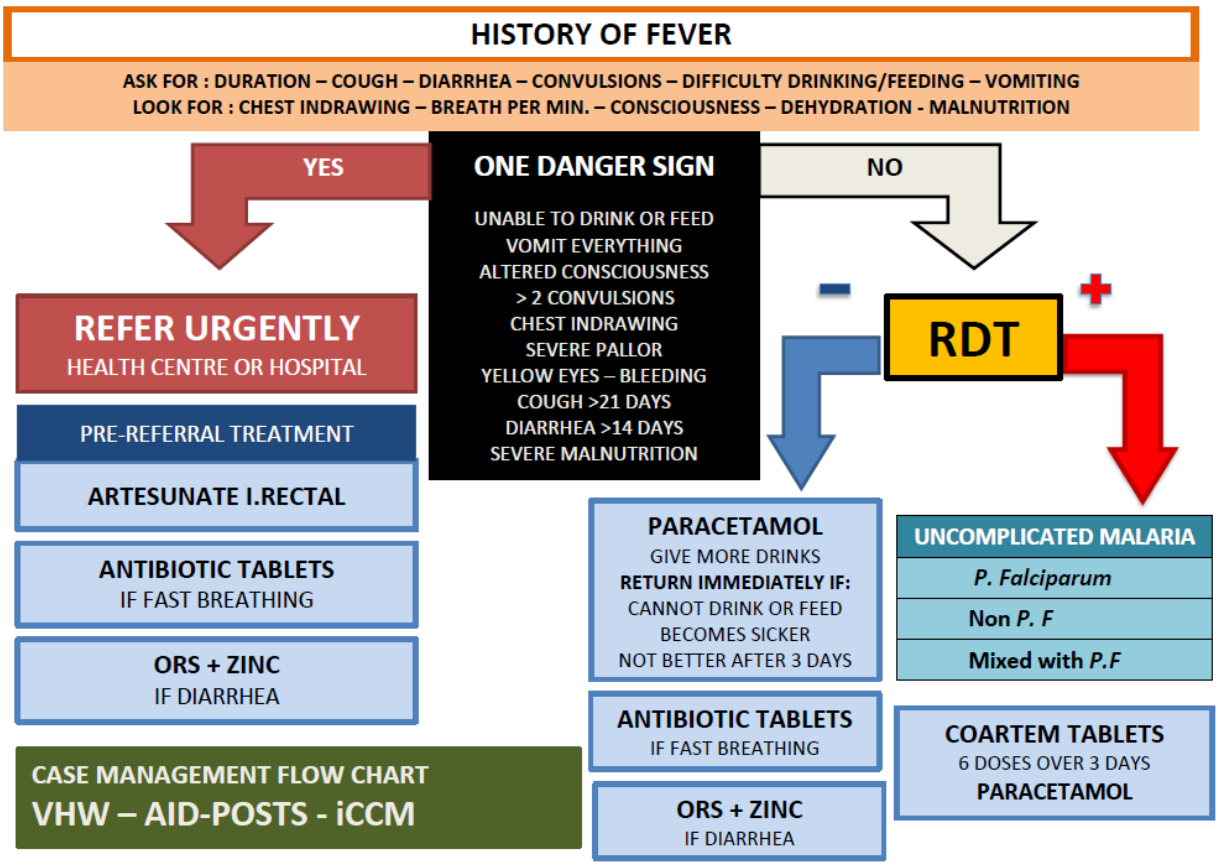
Patients **with one danger sign** should be given an appropriate pre-referral treatment and referred without delay to the nearest health center or hospital.

The pre-referral treatment recommended for iCCM includes:

- Artesunate suppositories for febrile patients with convulsions, repeated vomiting, unable to swallow or with altered consciousness
- Antibiotic for febrile patients with cough plus chest in-drawing
- ORS for patients with diarrhoea and who can drink.

If there is no danger sign or sign of severe malaria: perform a rapid diagnostic test (RDT)
Parasitological confirmation of malaria by microscopy or RDTs should be carried out for all febrile children and adults with no danger signs.

> See Flow chart about malaria case management in Aid-posts in Annex 5



3.2 Assessment of patient with fever by nurses in Dispensaries

The approach of integrated management of childhood illnesses (IMCI) is recommended.

All patients with fever as a main symptom (history of fever or feels hot or has an axillary temperature of 37.5°C or above) should be quickly checked for **general danger signs** and **features of severe malaria** for immediate care if any one of these signs or features is present.

Take case history with relevant general information:

- Age
- Place of residence, history of travel
- Pregnancy status in women of child-bearing age

Ask the patient and/or the accompanying person about:

- History of fever, chills
- Headache, neck stiffness
- Rash, skin problem
- Runny nose, earache, sore throat
- Cough, difficult breathing
- Drinking, eating, vomiting
- Diarrhoea

Examine the patient carefully:

- Temperature, pulse, blood pressure
- Respiration rate, chest auscultation
- Dehydration signs
- Rash or skin infection (wounds, abscess)
- Palmar pallor
- Weight, ratio weight/height (malnutrition)
- Throat, eyes and ears
- Cervical lymph nodes
- Abdomen palpation
- Neck stiffness, bulging fontanel (infant)

Look for IMCI general danger signs:

ASK the following:
1. Is the patient able to drink or breastfeed?
2. Does the patient vomit everything?
3. Has the patient had convulsions?

LOOK for the following:
4. Is the patient lethargic or unconscious?
5. Has the patient got respiratory distress?

Box 2: List of IMCI general danger signs

- **Repeated convulsions** (at least twice in 24h)
  Involuntary spasms of body parts

- **Prostration (**extreme weakness)
  Unable to drink or breastfeed (infant)
  Unable to sit unsupported

- **Coma or altered consciousness**
  Unable to fix/follow objects with eyes (infant)
  Unable to localize a painful stimulus

- **Respiratory distress**
  Deep breathing, in drawing of the lower chest wall
  Nasal flaring

Some patients may not have any of the 4 general danger signs but other signs of severe malaria

ASK and LOOK for the following:

1. Does the patient have any other sign of severe malaria?

- Severe palm pallor
- Passing dark or little urine
- Jaundice (yellow eyes)
- Bleeding from injection or venepuncture sites

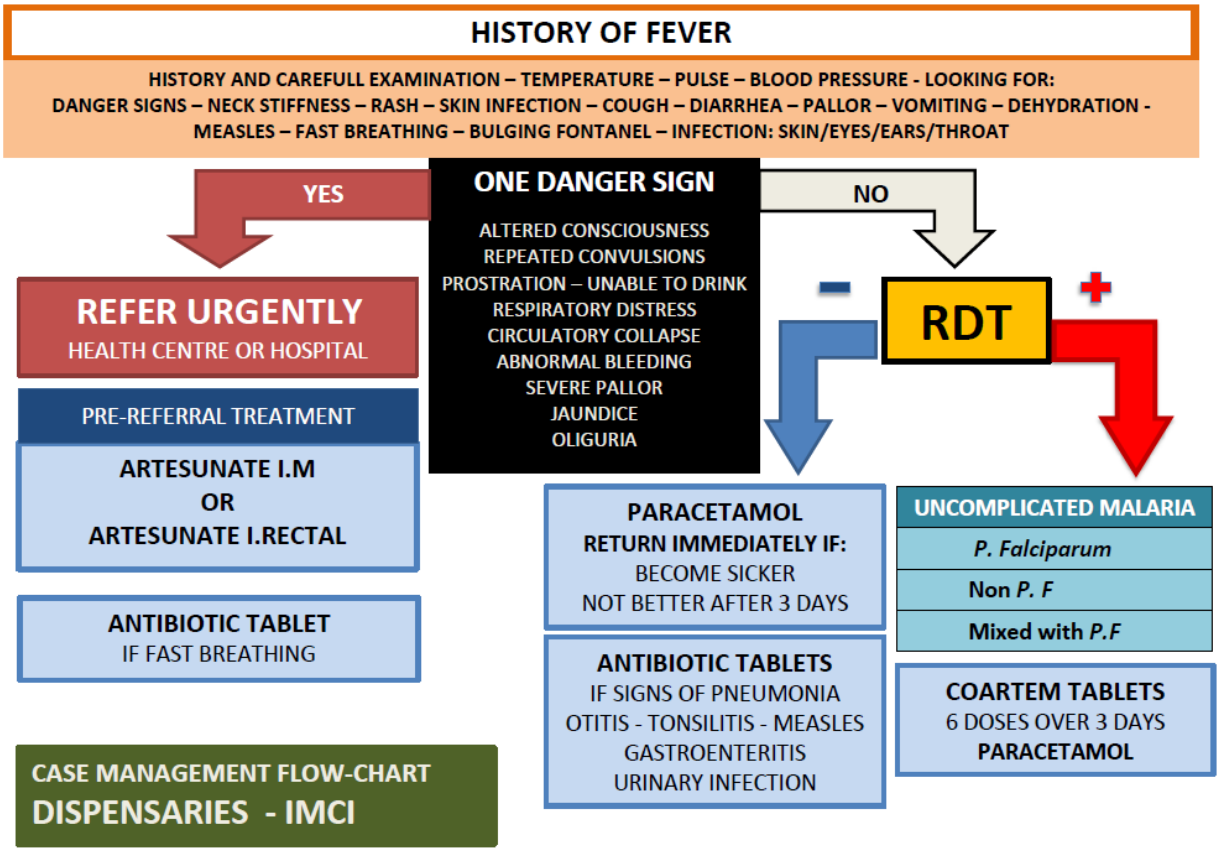
A patient with **a general danger sign** or any **signs of severe malaria** should be given pre-referral treatment without delay and referred immediately to the closest health center or hospital.

