

Ref: General Circular No:

Guidelines on malaria chemotherapy and management of patients with malaria

1. Background

With no indigenous malaria cases being reported since October 2012, Sri Lanka is currently in the malaria elimination and prevention of re-introduction phase. With progressively increasing incidence of imported malaria cases in recent years, early diagnosis and treatment of such cases have become the highest priority for prevention of re-introduction. Most of these infections have been acquired in India, Pakistan, South East Asian and African countries.

Currently, a low level of clinical suspicion in the backdrop of a very low disease burden has led to a significant delay in diagnosis of malaria cases. As a result, there were several patients who presented to the health care institutions with uncomplicated fever progressing to develop severe malaria while being at the hospital.

2. Patients likely to have malaria

Malaria should be suspected in:

1. any febrile individual (including foreign nationals):
 - with unexplained fever and a history of recent travel (within 1 year) to a malaria endemic country (esp. India, Pakistan, Haiti and African countries). Refer Annex II for a list of countries where malaria transmission occurs).
 - belonging to high risk groups e.g. businessmen, pilgrims and seamen returning from malaria endemic countries, re-settled communities, skilled and unskilled foreign workers, illegal/irregular migrants, refugees, asylum seekers, security forces returning from peace keeping missions etc.
 - with a history of malaria infection within the past 3 years
 - with fever of unknown origin
2. any individual presenting with clinical features of severe malaria (refer Annex I for clinical features of severe malaria)
3. Patients with anaemia of unknown cause
4. Patients with hepatomegaly and/or splenomegaly
5. Recipients of blood or blood products who develop fever within 3 months of transfusion

Please note:

- Malaria can present with non-specific symptoms even if there is no fever.
- Thrombocytopenia has been a frequent finding among patients with malaria reported in the recent years, yet a diagnosis of malaria has not been considered as a result of them being misdiagnosed as having dengue. This had led to a delayed malaria diagnosis resulting in adverse sequelae.

3. Notification of malaria patients

Any patient strongly suspected of having malaria should **immediately** be notified via telephone to the Regional Malaria Officer (RMO) and Anti Malaria Campaign Headquarters. In addition, it should be notified to the Medical Officer of Health (MOH) of the area where the patient resides following the standard notification procedure (Form H544).

The AMC will ensure:

- confirmation of diagnosis by species
- provision of appropriate anti-malarial drugs
- guidance on treatment
- initiation of rapid response to search for additional cases and prevent onward transmission of the disease
- follow up of the patient in the field in order to achieve radical cure.

The contact numbers of the AMC Headquarters and the RMOs are given in *Annex III*.

4. Diagnosis of malaria

- In every suspected case of malaria, laboratory confirmation by microscopic examination of blood smears and/or Rapid Diagnostic Test (RDT) is mandatory prior to initiation of anti-malarial treatment. Treating malaria based on clinical suspicion without laboratory confirmation should be avoided.
- If there is a strong clinical suspicion of malaria, and the blood smears/RDT are negative at the time of initial testing, a minimum of three consecutive blood smears/RDT should be done prior to concluding that the patient is negative for malaria.
- Blood should be collected for investigations prior to the administration of anti-malarials:
 - In all confirmed malaria patients
 - If anti-malarial treatment is required as a life saving measure based on clinical suspicion without laboratory confirmation of malaria
- Blood should be collected in the following manner:
 - 2ml of venous blood collected to an EDTA bottle and refrigerated until transported to the AMC headquarters.
 - Dried blood spots on filter paper: drop the blood in the syringe on the filter paper labeled with the patient's name; four blood spots with 3 drops per each spot. Air dry for one hour at room temperature. Place each filter paper in an individual envelope. Store at room temperature until transported to the AMC Headquarters. *(Please contact AMC Headquarters for details).*

5. Monitoring during treatment and follow up of patients

- To ensure an effective parasitological response to the anti-malarial drugs, a blood smear should be obtained daily and examined over the three day that the patient is admitted. If parasitaemia persists beyond 3 days blood smears should be taken daily until parasitaemia clears. In severe malaria cases, blood smears have to be taken at a higher frequency.
- Thereafter the patient will be followed up to one year (frequency and duration will depend on the species) by the AMC field staff.

