Revised Malaria Treatment Regimen-2017

6th Version

National Malaria Elimination & Aedes Transmitted Diseases Control Program
Directorate General of Health Services (DGHS)
Ministry of Health & Family Welfare, Bangladesh

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Background

Based on the Revised Malaria Control strategy of early diagnosis and prompt treatment (EDPT) the then National Malaria Control Program, Bangladesh adopted the treatment regimen in 1994 through a consensus workshop. Since then, the treatment regimen was revised at several occasions. As the necessity arose over the period of time, the national program adopted required changes and updated the malaria treatment regimen. Any revision, whenever it took place, was done through consultation meetings with relevant partners, collaborators and stakeholders and due endorsement was taken.

The treatment guideline, adopted in 1994, was in place until its 1st revision in 2004. By then, there were evidences from several studies on monitoring of antimalarial drug resistance that Chloroquine had been found to be resistant to treatment of Plasmodium falciparum malaria to the extent ranging from 40% to 70% in the high endemic areas of Bangladesh. Besides this, commonly used drugs Fansidar and occasionally used drugs like Mefloquine was found to be resistant. Results of those various drug efficacy studies, as well as accessibility issues, raised concern for the national program. It deemed necessary to update the Malaria Treatment Regimen and related operational issues for providing treatment of all malaria cases in the endemic areas of Bangladesh with effective drugs to ensure radical cure. Therefore, the multidrug resistant status of falciparum malaria treatment had led to the 1st revision of the regimen in 2004.

Based on epidemiological situation and changes in the malaria paradigm, further revision of the malaria treatment regimen was again warranted in 2009. The 2004 version of the regimen adopted treatment as UMC (Uncomplicated Malaria Confirmed), UMP (Uncomplicated Malaria Presumptive) and SM (Severe Malaria) for Plasmodium Falciparum cases and VM (Vivax Malaria) for Plasmodium Vivax cases. But UMP cases were still being treated with Chloroquine. It created many controversies, as this group of patients were receiving ineffective drugs. It virtually did lead to no effective treatment and patients remained at risk of developing severe malaria. By then, field researches, quality data and experiences revealed that diagnosis by Rapid Diagnostic Test (RDT) was within reach and prompt treatment with Artemisinin Based Combination Therapy (ACT) were also easily available at

the community level. So, it was decided to discourage UMP and treat malaria cases on confirmatory diagnosis only. The necessary revision had been made in 2009 after reaching at a consensus with all relevant stakeholders. The revised Malaria Treatment Regimen 2009 includes revision of case definition and management of malaria with flow chart.

The further revision in malaria treatment regimen was made in 2014. It was decided to provide single dose of Primaquine (0.75 mg/kg) on 1st day of ACT or Q7T7/Q7D7/Q7C7 treatment for Plasmodium falciparum cases. However, it would not be applicable for pregnant women, infants (< 6 months of age) and lactating mother upto 6 months. Again, the dose of Primaquine was revised in 2016 from 0.75 mg/kg to 0.25 mg/kg. The latest revision of malaria treatment regimen in 2017 included the provision of providing ACT at all stages of pregnancy and treating infants weighing < 5 kg for uncomplicated Plasmodium falciparum / Mixed cases with ACT at the same mg/kg body weight target dose as for children weighing 5 kg. The necessary revision had been done in 2017 through a series of consultations with clinicians, public health experts, epidemiologist, program managers and other stakeholders. The 6th version of the revised malaria treatment regimen was also endorsed by the National Malaria Technical Committee.

Objective:

To update and revise the existing Malaria Treatment Regimen in Bangladesh with provision of early definitive diagnosis, prompt and appropriate treatment of cases.

Issues considered:

The following issues were considered during updating:

- Universal access to early diagnosis (RDT and Microscopy) and provision of prompt and appropriate treatment with ACT
- Provision of newer effective antimalarial drugs
- Increased awareness through intensive Behavior Change Communication (BCC)
- Specific evidences related to diagnosis, treatment and pharmacovigilance
- Potential partnership for effective service delivery
- Generating further evidences on safety of newer antimalarial drugs in the first trimester of pregnancy and child <5kg

Malaria Treatment Regimen

Revised Treatment Regimen for malaria has been adapted for:

- Early Definitive Diagnosis and Prompt Treatment (EDPT)
- Prevention or delay in development of durg resistance
- Interruption of transmission
- Reduction of morbidity and mortality.