2. Does the patient have any other signs suggesting another cause of fever?

Check for a stiff neck.
Look for signs of measles (especially for children below 5 years).
Look for other signs of local infection (skin, eyes, ears and throat)

If there is no danger sign or sign of severe malaria: perform a rapid diagnostic test (RDT)
Parasitological confirmation of malaria by microscopy or RDTs should be carried out for all febrile children and adults with no danger signs.

> See Flow chart about malaria case management in Dispensaries in Annex 5



3.3 Parasitological diagnosis of malaria

Two parasite-based methods are available in Vanuatu to confirm the presence of malaria: Standard microscopy, and malaria rapid tests (RDTs).

Until recently, the diagnostic coverage in Vanuatu was only low, due to difficulty in maintaining microscopic services in all provinces. With the countrywide distribution of RDTs to all health facilities, access to diagnostic test for malaria is now possible to all patients.

Why should we test patients with fever?
In Vanuatu, the great majority of febrile illnesses are not due to malaria. The aim of testing a sick person for malaria is not just to confirm the presence of an infection with Plasmodium but in most cases is to give more appropriate treatment for non-malarial fevers.

Parasitological testing of fever episodes has many advantages over presumptive treatment:

- improved care of parasite-positive patients owing to greater certainty that the cause of the present illness is malaria
- another treatment can be sought for parasite-negative patients
- avoid antimalarial drug in parasite-negative patients reducing side effects and drug resistance
- confirmation of treatment failures
- improved malaria case detection and reporting

Who should be tested for malaria?

Every patient presenting with a history of fever or elevated temperature should be tested for malaria. Do not delay in referring patients with danger signs.

When should patient with danger signs be tested?
In any suspected case of severe febrile illness (with danger sign), parasitological confirmation of the malaria diagnosis is strongly recommended; however, in the absence or delay in obtaining a parasitological diagnosis, admission or reference to hospital should organised immediately and presumptive treatment started. Other investigations to determine illness severity, complications and prognosis should be undertaken where feasible.

Which method should be used to test for malaria?
The two main methods in routine use for parasitological confirmation of malaria are light microscopy and rapid diagnostic tests (RDTs). For the management of a new fever episode, quality-assured **microscopy and RDTs are equivalent** in terms of performance for the diagnosis of uncomplicated malaria.

High-quality **microscopy** services for the diagnosis of malaria will **only be available in hospitals**. It requires trained staff, well-maintained equipment, a regular supply of reliable reagents, clean water and electricity, and a well-executed quality management system.

In hospitals, RDTs are an option for ensuring malaria testing in outpatient departments with a high malaria caseload. RDTs are also needed for diagnostic testing for malaria when a laboratory is closed or microscopy is not available (after working hours).

Microscopy is necessary for severe cases for the initial quantification of parasite density because density is a marker of severity. Microscopy is also needed for follow-up of parasite density until full parasite clearance.

Microscopy is also needed for investigating **treatment failure** in outpatients, especially to assess patients referred from health-care facilities that do not have microscopy.

Quality standards for malaria microscopy

Microscopy has a high degree of sensitivity and specificity when performed well. In addition, it allows quantification of malaria parasites and identification of the infecting species.

Which microscopists are qualified to read slides?
A skilled microscopist is able to detect asexual parasites at densities of fewer than 10 per microliter (µl) of blood but under typical field conditions the limit of sensitivity is approximately 100 parasites per µl.

Malaria microscopist should be assessed by standard WHO External Competency Assessment. They should be graded **at least a Level 3** to be qualified for slide reading. If such a competent microscopist is not available, RDTs should be used.

What are the advantages of microscopy?
The following are added values from the microscopy:

- Differentiation between species and the stages of the parasite;
- Determination of parasite densities
- Diagnosis of other conditions like leukaemia, leucocytosis, eosinophilia (thick film) and various types of anaemia (thin film).

How should malaria microscopy be performed?
This is done by examining a stained thick and thin blood film for the presence of malaria parasites.

Giemsa stain should be used for its stability during storage and quality over a range of temperatures.

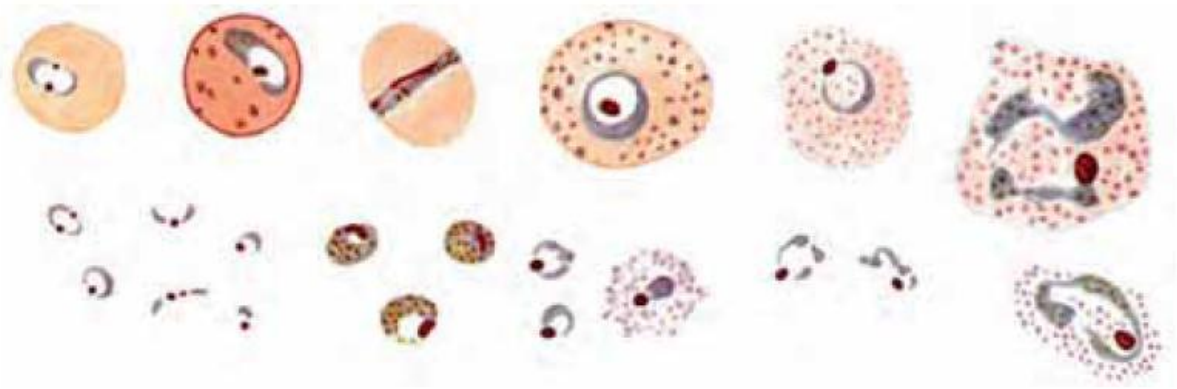
Thick films are recommended for parasite detection and quantification and can be used to monitor response to treatment. Before starting parasite count, 100 fields of the thick smear at a magnification of 700 (equivalent to 0.25µl of blood) are examined to establish presence of parasites and their species. If diagnosis of species is uncertain, a further 100 fields should examined to identify a potential mixed infection.

Thin films are recommended for species identification and can also be used for parasite quantification. Thin smears are not routinely examined to diagnose malaria in a patient except when there are technical problems with the thick smears, when confirmation of the species is difficult or uncertain in the thick smear or when the parasite density is very high.

> See SOP for malaria microscopy

Why do we need to measure parasite density?
It has a valuable prognostic value in cases of **severe malaria** infection and also helps in following up the changes produced by treatment.

Parasites are commonly quantified by counting ring forms against white blood cells (WBCs). The results are expressed as parasite count/200 WBCs or parasite count/µl of blood (assuming a WBC count of 8000/µl).



Quality assurance (QA) of malaria microscopy
The primary aim of malaria microscopy QA programmes is to ensure that microscopy services employ competent staff. Technical skills of malaria microscopist should be evaluated with at least a Level 3 by standard WHO External Competency Assessment (ECA).

A **National Reference Laboratory** (NRL) with a QA coordinator based in Port Vila hospital oversees QA programme training and validation standards including:

- Systematic cross-checking (validation) system with feed-back of results
- Regular retraining and assessment of competency, supported by a reference slide set
- Supervision of the laboratory in the 6 hospitals
- Logistical management and supply of consumables and maintenance of micro-scopes
- Clear standard operating procedures (SOPs) at all levels of the system.

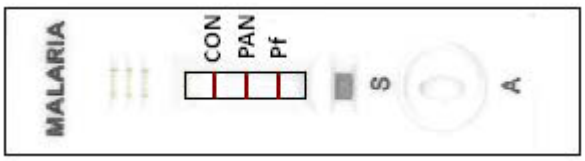
> See SOP for NRL and malaria microscopy QA

Quality standards for rapid diagnostic tests (RDTs)

How do RDTs work?
Whole blood obtained from a finger-prick is used for the tests. Malaria RDTs are based on the detection of specific parasite antigens, which are present in the blood of infected patients. If present, the antigens cause microscopic particles to stick to a band on the RDT, eventually forming a visible, coloured line in the 'test' area.

Which kind of RDTs should be used?
Selection and procurement should be guided by the WHO/FIND RDT Product Testing Programme which provides comparative performance data through the evaluation of products against well-characterized, cryopreserved, native and cultured *P.falciparum* and *P.vivax* samples.

In Vanuatu, a combination RDTs that distinguish *P. falciparum* and non-falciparum malaria is required. Common available products combine Histidine-Rich Protein 2 (HRP2) for *P. falciparum* and different variants of *Plasmodium* lactate dehydrogenase (pLDH): pLDH-Pan (common to all species) or pLDH-Pv (only for *P. vivax*).



Selection of product should be based on the following **performance criteria**:

- For the detection of *Plasmodium falciparum*, the panel detection score (PDS) should be **at least 75% at 200 parasites/µL**.
- For the detection of *Plasmodium vivax*, the panel detection score (PDS) should be **at least 75% at 200 parasites/µL**.
- The false positive rate should be **less than 10%**.
- The invalid rate should be **less than 5%**.

In addition the **other important features** are to be taken into consideration:

- Cassette format is preferred because of ease of use.
- Sequence of lines (C/Pv/Pf)
- 2 drops buffer
- Time for result 20 min
- Complete kits (with lancets, pipette, buffer and alcohol swabs) are required
- Heat stability (at 35-45°C 60 days incubation)

Once all these factors have been considered, other parameters should also be evaluated but price alone should not be the determining factor for the procurement of RDTs.