6. Treatment of patients with malaria

Specific treatment and management of malaria will depend on the parasite species causing infection, severity of disease and the biological factors of the patient.

- Objectives of treatment:
 - Primary objective of treatment: to ensure rapid and complete elimination of the Plasmodium parasite from the patient's blood in order to prevent progression of uncomplicated malaria to severe disease or death.
 - From a public health perspective: to reduce transmission of the infection to others by reducing the infectious reservoir and to prevent the emergence and spread of resistance to anti-malarial medicines.
- All confirmed malaria patients should be admitted to a medical institution for a minimum of 3 days to be managed under supervision.
- If facilities are available, a test for G6PD deficiency should be carried out prior to administration of primaquine.

6.1 Mono-infection with *Plasmodium vivax*

- For radical cure of *P. vivax* malaria, the patient should be treated with chloroquine and primaquine.
- **Chloroquine:** base at a total dose of 25 mg/kg body weight (bw) over three days. This dose should be divided as 10mg/kg on the first and second day followed by 5 mg/kg bw on the third day.
- **Primaquine:** the adult dose is 15mg base (0.25mg/kg per day) for fourteen days unless it is contraindicated. The administration of primaquine is not recommended during pregnancy and lactation, infancy and in severe G6PD deficiency (<10% of residual enzyme activity).
- In patient with mild to moderate G6PD deficiency (10-60% of residual enzyme activity) primaquine can be administered in a dosage of 0.75 mg/kg weekly for 8 weeks under specialized supervision.

6.2 Uncomplicated mono-infection with *Plasmodium falciparum*

- For radical cure of falciparum malaria, the patient should be treated with ACT and primaquine.
- **Artemisinin based combination Therapy (ACT):** Weight appropriate dose. Coartem® (containing 20mg of artemether and 120mg of lumefantrine) is the ACT used in Sri Lanka.
- Artemisinin and its derivatives should never be used as monotherapy.
- Coartem® tablets are packed in four colour coded blister packs. The recommended treatment is 6-dose regimen over a three day period according to the weight of the patient as indicated in table 1.

Table 1. Number of ACT (Coartem®) tablets administered based on weight of patient

Interval between doses	5 -14 kg (Yellow Pack)	15 -to 24 kg (Blue Pack)	25- 34 kg (Orange pack)	>35 kg (Green pack)
0 Hours	1	2	3	4
8 Hours	1	2	3	4
24 Hours	1	2	3	4
36 Hours	1	2	3	4
48 Hours	1	2	3	4
60 Hours	1	2	3	4
Total	6	12	18	24

ACT should be taken immediately after a meal or drink containing at least 1.2g of fat (e.g. a glass of milk) since its absorption is enhanced by co-administration with fat. As low blood levels of ACT with treatment failure could potentially result from inadequate fat intake, it is essential that patients or carers are informed of the need to take Coartem® with milk or fat containing food, particularly on the second or third day of treatment.

- **Primaquine:** A weight appropriate single dose of primaquine (0.75mg/kg bw) should be administered **unless contraindicated**, on day 3 of treatment or prior to discharge from hospital to destroy gametocytes.

Uncomplicated *P. falciparum* malaria in infants and young children

- ACT (Coartem®) is the first line treatment in infants and young children.
- Primaquine should be avoided in children less than 1 year of age.
- An acutely ill child requires careful clinical monitoring as she/he may deteriorate rapidly.
- Please contact Anti Malaria Campaign Headquarters for further guidance.

Uncomplicated *P. falciparum* malaria in Pregnancy

- **1st Trimester:** Uncomplicated falciparum malaria is treated with oral quinine sulfate 10mg/kg bw at 8 hourly intervals plus clindamycin 10 mg/kg bw twice a day for 7 days. If clindamycin is unavailable, quinine monotherapy may be given.
- **2nd and 3rd Trimester:** Uncomplicated falciparum malaria is treated with Coartem®.
- Primaquine should not be administered during pregnancy.