Malaria case definition

1. Falciparum Malaria (FM)

a. Uncomplicated malaria (UM)--

- Fever or history of fever within last 48 hours
  and
- Absence of convincing evidence of any other febrile illness
  and
- No features of severe malaria
  and
- High index of suspicion based on time, place and person – (Enquiring about high risk groups – Jhum Cultivator, Forest goers, new arrival, H/O travel to endemic area, short term travelers)
  and
- Presence of asexual form of Plasmodium falciparum in Blood Slide Examination (BSE) or Rapid Diagnostic Test (RDT) +ve for *P. falciparum*

The diagnosis of malaria should be confirmed through RDT or BSE as symptom based clinical diagnosis of malaria may be unreliable.

b. Severe Malaria (SM)--

- Fever or history of fever within last 48 hours
  and
- One or more of the following clinical or lab features of severity:

Clinical features:

- Change of behavior, confusion or drowsiness
- Altered consciousness or coma (cerebral malaria)
- Generalized convulsions > 2 episodes in 24 hours
- Difficulty in breathing due to acute pulmonary oedema (with a respiratory rate > 30/min, often with chest indrawing and crepitations on auscultation)
- Acute Respiratory Distress Syndrome (ARDS) or deep breathing (acidotic breathing) (rapid, deep, laboured breathing).
- Circulatory collapse or shock: Compensated shock is defined as capillary refill ≥ 3 s or temperature gradient on leg (mid to proximal limb), but no hypotension. Decompensated shock is defined as systolic blood pressure < 70 mm Hg in children or < 80 mm Hg in adults, with evidence of impaired perfusion (cool peripheries or prolonged capillary refill) or (algid malaria)
- Clinical Jaundice
- Severe prostration, i.e. extreme generalized weakness, so patient cannot walk, stand or sit without assistance and in small child failure to feed
- Severe vomiting leading to 'non per os'.
- Bleeding tendency or abnormal spontaneous bleeding including recurrent or prolonged bleeding from nose, gums or venipuncture sites; Hematemesis or melaena
- Severe Anaemia
- Oliguria (<400 ml/24 hrs or 0.5 ml/kg/hr over 6 hours)

Laboratory features:

- Acidosis: A base deficit of > 8 mEq/L or, if not available, a plasma bicarbonate level of < 15 mmol/L or venous plasma lactate ≥ 5 mmol/L.
- Hypoglycaemia: Blood or plasma glucose < 2.2 mmol/L (< 40 mg/dL)
- Severe malarial anaemia: Haemoglobin concentration ≤ 5 gm/dl or a haematocrit of ≤ 15% in children < 12 years of age (< 7 gm/dl and <20%, respectively, in adults) with a parasite count > 10 000/μL

- ❖ Renal impairment: Plasma or serum creatinine > 265 µmol/L (3 mg/dL) or blood urea > 20 mmol/L
- ❖ Jaundice: Plasma or serum bilirubin > 50 µmol/L (3 mg/dL) with a parasite count 100 000/ µL,
- ❖ Pulmonary oedema: Radiologically confirmed or oxygen saturation <92% on room air
- ❖ Hyperparasitaemia: P. falciparum parasitaemia > 10% and
- ❖ Presence of asexual form of P. falciparum in BSE or +ve RDT for *P. falciparum*

II. Vivax Malaria (VM):

- ❖ Fever or history of fever within last 48 hours
  and
- ❖ Absence of convincing evidence of any other febrile illness
  and
- ❖ High index of suspicion based on time, place and person– (Enquiring about high risk groups – Jhum Cultivator, Forest goers, new arrival, No travel to endemic area, short term travellers)
  and
- ❖ Presence of asexual form of Plasmodium vivax in Blood Slide Examination (BSE) or Rapid Diagnostic test (RDT) +ve for *P. vivax*

III. Mixed Infection:

Mixed malaria infections are common in endemic areas. In Bangladesh Plasmodium falciparum and vivax are common mixed malarial infections. Mixed infections are best detected by nucleic acid-based amplification techniques, such as PCR; they may be underestimated with routine microscopy.

Several RDTs can't detect mixed infection or have low sensitivity for detection of vivax malaria. BSE is preferable over RDT in mixed infection.

N.B:

- ❖ Results of RDT may be false positive in patient who received antimalarial drugs over 4 weeks.
- ❖ Very low parasite count may be missed by RDT.

Revised Malaria Treatment Regimen:

1. Falciparum Malaria (FM):

a. Uncomplicated Malaria (UM)--

Objective of Treatment of Uncomplicated Malaria:
The clinical objectives of treating uncomplicated malaria are to cure the infection as rapidly as possible and to prevent progression to severe disease. "Cure" is defined as elimination of all parasites from the body. The public health objectives of treatment are to prevent onward transmission of the infection to others and to prevent the emergence and spread of resistance to antimalarial drugs.