Why should we do lot-testing?
The performance of individual products is likely to vary between lots over time. Prior to large-scale deployment in the field, lots of procured products will be checked for quality by a laboratory accredited for WHO-FIND lot testing.

How RDTs should be stored?
RDTs require important attention to store them properly at temperature below 4O°C in a shade area (ensure that they are not directly exposed to sunlight and that the environment does not exceed the temperature range mentioned on the box.

What are the limitations of RDTs?
RDTs cannot tell how many malaria parasites are present in the blood. They can only test whether parasites are present or absent.

RDTs that detect HRP2 antigen from *P. falciparum* cannot be used to check for effectiveness of treatment because it remains in the blood for at least two weeks after the parasites are killed by drugs and the test will remain positive even though the patient is cured.

RDTs can be damaged by heat and humidity, so an RDT should not be removed from its sealed packet until right before you are ready to use it.

How do we best perform RDTs?
For more detailed information on the practical use of RDTs.

> See job-aid to perform RDTs in Annex 5

3.4 Classification of malaria

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

Uncomplicated malaria
This is symptomatic malaria with parasitaemia without signs of severity or evidence of vital organ dysfunction. The main manifestations of uncomplicated malaria include fever, chills, rigors, headaches, and body pains. Others are malaise, nausea, vomiting, and joint weakness. These features may occur alone or in combination. Physical examination may reveal pallor and hepatosplenomegaly.

Severe febrile disease
This is a patient with history of recent fever and a danger sign (see section 3.2 above).

Severe falciparum malaria
This refers to acute *P. falciparum* malaria with signs of severity or evidence of vital organ dysfunction. A patient is regarded as having severe falciparum malaria if there are asexual forms of P. falciparum in a blood film and any of the following clinical or laboratory features:

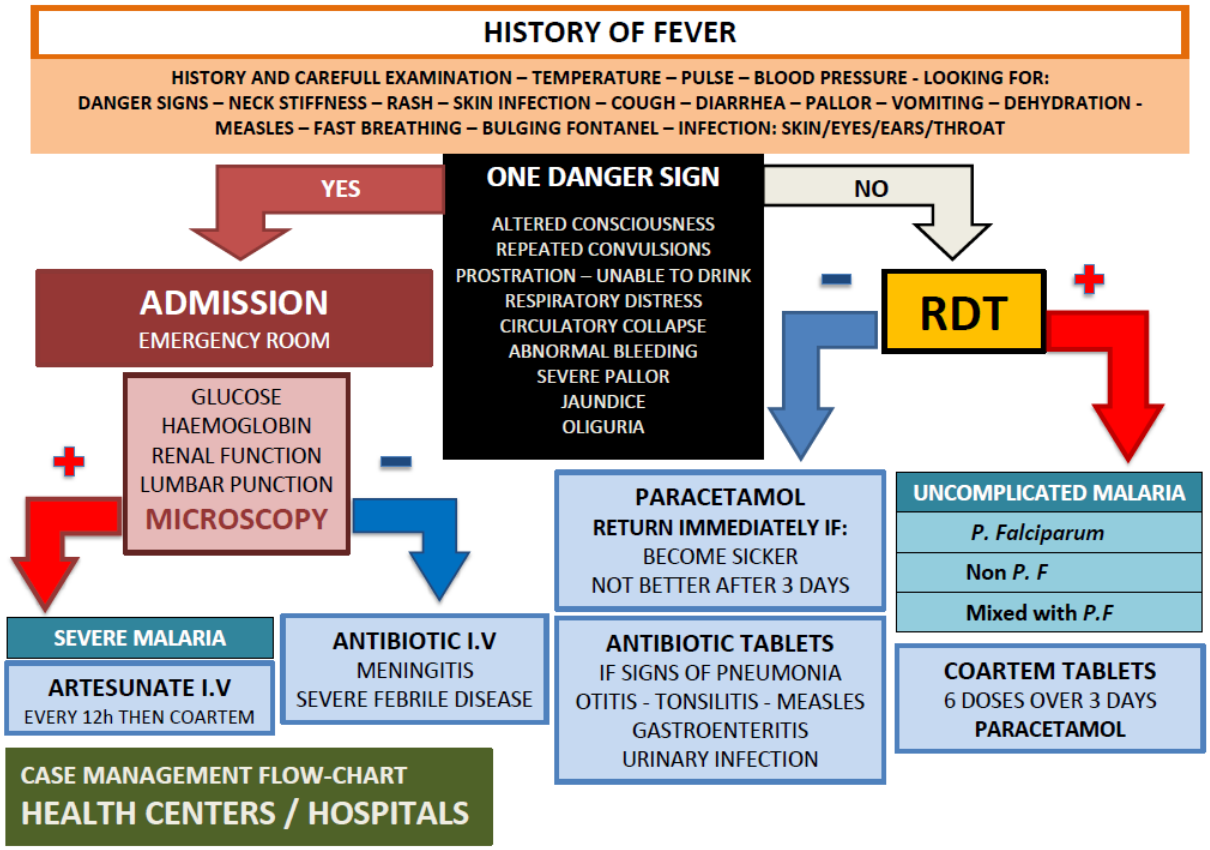
Clinical features:
- impaired consciousness or unrousable coma
- prostration, i.e. generalized weakness so that the patient is unable walk or sit up without assistance
- failure to feed
- multiple convulsions – more than two episodes in 24 h
- deep breathing, respiratory distress (acidotic breathing)
- circulatory collapse or shock, systolic blood pressure < 70 mm Hg in adults and < 50 mm Hg in children
- clinical jaundice plus evidence of other vital organ dysfunction
- haemoglobinuria
- abnormal spontaneous bleeding
- pulmonary oedema (clinical and radiological)

Laboratory findings:
- hypoglycaemia (blood glucose < 2.2 mmol/l or < 40 mg/dl)
- metabolic acidosis (plasma bicarbonate < 15 mmol/l)
- severe normocytic anaemia (Hb < 5 g/dl, packed cell volume < 15%)
- haemoglobinuria
- hyperparasitaemia (> 2% or 100 000/µl)
- hyperlactataemia (lactate > 5 mmol/l)
- renal impairment (serum creatinine > 265 µmol/l).

Severe non-falciparum malaria

P. vivax and more recently P. knowlesi have been recognized as causes of severe malaria particularly in Asia and in certain forested areas of South-East Asia respectively. Severe vivax malaria may present with pathologies similar to severe P. falciparum malaria and can be fatal.

> See Flow chart about malaria case management in Health Centers and hospitals



4. TREATMENT OF UNCOMPLICATED MALARIA

The objective of effective treatment of uncomplicated malaria is to:

- prevent progression to severe disease
- cure the infection
- reduce transmission of the infection to others
- prevent the emergence and spread of resistance to antimalarial

4.1 Who should be treated for malaria?

In uncomplicated cases, **only patients with a positive diagnostic test** for malaria should receive antimalarial treatment.

Presumptive treatment may only be used exceptionally where no diagnostic facilities are available, and for suspected severe cases where delay in treatment is considered unacceptable due to the clinical condition of the patient.

When the **diagnostic test for malaria is negative**, an antimalarial medicine **should NOT be given**. The patient should be assessed for other causes of fever, and specific treatment should be given only for those conditions identified.

A child with cough plus fast breathing and/or chest in-drawing should be classified as pneumonia. An antibiotic should be given to the patients if they can take oral medication.

A child with loose stools (3 or more in 24 h) for less than 7 days should be classified as having diarrhoea. These patients should receive ORS and zinc if they can drink.

Patients with **negative RDT and without any signs of other diseases** should be instructed to return for **a follow-up visit within 3 days** and/or anytime if the child is still sick.

During the follow-up visit, look for signs of illness again and perform a new test.

> See Flow chart about malaria case management in Aid-posts
> See Flow chart about malaria case management in Dispensaries
> See Flow chart about malaria case management in Health Centers and hospitals

4.2 Artemisinin-based combination therapy (ACT) as first-line treatment

Artemisinin-based combination therapy should be used because:

- is more effective than a monotherapy
- prevent or delay the emergence of resistance
- artemisinins have marked effects on all stages of the parasite
- artemisinins have gametocytocidal effects on P. falciparum, and this may help to reduce transmission

Treatment is the same for *P. faciparum* and *P. vivax* or other species

The recommended first-line treatment for uncomplicated malaria in Vanuatu is oral treatment with tablets of **artemether-lumefantrine (ALU)**, also known as Coartem®.

An advantage of this combination is that lumefantrine is not available as a monotherapy and has never been used alone for the treatment of malaria.

Artemether-lumefantrine (ALU) is administered:
As a **fixed-dose** combined tablet (artemether 20mg & lumefantrine 120mg)
In **six doses over 3 days** (0h, 8h, 24h, 36h, 48h & 60h)

Different blister packages exist for different patient weight groups, providing exactly the required number of tablets per dose for each age group (see dosing table below).

Artemether-lumefantrine dosing table for uncomplicated falciparum-malaria (Fixed-dose tablets of 20mg artemether & 120mg lumefantrine)

Patient body weight (Kg)	Age (if weight not available)	Tablet per dose
< 5	<6 months	1 (D*)
5-14	6 months – 3 years	1 (D*)
15-24	4 years – 8 years	2 (D*)
25-34	9 years – 14 years	3
> 35	More than 14 years	4

D* is for dispersable tablets for children
A flavoured dispersible tablet paediatric formulation of artemether-lumefantrine is now available, facilitating its use in young children. Mix the tablet with about 10ml of water.