Uncomplicated *P. falciparum* malaria during Lactation

- Lactating women can receive the recommended dose of Coartem®.
- Primaquine should not be given during lactation.

6.3 Uncomplicated mixed infections with *P. falciparum* and *P. vivax*

- Artemisinin based combination therapy: Coartem® is given at a weight appropriate dose.
- Primaquine base: at a dose of 0.25mg/kg bw per day for fourteen days unless it is contraindicated.

6.4 Severe *P. falciparum* malaria

Severe malaria is a medical emergency. After rapid clinical assessment and confirmation of the diagnosis, full doses of parenteral antimalarial treatment should be started without delay. Patients with severe malaria require intensive nursing care, preferably in an intensive care unit where possible. Clinical observations should be made as frequently as possible. These should include monitoring of vital signs, coma score, and urine output. Blood glucose should also be monitored every four hours, if possible, particularly in unconscious patients.

- **Intravenous artesunate**, 2.4mg/kg bw given on admission (time = 0), then at 12 hour and 24 hour, then once a day until the patient is able to take oral medication. If intra venous administration is not possible, it can also be given as an intramuscular injection.

If parenteral artesunate is **NOT** available:

- **Quinine dihydrochloride**, 20mg salt/kg bw (loading dose) on admission, then 10mg/kg every 8 hours. Each dose is given as a rate controlled intra venous infusion diluted in 10ml/kg bw of isotonic fluid over 2-4 hours at an infusion rate that should not exceed 5mg salt/kg body weight per hour.

The most important adverse effect is hyperinsulinaemic hypoglycaemia. Hypotension and cardiac arrest may result from rapid intravenous injection. Quinine causes prolongation of the electrocardiograph QT interval. Therefore; this administration should be accompanied by frequent blood glucose monitoring to prevent hypoglycaemia and cardiac monitoring.

Duration of parenteral treatment

Give parenteral antimalarials in the treatment of severe malaria for a minimum of 24 hours, even if the patient can tolerate oral medication.

Follow up on oral treatment

Complete the treatment by giving a full course of Coartem® as soon as the patient is able to take oral medication, but not before a minimum of 24 hours of parenteral treatment. This should be followed by a single dose of primaquine.

Artesunate is dispensed as a powder of artesunic acid. This powder is dissolved in 1ml of 5% sodium bicarbonate to form sodium artesunate. The solution is then diluted with 5 ml of 5% dextrose and given immediately by intravenous bolus ('push') injection or by intramuscular injection (to the anterior thigh). The solution should be prepared freshly for each administration and should not be stored.

Severe *P. falciparum* malaria in pregnancy

- 1st Trimester: should be treated with parenteral quinine until clinical improvement, followed by oral quinine therapy for a total of 7 days.
- 2nd and 3rd Trimester of pregnancy: parenteral artesunate/quinine can be administered as above. After clinical improvement, Coartem® should be administered in the weight appropriate dose.

Please note: Primaquine should not be administered during pregnancy.

Severe *P. falciparum* and *P. vivax* mixed infections

- Parenteral administration of artesunate or quinine dihydrochloride followed by a full course of oral Coartem® (as described in management of severe falciparum malaria).
- These patients should be given a course of primaquine base at a dose of 0.25mg/kg per day for fourteen days unless it is contraindicated.

6.5 Patients infected with other malaria parasites

The recommended treatment for malaria caused by *P. ovale* is the same as that given to achieve radical cure in *P. vivax* malaria, i.e. with chloroquine and primaquine.

P. malariae should be treated with the standard regimen of chloroquine as for *P. vivax* malaria, but it does not require radical cure with primaquine.

7. Chemoprophylaxis for malaria

Chemoprophylaxis is not needed for visitors to Sri Lanka and anyone living within the country including pregnant women.

Chemoprophylaxis is recommended for travelers to malaria endemic countries (the list of countries where malaria transmission occurs is given in Annex II). Contact Anti Malaria Campaign to obtain chemoprophylactic drugs and for further details.