> See job-aid about administration of Coartem in Annex 5

4.3 Counselling for effective treatment

Patient with malaria should be counselled as follows:

Timing of doses
The second dose should be administered 8 hours after the first one. It is important that patients are advised well on when to take their medicine according to the treatment schedule in this protocol.

Take treatment with some food
Lumefantrine absorption is enhanced by co-administration with fat. It is essential that patients or caregivers are informed of the need to take this ACT immediately after a meal or a glass of milk – particularly on the second and third days of treatment.

Drink plenty of fluids
Water, coconut juice, or ORS (Oral Rehydration Solution) should be given regularly to prevent dehydration.

Supportive care with antipyretics:
Fever is a cardinal feature of malaria. For fever management, tepid sponging of the body is recommended and antipyretics could be used if necessary. Paracetamol at a dose of 15mg/kg given at 4-hour intervals has been effective in fever management. Ibuprofen (5mg/kg) may also be used.

Vomiting
If vomiting occurs within 1 hour of taking a dose, another dose must be taken or given.

4.4 Quinine for pregnant women in first trimester

Quinine is administered in the dose of 10 mg sulphate salt/kg **three times a day for 7 days**

Dosing table for quinine sulphate salt (300 mg tablets)

Patient body weight (Kg)	Tablet per dose
50-69	2
70-89	2½
>90	3

The first line ACT treatment is indicated if quinine is not available or if there is uncertainty about patient compliance with a 7-days treatment.

4.5 Management of suspected treatment failure

Malaria treatment failure is defined as failure to achieve an adequate clinical and parasitological response to treatment.

Recurrence of fever and parasitemia after 14 days
Recurrence of fever and parasitaemia more than two weeks after treatment could result either from recrudescence, a relapse of *P. vivax* or new infection. It should be treated a second time with the first-line ACT.

Management of suspected treatment failure within first 14 days:
Treatment failure should be suspected if malaria symptoms persist or reappear 3-14 days after initiation of the initial malaria treatment.

Importantly, it should be remembered that a treatment failure could also be explained by a wrong diagnosis in the first place, and therefore the wrong treatment.

Although treatment failure could be due to drug resistance, it is more likely the result of inadequate medication, often arising from poor patient compliance with the treatment. Therefore, it is important to determine from the patient's history whether the antimalarial medicine was vomited or whether the full course was not completed.

If the treatment failure is explained by poor treatment compliance, the patient should receive a repeat full course of first-line treatment, as well as careful counselling.

Suspected treatment failure:
A treatment failure will be suspected if the 3 following criteria are verified:

- The initial diagnosis has been parasitologically confirmed and reliable
- The patient has completed the full course of artemether-lumefantrine
- The patient did not vomit within 1 hour after taking any of the doses

Confirmed treatment failure:
Any patient with suspected treatment failure must be referred to the nearest hospital with malaria microscopy available for parasitological confirmation.

Treatment failure should be confirmed by the presence of malaria parasites in blood confirmed by malaria microscopy within 14 days after finishing a full course of first-line treatment.

HRP-2-based tests cannot be used because they remain positive for several weeks after the initial infection even without recrudescence.

Confirmed cases of treatment failure should be treated with the recommended second-line treatment drug (see section 4.6). Other potential causes of illness must also be considered and adequately managed.

4.6 DHA-PPQ as second-line treatment for uncomplicated malaria

Second line treatment should only be prescribed to patients with **confirmed treatment failure** after complete investigation and confirmation of failure by microscopy.
The treatment will be **only available in hospitals**.

The second line treatment is an alternative artemisinin-based combination therapy (ACT) with combined dihydroartemisinin and piperaquine. The target dose is of 4mg/kg/day dihydroartemisinin and 18mg/kg/day piperaquine **once a day for 3 days**.

It is currently available as a fixed dose combination with tablets containing 40 mg of dihydroartemisinin and 320 mg of piperaquine.

Dosing table for dihydroartemisinin plus piperaquine (DHA-PPQ)
(Fixed dose tablets with 40 mg of dihydroartemisinin and 320 mg of piperaquine)

Patient body weight (Kg)	Tablet per dose
5-9	1/2
10-19	1
20-39	2
>40	3

4.7 Antigametocyte treatment for *P.falciparum* in elimination areas

The addition of a **single dose primaquine (0.25mg/kg)** to ACT treatment for uncomplicated falciparum malaria as an antigametocyte medicine, is recommended as a component of the elimination programme.

Dosing table for single dose primaquine for *P.falciparum* infection in elimination areas (0.25mg base/kg/day).

Patient body weight (Kg)	7.5mg tablet per day	15mg tablet per day
10-20	½	¼
21-40	1	½
41-60	1 ½	¾
>60	2	1

5. RADICAL TREATMENT OF VIVAX and MIXED INFECTIONS

Plasmodium vivax remains responsible for a large proportion of malaria cases in Vanuatu. Due to its ability to cause relapses from dormant hypnozoite stages in the liver, additional treatment with primaquine needs to be given in addition to artemether-lumefatrine to prevent relapses (radical cure).

For mixed infections (*P. falciparum* and *P. vivax* together at the same time), treatment recommendations are the same as for *P. vivax* mono-infections.

Other *Plasmodium* species are extremely rare in Vanuatu. The treatment of *P. ovale* is the same as for P. vivax. *P. malariae* does not cause relapses and do not need radical treatment.

5.1 G6PD testing

G6PD status should be ascertained if possible before administering daily primaquine therapy for 14 days to prevent relapses in patients with confirmed acute P. vivax infection.

G6PD qualitative point-of-care tests to identify G6PD non-deficient patients prior to primaquine administration should be >95% sensitive compared to spectrophotometry or equivalent quantitative tests, stable at temperatures expected in tropical settings (35–40°C) and have a negative predictive value of >95% at G6PD enzyme activity levels <30% of normal.

Males who have a history of testing normal using a reliable G6PD test should receive standard daily primaquine therapy, as they are not expected to experience harmful adverse drug effects.

G6PD qualitative tests will not identify the majority of heterozygous females some of whom may be at risk of developing acute haemolysis secondary to primaquine therapy. Therefore, females who test G6PD normal with a qualitative test should only receive daily primaquine therapy if they can be monitored for signs and symptoms of acute haemolysis during the first week of treatment.

5.2 Contra-indication of primaquine

Primaquine radical treatment is recommended for any confirmed case of vivax-malaria, with the important exceptions of the following patient groups:

Contra-indication of primaquine

- Pregnant or lactating women
- Infants younger than 1 year or with a bodyweight less 10 kg.

5.3 Radical treatment with primaquine

Primaquine is administered **once daily for 14 days**.

It should be **started on the same day** of artemether-lumefantrine treatment.

It can be available in **7.5 mg base or 15 mg base tablets** and should always be given together with food. (7.5 mg primaquine base is equivalent to 13.2 mg primaquine phosphate).

Primaquine dosing and monitoring should be done according to patient G6PD deficiency status as follows:

a) Patients with known G6PD deficiency:

- Patients with known G6PD deficiency based on testing, or with suspected G6PD deficiency based on a history of previous primaquine treatment associated with side effect including acute haemolysis, **should NOT be treated with primaquine**.

- However, these patients may receive **a weekly dose of 0.75 mg/kg for 8 weeks** provided they are **under close medical supervision** for signs and symptoms of acute hemolytic anaemia **during the first 3 weeks** of treatment; and provided they have access to health facilities **with capacity for safe blood transfusion**.

b) Male patients with normal G6PD function:

- Male patients with normal G6PD status, based either on G6PD testing or based on a history of previous safe and succesful primaquine treatment, should receive the **standard primaquine regimen (0.50 mg/Kg daily for 14 days)** without any specfic precautions in terms of clinical monitoring.

Dosing table for primaquine for patients with normal G6PD function (0.5mg base/kg/day).

Patient body weight (Kg)	7.5mg base tablet per day	15mg base tablet per day
10-20	1	½
21-40	2	1
41-60	3	1½
>60	4	2

c) Female patients or male patients with unknown G6PD function:

- Patients with **unknovn G6PD deficiency status** may receive primaquine, but in a **reduced dose of 0.25 mg/Kg daily for 14 days**. Furthermore the patient should be observed clinically at a higher-level health facility (Hospital or Health Centre) during the first 3-4 days of treatment. If a patient should be G6PD deficient, side-effects (in particular haemolysis) will normally appear within the first couple of days.

- If the patient's urine becomes dark (reddish brown) during treatment, **primaquine treatment must be stopped.**

- Similarly, after the first days of direct clinical observation, the patient must be instructed that if he/she should later observe that his/her urine becomes dark (reddish brown), **the primaquine treatment should be stopped and the patient should return to the nearest health facility for advice**.

Dosing table for primaquine for patients with unknown G6PD function (0.25mg base/kg/day).

Patient body weight (Kg)	7.5mg base tablet per day	15mg base tablet per day
10-20	½	¼
21-40	1	½
41-60	1 ½	¾
>60	2	1

> See job-aid about administration of primaquine in Annex 5

6. PRE-REFERAL TREATMENT OF PATIENTS WITH DANGER SIGNS

Any **suspected case of severe malaria** must wherever possible be immediately referred to **the nearest health centre or hospital** for parenteral antimalarial treatment, as well as other supportive treatment and close clinical monitoring.

Pre-referral administration of artesunate rectal suppositories to severely ill malaria patients have shown to reduce the risk for complications and death. The advantage of artesunate suppositories is that they can be given easily and rapidly to both children and adults without the need for extra materials or much staff training.

6.1 Rectal artesunate at Dispensary and Aid Post level

Recommendations for the management and referral of patients with danger signs or suspected severe malaria are as follows:

- Give **artesunate suppositories** to any patients with suspected severe malaria according to the weight of the patient.
- Thereafter, **refer the patient immediately** to the nearest Health Centre or Hospital to initiate parenteral antimalarial treatment, further clinical observation and additional supportive therapy, as necessary.

Artesunate suppositories should be given as follows:

- Give artesunate suppository 10mg/kg once. Artesunate suppositories are available in 50mg & 200mg strengths (see dosing table below).
- To ensure absorption, hold the buttocks of the patient together for 10 minutes. If suppository is expelled within 30 minutes, give another suppository.
- After inserting 3 suppositories, wait at least 10 min. before inserting another one.

Dosing table for artesunate suppositories for pre-referral treatment of severe malaria

Patient body weight (Kg)	Age (if weight not available)	Rectocap. 50mg	Rectocap. 200mg
3-5	0-3 months	1	
6-10	6-11 months	2	
11-20	1-6 years		1
21-40	7-16 years		2
41-60	Small adult		3
>60	Large adult		4

Repeat the dose of artesunate suppository **every 12 hours** if referral has still not been possible.

> See job-aid about administration of Artesunate rectocaps in Annex 5

7. TREATMENT OF SEVERE MALARIA

Severe malaria is a **medical emergency**. Early recognition, repeated assessment, and appropriate and prompt antimalarial treatment and supportive therapy is key to successful management. Any delay in diagnosis and inappropriate treatment, especially in infants and children, can rapidly lead to a worsening of the patient's condition.

Treatment of severe malaria should be given **parenterally**. If parenteral treatment is not possible, artesunate suppositories should be given.

7.1 Immediate supportive treatment and assessment

An open airway should be secured in unconscious patients and breathing and circulation assessed.

The patient should be weighed, so that medicines and fluids can be given accordingly.

An intravenous cannula should be inserted and immediate measurements of blood glucose (stick test), haematocrit/haemoglobin, parasitaemia and, in adults, renal function should be taken.

A detailed clinical examination should be conducted, including a record of the coma score.

Unconscious patients should have a lumbar puncture for cerebrospinal fluid analysis to exclude bacterial meningitis.

The degree of acidosis is an important determinant of outcome; the plasma bicarbonate or venous lactate level should, therefore, be measured, if possible. If facilities are available, arterial or capillary blood pH and gases should be measured in patients who are unconscious, hyperventilating or in shock.

7.2 Injectable artesunate in health centers and hospitals

Parenteral artesunate (i.v. or i.m.) is the medicine of choice **for severe for all adults and children (including infants, pregnant women in all trimesters, and lactating women)**.

Compared to quinine, artesunate significantly reduces the risk of death, and lowers the risk of treatment-associated side effects including hypoglycaemia.

Intravenous drug administration should be preferred and used wherever possible; however, if i.v. treatment is not feasible, intramuscular drug administration should be applied. The most important is not to waste time in starting the antimalarial treatment.

Parenteral artesunate treatment should always be followed by a **full standard course of oral treatment with ALU**.

Artesunate treatment schedule

Dose 1: on admission

Continue parenteral artesunate for **a minimum of 24 hours** (3 doses)

Dose 2: 12 hours after first dose
Dose 3: 24 hours after first dose

One dose daily thereafter until oral treatment is possible

Schedule for administration of parenteral artesunate (hours after first injection)						
0	12	24	36	48	60	72
①	②	③		④		⑤

Full course of oral ACT treatment after 24h if possible
When the patient can take oral treatment, give a full course of oral artemether-lumefatrine (6-doses over 3 days).

Preparation of Artesunate for intravenous (i.v.) route

Reconstitute the 1 ml solution of artesunate powder with bicarbonate solution

Dilute in **5 ml of saline solution** (or dextrose 5%) – do not use water for injection

Calculate the dose and volume required (dilution of **60mg in 6ml**)

Administer i.v. with slow bolus 3-4ml per minute.

> See Annex 3 and job-aid about preparation of Artesunate injections in Annex 5

Preparation of Artesunate for intramuscular (i.m.) route

Reconstitute the 1 ml solution of artesunate powder with bicarbonate solution

Dilute in **2 ml of saline solution** (or dextrose 5%) – do not use water for injection

Calculate the dose and volume required (dilution of **60mg in 3ml**)

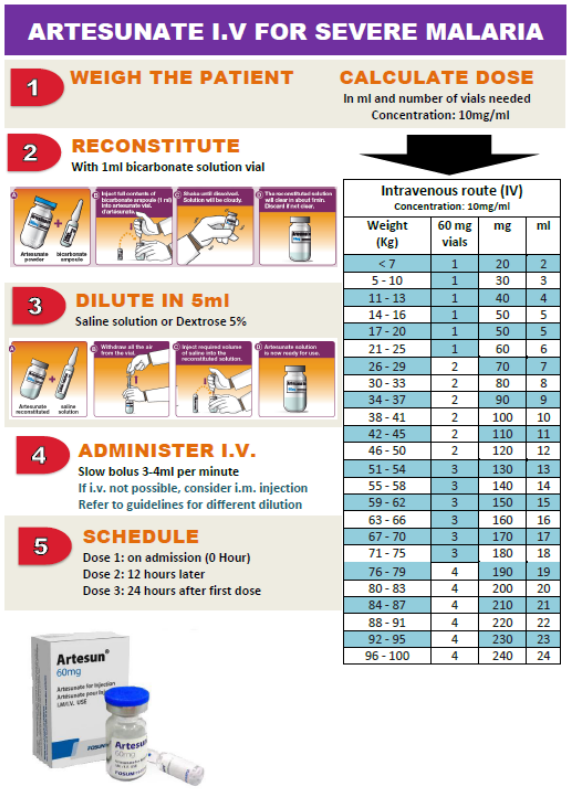
Administer i.m. slowly in the anterior thigh. One half should be injected in each thigh if volume is more than 5ml.

Dosing tables for Artesunate injections

While the dosage of 2.4 mg/kg is the same for i.v. and i.m. administration, the **concentration** of the mixtures is different because of the different ways in which the mixtures are prepared:

Children weighing less than 20 kg should receive a higher dose of artesunate (3 mg/kg/dose) than larger children and adults (2.4 mg/kg/dose) to ensure an equivalent drug exposure.

> See Annex 3 and job-aid about preparation of Artesunate injections



Intravenous route (IV)
Concentration: 10mg/ml

Weight (Kg)	60 mg vials	mg	ml
< 7	1	20	2
5 - 10	1	30	3
11 - 13	1	40	4
14 - 16	1	50	5
17 - 20	1	50	5
21 - 25	1	60	6
26 - 29	2	70	7
30 - 33	2	80	8
34 - 37	2	90	9
38 - 41	2	100	10
42 - 45	2	110	11
46 - 50	2	120	12
51 - 54	3	130	13
55 - 58	3	140	14
59 - 62	3	150	15
63 - 66	3	160	16
67 - 70	3	170	17
71 - 75	3	180	18
76 - 79	4	190	19
80 - 83	4	200	20
84 - 87	4	210	21
88 - 91	4	220	22
92 - 95	4	230	23
96 - 100	4	240	24

7.3 Quinine infusion as alternative treatment

Indications of alternative treatment with quinine i.v. infusions:

1. Artesunate injectable is not available
2. Treatment failure of the artemisinin derivatives
3. Known patient hypersensitivity to artemisinins

Administration of Quinine by intravenous (i.v.) route

CAUTION: Quinine must never be given by intravenous bolus injection, as lethal hypotension may result. Quinine should be given by **rate-controlled infusion** in saline or dextrose solutions at a rate not exceeding 5 mg salt/kg body weight per hour.

Dosing of quinine by intravenous (i.v.) route

Quinine dihydrochloride 600mg

- First **loading dose**: i.v. **20mg/kg diluted in 10ml/kg**
  given in dextrose/saline infusion rate-controlled over 4 hours.

- **Maintenance dose**: i.v. **10mg/kg diluted in 10ml/kg**
  given in dextrose/saline infusion rate-controlled over 4 hours.

- Maintenance dose is given **every 8 hours** for both adults and children

Schedule of quinine by intravenous (i.v.) route

Schedule for administration of quinine i.v. (hours after first injection)						
0	**4**	**8**	**12**	**16**	**20**	**24**
Maintenance dose every 8 hours						
Loading		**Maintenance**		**Maintenance**		**Maintenance**

Full course of oral ACT treatment after 24h if possible
When the patient can take oral treatment, give a full course of oral artemether-lumefatrine (6-doses over 3 days).

8. PREVENTION OF MALARIA FOR PREGNANT WOMEN

Weekly chemoprophylaxis during pregnancy:

Chloroquine tablets **5mg base/kg once a week**, from the first antenatal visit and for the remaining pregnancy period.

Chloroquine is available by 150mg base tablets

9. PREVENTION FOR TRAVELLERS

Depending on the malaria risk in the area to be visited and the local patterns of resistance to antimalarial medicine, the recommended medicine may be chloroquine, chloroquine plus proguanil, atovaquone-proguanil or doxycycline:

- **Chloroquine alone** can only be recommended for areas where malaria is due exclusively to P. vivax or fully chloroquine-sensitive P. falciparum.