Annex I. Severe malaria

Definition of Severe malaria

Severe malaria is defined by clinical or laboratory evidence of vital organ dysfunction (WHO, 2012), in a patient with *P. falciparum* asexual parasitaemia and no other obvious cause of symptoms, the presence of one or more clinical or laboratory features classifies the patient as suffering from severe malaria.

Clinical features of severe malaria

- impaired consciousness (including unarousable coma);
- prostration, i.e. generalized weakness so that the patient is unable to walk sit up without assistance;
- multiple convulsions - more than two episodes in 24h;
- deep breathing, respiratory distress (acidotic breathing);
- acute pulmonary oedema and acute respiratory distress syndrome;
- circulatory collapse or shock, systolic blood pressure <80 mm Hg in adults and < 50 mm Hg in children;
- acute kidney injury;
- clinical jaundice plus evidence of vital organ dysfunction; and
- abnormal bleeding

Laboratory findings

- hyperparasitaemia
- hypoglycaemia (blood glucose <2.2 mmol/l or <40mg/dl);
- metabolic acidosis (plasma bicarbonate < 15 mmol/l);
- severe normocytic anaemia (in children: Hb <5g/dl, packed cell volume <15%. in adults: Hb<7g/dl, packed cell volume, PCV< 20%)
- haemoglobinuria;
- hyperlactataemia (lactate > 5 mmol/l);
- renal impairment (serum creatinine> 265 µmol/l);
- pulmonary oedema (radiological)

Reference:

WHO, 2012, *Management of severe malaria, A practical handbook*, 3rd Ed., World Health Organization

Annex II. Countries where malaria transmission occurs

Afghanistan	Dominican Republic	Madagascar	Saudi Arabia
Angola	Ecuador	Malawi	Senegal
Bangladesh	Equatorial Guinea	Malaysia	Sierra Leone
Belize	Eritrea	Mali	Solomon Islands
Benin	Ethiopia	Mauritania	Somalia
Bhutan	French Guiana	Mayotte	South Africa
Bolivia	Gabon	Mozambique	Sudan
Botswana	Gambia	Myanmar	Swaziland
Brazil	Ghana	Mexico	Suriname
Burkina Faso	Guatemala	Namibia	Thailand
Burundi	Guinea	Niger	Timor Leste
Cambodia	Guinea-Bissau	Nigeria	Togo
Cameroon	Guyana	Nepal	Tajikistan
Central African Rep.	Haiti	Nicaragua	Turkey
Chad	Honduras	Pakistan	Uganda
China	India	Panama	Tanzania
Colombia	Indonesia	Papua New Guinea	Vanuatu
Comoros	Iran	Peru	Vietnam
Congo	Iraq	Philippines	Venezuela
Costa Rica	Kenya	Paraguay	Yemen Socotra Island
Cote d'Ivoire	Lao PDR	Rwanda	Zambia
Djibouti	Liberia	Sao Tome & Principe	Zimbabwe

Note: There are some other countries with very limited malaria risk. For more details please refer International Travel and Health-2012 at http://www.who.int/ith/chapters/ith2012en_countylist.pdf

Annex III. Telephone numbers related to Anti Malaria Campaign

Anti Malaria Campaign Headquarters:

Tele: (011) 2588408, (011) 2368173
(011) 2368174
(011) 7626626 (hotline)
e-mail: antimalariacampaignsi@gmail.com
Website: www.malariacampaign.gov.lk

Regional Malaria Offices

Ampara	(063) 2223464	Kandy	(081) 2210687	Monaragala	(055) 2276698
Anuradhapura	(025) 2221844	Kegalle	(035) 2222549	Mullaitivu	(024) 3248341
Badulla	(055) 2226018	Kilinochchi	(024) 3247236	Polonnaruwa	(027) 2226018
Batticaloa	(065) 2222931	Kurunegala	(037) 2222193	Puttalam	(032) 2265319
Hambanthota	(047) 2220135	Maha	(037) 2275254	Ratnapura	(047) 2230301
Jaffna	(021) 2227924	Mannar	(023) 2222326	Trincomalee	(026) 2222584
Kalmunai	(067) 2220206	Matale	(066) 2222295	Vavuniya	(024) 2222954