- **Chloroquine + proguanil** can be recommened for areas where both P. vivax and P. falciparum malaria transmission co-exist and where chloroquine resistance is emerging.

- **Atovaquone-proguanil or doxycycline** (selected according to reported resistance pattern) are recommended for areas with (i) high risk of P. falciparum malaria, in combination with reported antimalarial drug resistance; (ii) moderate/low risk of P. falciparum malaria, in combination with reported high levels of drug resistance.

These drugs are not on Essential Drug List. Consider purchase from private pharmacies.

10. ANNEXES

ANNEX 1: REFERENCES

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http://www.who.int/malaria/publications/atoz/policy-brief-withdrawal-of-oral-artemisinin-based-monotherapies/en/

ANNEX 2: PERFORMING A MALARIA RAPID TEST (RDT)

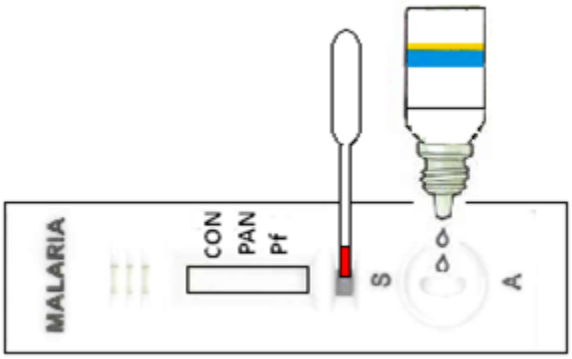
1- Instructions to perform an RDT

Step 1: Preparation
Prepare all materials needed to perform the test and to record the result, such as the RDT device itself, pipette, pencil/marker, timer.
Write the patient ID and date on the back side of the cassette test.
Record the patient name and date on the RDT record book.
Always check the expiry date on the packet, to make sure it is valid to use.

Step 2: Blood collection
Open the alcohol swab. Clean the patient's 4th finger.
Once the patient's finger is dry, open the lancet.
Prick the patient's finger, preferably towards the side of the pulp.
Collect a small volume of blood from a finger-prick, using pipette. Get the tip of the pipette onto the blood drop and gently suck up the blood up to the line (5 µl).

Step 3: Transfer blood into the cassette
Transfer blood into cassette by putting the drop of blood into « S » square window squeezing the pipette bulb.

Step 4: Insert buffer into the cassette
Holding the buffer bottle vertically, slowly put **2 drops** of buffer into the circle marked "A"



Step 5: Wait for 20 minutes

Step 6: Read the result after 20 minutes

2- Interpretation and recording of malaria RDT results

The rectangular hole is where you read the test results.

The CON section tells you whether the test has worked correctly. A line must appear for the test to be valid. If no line appears here, the test is not working properly and the result is invalid. You must discard the cassette and test the patient again using a new test.

No line in « CON »
= Invalid
CONCLUSION: The patient must be re-tested!

A line in « CON » only
= Negative
CONCLUSION: The patient does not have malaria. Malaria treatment is NOT required!

A line in « CON » and a line in « Pf »
= Positive for falciparum malaria
CONCLUSION: The patient has falciparum-malaria.

A line in « CON » and a line in « PAN »
= Positive for non-falciparum malaria
CONCLUSION: The patient has a malaria infection OTHER than falciparum, typically vivax-malaria.

Lines in « CON » and a line in « PAN » and « Pf »
= Positive for falciparum malaria and other species
CONCLUSION: The patient has a mixed infection of falciparum and another malaria species, typically vivax-malaria.

Note: test is positive even if the “Pf or PAN” lines in the test window are very faint.

> See job-aid on RDT testing

3- Record RDT result and treatment

Record the RDT result into the RDT record book
Complete the Malaria Line List if you give antimalarial treatment to the patient.

4- Dispose waste correctly

After performing the blood test, dispose all medical waste appropriately.

ANNEX 3: PREPARATION OF ARTESUNATE INJECTIONS

Artesunate injection will be available in Hospitals, Health Centres and Dispensaries.

Preparation of **ARTESUNATE INJECTIONS**:

Each pack of artesunate Injection contains:

- Vial of **60 mg of artesunate powder**
- Vial of **1 ml of sterile sodium bicarbonate (5%)** fluid

In addition you need:

- 1 or 2 vials of 5 ml of sterile normal saline (0.9%) OR 5ml of sterile dextrose (5%) fluid.

Important points in using artesunate injection (i.v. or i.m.):

- The prepared Artesunate injection should always be used immediately after mixing.
- The required amount of injection should be given slowly (over 2 - 3 minutes).
- Partially used vials should be discarded.
- Artesunate powder for injection is difficult to dissolve and care must be taken to ensure that it is completely dissolved before i.v. or i.m. injection. If the solution is cloudy or a lump is present, it should be discarded!

Preparation:

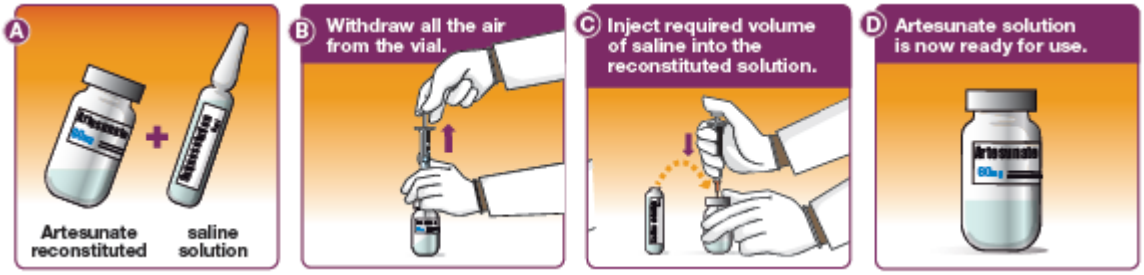
For Intravenous Use:

- Insert **1ml of sterile sodium bicarbonate (5%)** into the **artesunate powder** vial and SHAKE WELL 2-3 minutes until completely dissolved and the solution becomes clear.

CAUTION: If a completely clear solution cannot be obtained, it should be discarded.

- Add **5 ml of sterile sodium chloride (0.9%) OR 5 ml dextrose (5%)** - as available - to the same artesunate vial and SHAKE WELL again.

- This gives a concentration of **artesunate 10mg per ml of injectable solution**.



Can regular water for injection be used as a dilutant?
There is no data to show that water for injection is an appropriate dilutant. Artesunate should only be diluted with either 5% dextrose or normal saline.

How to proceed with preparation of more than 1 artesunate vial?
1. Line up your reconstituted vials for one patient.
2. Use one syringe to reconstitute each vial with the bicarbonate and carefully set each reconstituted vial to one side.
3. Use a new syringe to dilute each vial with the correct volume of saline and set aside
4. Administer the contents of vials to the patient by using a new syringe that is large enough to draw up the full dose from each of your reconstituted and diluted vials.

Administration

Inject intravenously slowly over 2-3 minutes.

For Intramuscular Use

- Insert **1ml of sterile sodium bicarbonate (5%)** into the **artesunate powder** vial and SHAKE WELL 2-3 minutes until completely dissolved and the solution becomes clear.

CAUTION: If a completely clear solution cannot be obtained, it should be discarded.

- Add **2 ml of sterile sodium chloride (0.9%) OR 2 ml of dextrose (5%)** - as available -to the same artesunate bottle and SHAKE WELL again.

- This gives a concentration of **artesunate 20 mg per ml of injectable solution.**

- Withdraw the necessary amount of the solution into a syringe and inject in the anterior thigh.

Intravenous route (IV) Concentration: 10mg/ml			
Weight (Kg)	**60 mg vials**	**mg**	**ml**
< 7	1	20	2
5 - 10	1	30	3
11 - 13	1	40	4
14 - 16	1	50	5
17 - 20	1	50	5
21 - 25	1	60	6
26 - 29	2	70	7
30 - 33	2	80	8
34 - 37	2	90	9
38 - 41	2	100	10
42 - 45	2	110	11
46 - 50	2	120	12
51 - 54	3	130	13
55 - 58	3	140	14
59 - 62	3	150	15
63 - 66	3	160	16
67 - 70	3	170	17
71 - 75	3	180	18
76 - 79	4	190	19
80 - 83	4	200	20
84 - 87	4	210	21
88 - 91	4	220	22
92 - 95	4	230	23
96 - 100	4	240	24

Intramuscular route (IM) Concentration: 20mg/ml			
Weight (Kg)	**60 mg vials**	**mg**	**ml**
< 7	1	10	1
7 - 10	1	20	2
11 - 13	1	30	2
14 - 16	1	40	3
17 - 20	1	50	3
21 - 25	1	60	3
26 - 29	2	70	4
30 - 33	2	80	4
34 - 37	2	90	5
38 - 41	2	100	5
42 - 45	2	110	6
46 - 50	2	120	6
51 - 54	3	130	7
55 - 58	3	140	7
59 - 62	3	150	8
63 - 66	3	160	8
67 - 70	3	170	9
71 - 75	3	180	9
76 - 79	4	190	10
80 - 83	4	200	10
84 - 87	4	210	11
88 - 91	4	220	11
92 - 95	4	230	12
96 - 100	4	240	12

ANNEX 4: MANAGEMENT OF SEVERE CASES

Continued supportive treatment:

1- **Correct hypoglycaemia**:

Infusion of dextrose over a period of 3–5 minutes. This can be done by any one of the following procedures:

- 0.5–1ml/kg of 50% dextrose diluted with an equal volume of normal saline given by slow intravenous infusion over several minutes in children;
- 20–50ml of 50% dextrose given as intravenous bolus in adults;
- for other strengths of dextrose, calculate the volume accordingly;
- where intravenous access is impossible, give sugar solution by nasogastric tube
- re-check blood glucose 2–4 hourly during the course of treatment, particularly in comatose patients.

2- **Control convulsions:**

Correct hypoglycaemia if it is present.

Give rectal paracetamol if the temperature is above 39°C.

If the convulsions continue for more than 5 minutes give diazepam by slow intravenous injection (0.2-0.3 ml/kg bw, maximum 10mg for adults).

In children always calculate according to weight in order to avoid dangerous respiratory depression. Diazepam can be given rectally (0.3–0.5 mg/kg bw) only if injection is not possible. Monitor the breathing carefully. If the first dose of diazepam fails to control convulsions, a second dose may be given after 10 minutes. If seizures continue, give phenytoin (18mg/kg infused over 20 minutes as a loading dose, followed by 2.5mg/kg twice daily for 48 hours). If you have given two doses of diazepam and seizures continue, and if phenobarbitone is the only additional anticonvulsant drug available, you may give phenobarbitone (15 mg/kg im or iv loading dose, then 3-4 mg/kg daily for 48 hours), but extreme vigilance is necessary because these two drugs (phenobarbitone and diazepam) in combination may cause respiratory arrest - monitor breathing continuously and be ready to give assisted ventilation, by bag-and-mask if a manual ventilator is not available.

3- **Assess the patient's fluid requirements:**

Look for evidence of fluid depletion or overload in order to determine the appropriate rate of infusion. Children with severe metabolic acidosis may benefit from a resuscitation bolus of fluid, preferably a plasma expander, e.g. normal saline.

The usual route for fluid infusion is intravenous; if this cannot be achieved alternatives are intraosseous or nasogastric infusions. Intra-osseous infusion may be performed when there is life threatening hypovolaemia, under strict sterile procedure.

Reduce body temperature if greater than 39.5ºC. This is best done by giving paracetamol by mouth if possible, alternatively by suppository. In addition, remove the patient's clothes and start tepid sponging. Relatives can help with this task.

4- Consider the need for blood transfusion:

The most common indication for blood transfusion is severe anaemia (Hb < 5g/dl). Assess the patient's clinical condition rather than relying on the haemotocrit and/or Hb level. "Does the patient need blood?" is a more important question than "What is the PCV/Hb?"
If the patient's life is threatened by anaemia-associated acidosis, or by shock, or the parasitaemia is so high that a critical drop is predictable, packed cells (10ml/kg in children) or whole blood transfusion should be given urgently with furosemide as follows:
▷▷ if the patient has spontaneous bleeding give whole fresh blood if available or a platelet transfusion if possible;
▷▷ where blood is unavailable, give pre-referral treatment and refer the patient;
▷▷ if the patient is unconscious, insert a nasogastric tube and start the procedures for management of the comatose patient.

5- Continuing treatment and nursing care:

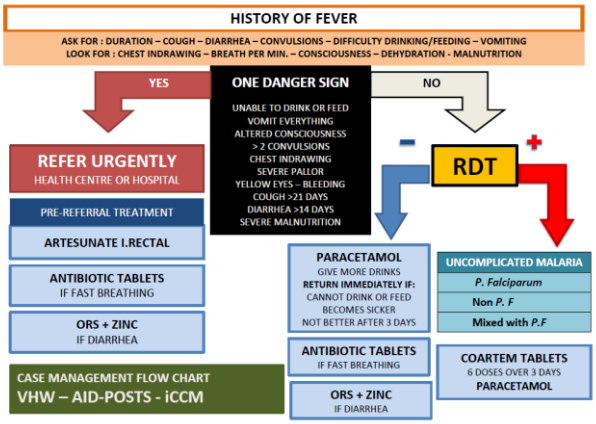
Continuing care calls for close cooperation between medical and nursing staff. Responsibility for various observations must be allocated according to the availability and expertise of personnel. Proper nursing care of the unconscious patient, in an intensive care unit if available, is of utmost importance in patients with cerebral malaria. The patient must be turned every two hours and not allowed to lie in a wet bed. Particular attention must be paid to pressure points and the patient should be nursed on his/her side to avoid aspiration of fluids. Sufficient nutritional support is necessary for patients who have a prolonged illness.

Following are the parameters to be monitored on a routine basis:

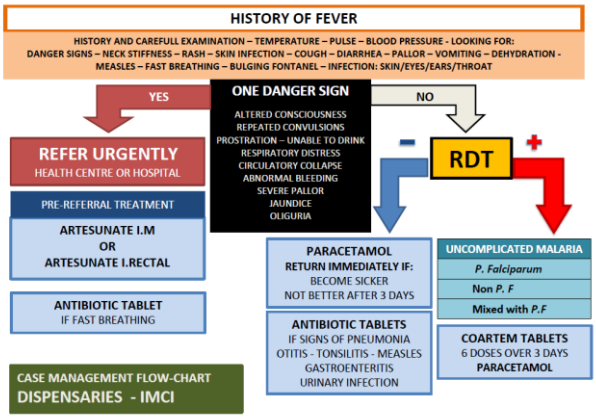
- level of consciousness (see Blantyre and Glasgow coma scales in Annex 1);
- vital signs: blood pressure, temperature, pulse rate and respiratory rate;
- fluid input and output. Examine regularly for signs of dehydration or fluid over load;
- urine volume, colour and specific gravity;
- blood glucose;
- parasitaemia;
- haemoglobin (Hb/Ht) if anaemia is suspected to be worsening;
- occurrence of convulsions;
- uterine contractions and fetal heart rate in pregnant women.

ANNEX 5: LIST OF JOB-AID AND STANDARD PROCEDURES

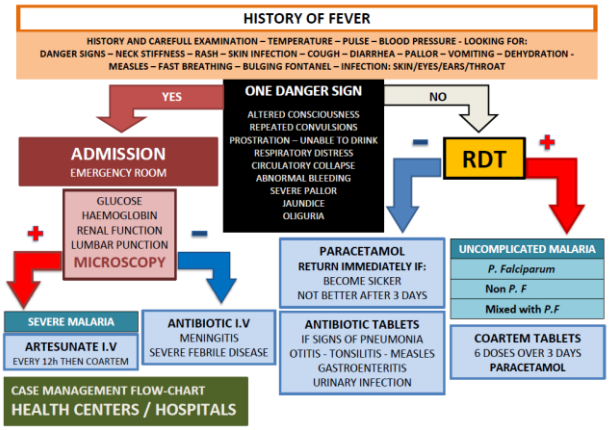
Flow chart about malaria case management in Aid-posts



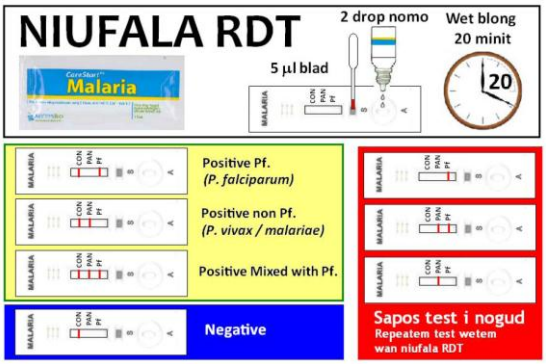
Flow chart about malaria case management in Dispensaries



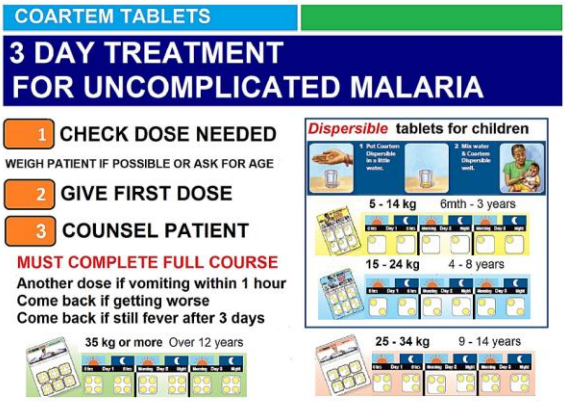
Flow chart about malaria case management in Health Centers and hospitals



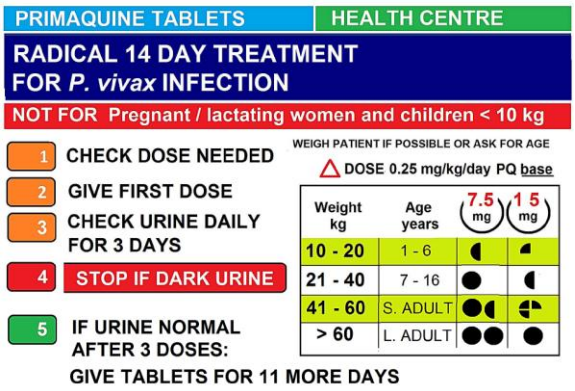
Job-aid to perform RDTs



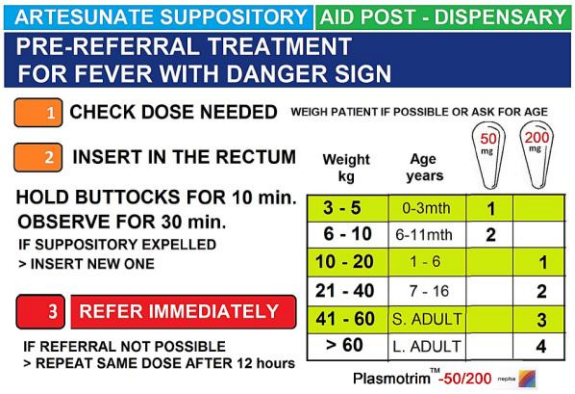
Job-aid about administration of Coartem



Job-aid about administration of primaquine



Job-aid about administration of rectal artesunate



ARTESUNATE SUPPOSITORY | AID POST - DISPENSARY

PRE-REFERRAL TREATMENT
FOR FEVER WITH DANGER SIGN

1 CHECK DOSE NEEDED — WEIGH PATIENT IF POSSIBLE OR ASK FOR AGE

2 INSERT IN THE RECTUM

HOLD BUTTOCKS FOR 10 min.
OBSERVE FOR 30 min.
IF SUPPOSITORY EXPELLED
> INSERT NEW ONE

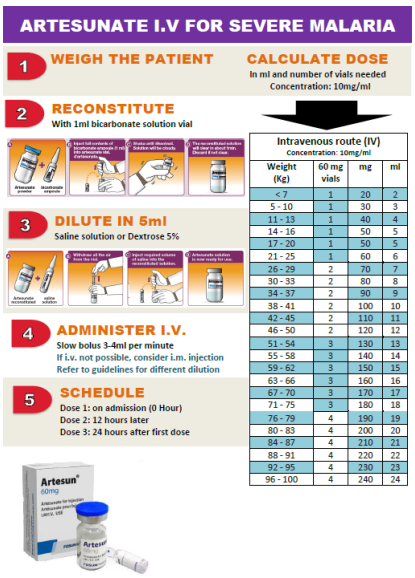
3 REFER IMMEDIATELY

IF REFERRAL NOT POSSIBLE
> REPEAT SAME DOSE AFTER 12 hours

Weight kg	Age years	50 mg	200 mg
3 - 5	0-3mth	1	
6 - 10	6-11mth	2	
10 - 20	1 - 6		1
21 - 40	7 - 16		2
41 - 60	S. ADULT		3
> 60	L. ADULT		4

Plasmotrim™ -50/200

Job-aid about administration of injectable artesunate



ARTESUNATE I.V FOR SEVERE MALARIA

1 WEIGH THE PATIENT — CALCULATE DOSE
In ml and number of vials needed
Concentration: 10mg/ml

2 RECONSTITUTE
With 1ml bicarbonate solution vial

3 DILUTE IN 5ml
Saline solution or Dextrose 5%

4 ADMINISTER I.V.
Slow bolus 3-4ml per minute
If i.v. not possible, consider i.m. injection
Refer to guidelines for different dilution

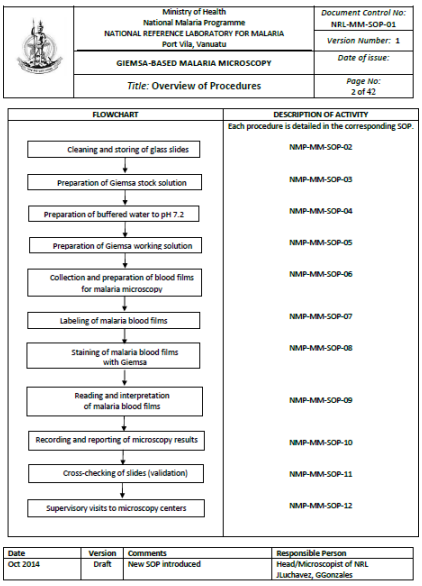
5 SCHEDULE
Dose 1: on admission (0 Hour)
Dose 2: 12 hours later
Dose 3: 24 hours after first dose

Intravenous route (IV)
Concentration: 10mg/ml

Weight (Kg)	60 mg vials	mg	ml
< 7	1	20	2
5 - 10	1	30	3
11 - 13	1	40	4
14 - 16	1	50	5
17 - 20	1	50	5
21 - 25	1	60	6
26 - 29	2	70	7
30 - 33	2	80	8
34 - 37	2	90	9
38 - 41	2	100	10
42 - 45	2	110	11
46 - 50	2	120	12
51 - 54	3	130	13
55 - 58	3	140	14
59 - 62	3	150	15
63 - 66	3	160	16
67 - 70	3	170	17
71 - 75	3	180	18
76 - 79	4	190	19
80 - 83	4	200	20
84 - 87	4	210	21
88 - 91	4	220	22
92 - 95	4	230	23
96 - 100	4	240	24

Artesun® 60mg

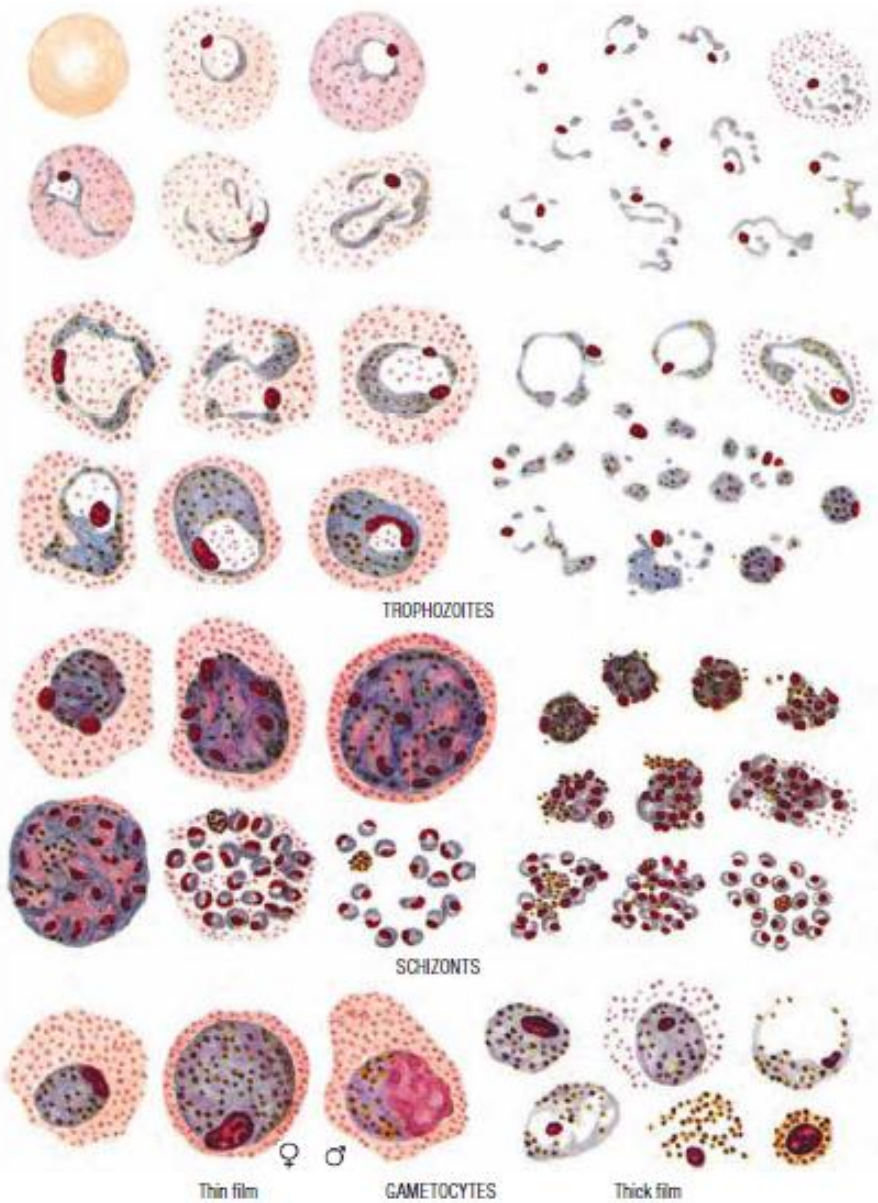
SOP for malaria microscopy NRL and QA



Ministry of Health National Malaria Programme NATIONAL REFERENCE LABORATORY FOR MALARIA Port Vila, Vanuatu	Document Control No: NRL-MM-SOP-01
	Version Number: 1
GIEMSA-BASED MALARIA MICROSCOPY	Date of issue:
Title: Overview of Procedures	Page No: 2 of 42

FLOWCHART	DESCRIPTION OF ACTIVITY Each procedure is detailed in the corresponding SOP.
Cleaning and storing of glass slides	NMP-MM-SOP-02
Preparation of Giemsa stock solution	NMP-MM-SOP-03
Preparation of buffered water to pH 7.2	NMP-MM-SOP-04
Preparation of Giemsa working solution	NMP-MM-SOP-05
Collection and preparation of blood films for malaria microscopy	NMP-MM-SOP-06
Labeling of malaria blood films	NMP-MM-SOP-07
Staining of malaria blood films with Giemsa	NMP-MM-SOP-08
Reading and interpretation of malaria blood films	NMP-MM-SOP-09
Recording and reporting of microscopy results	NMP-MM-SOP-10
Cross-checking of slides (validation)	NMP-MM-SOP-11
Supervisory visits to microscopy centers	NMP-MM-SOP-12

Date	Version	Comments	Responsible Person
Oct 2014	Draft	New SOP introduced	Head/Microscopist of NRL JLuchavez, GGonzales


TROPHOZOITES
SCHIZONTS
♀ ♂
Thin film
GAMETOCYTES
Thick film