First line treatment:
Artemether +Lumefantrine combination (ACT) in 6 divided doses over 3 days

Drug	Day	No of Dose	Time at	5-<15 Kg	15-<25 Kg	25-<35 Kg	>35-Kg
Artemether +Lumefantrine combination (ACT)	Day-1	1st	0 hour	1	2	3	4
		2nd	8 hour	1	2	3	4
	Day-2	3rd	24 hour	1	2	3	4
		4th	36 hour	1	2	3	4
	Day-3	5th	48 hour	1	2	3	4
		6th	60 hour	1	2	3	4

Artemether + Lumefantrine combination (ACT) (20mg +120 mg) should be started immediately after confirming the diagnosis (0 hours). The second dose should be given 8 hours after the first dose. The subsequent dose will be given 24 hours after first dose or 16 hours after giving second dose. Then the dose are to be given 12 hourly until the total 6 doses have been achieved. The calculated dose for adults and children are given in the box (e.g. for adults 4 tab stat. Second dose is given 8 hours after first dose. Then 4 tab 12 hourly for next two days).

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

If Artemether +Lumefantrin combination (ACT) cannot be given for any reason then follow alternative treatment.

Alternative treatment:

i) Artesunate + Amodiaquine*

Formulations currently available: A fixed-dose combination in tablets containing 25 + 67.5 mg, 50 + 135 mg or 100 + 270 mg of artesunate and amodiaquine, respectively

Target dose and range: The target dose (and range) are 4 (2–10) mg/kg bw/day artesunate and 10 (7.5–15) mg/kg bw/day amodiaquine once a day for 3 days. A total therapeutic dose range of 6–30 mg/kg kw/day artesunate and 22.5–45 mg/kg bw/dose amodiaquine is recommended.

Body weight (kg)	Artesunate + amodiaquine dose (mg) given daily for 3 days
4.5 to < 9	25 + 67.5
9 to < 18	50 + 135
18 to < 36	100 + 270
≥ 36	200 + 540

Treatment failure after amodiaquine monotherapy was more frequent among children who were underweight for their age. Therefore, their response to artesunate + amodiaquine treatment should be closely monitored.

◆ Artesunate + Amodiaquines associated with severe neutropenia, particularly in patients co-infected with HIV and especially in those on zidovudine and/or cotrimoxazole. Concomitant use of efavirenz increases exposure to amodiaquine and hepatotoxicity. Thus, concomitant use of artesunate + amodiaquine by patients taking artesunate + amodiaquine by patients taking zidovudine, efavirenz and cotrimoxazole should be avoided, unless this is the only ACT promptly available.

No significant changes in the pharmacokinetics of amodiaquine or its metabolite desethylamodiaquine have been observed during the second and third trimesters of pregnancy; therefore, no dosage adjustments are recommended.

No effect of age has been observed on the plasma concentrations of amodiaquine and desethylamodiaquine, so no dose adjustment by age is indicated. Few data are available on the pharmacokinetics of amodiaquine in the first year of life.

ii) Artesunate + Mefloquine

Formulations currently available: A fixed-dose formulation of paediatric tablets containing 25 mg artesunate and 55 mg mefloquine hydrochloride (equivalent to 50 mg mefloquine base) and adult tablets containing 100 mg artesunate and 220 mg mefloquine hydrochloride (equivalent to 200 mg mefloquine base).

Target dose and range: Target doses (ranges) of 4 (2–10) mg/kg bw/day artestmate and 8.3 (7–11) mg/kg bw/day mefloquine, given once a day for 3 days.

Body weight (kg)	Artesunate + amodiaquine dose (mg) given daily for 3 days
4.5 to < 9	25 + 67.5
9 to < 18	50 + 135
18 to < 36	100 + 270
≥ 36	200 + 540

Mefloquine increases incidence of nausea, vomiting, dizziness, dysphoria and sleep disturbance in clinical trials, but these symptoms are seldom debilitating and where this ACT has been used, it has generally been well tolerated.

To reduce acute vomiting and optimize absorption, the total mefloquine dose should preferably be split over 3 days, as in current fixed-dose combinations.

As concomitant use of rifampicin decreases exposure to mefloquine, potentially decreasing its efficacy, patients taking this drug should be followed up carefully to identify treatment failures.

iii) Dihydroartemisinin + Piperaquine

Children weighing <25kg treated with dihydroartemisinin + piperaquine should receive a minimum of 2.5 mg/kg bw/day of dihydroartemisinin and 20 mg/kg bw/day of piperaquine daily for 3 days.

Body weight (kg)	Dihydroartemisinin + Piperaquine dose (mg) given daily for 3 days
5 to < 8	20 + 160
8 to < 11	30 + 240
11 to < 17	40 + 320
17 to < 25	60 + 480
25 to < 36	80 + 640
36 to < 60	120 + 960
60 to < 80	160 + 1280
≥ 80	200 + 1600

Other alternative treatment:

- ❖ Quinine 7 days + Tetracycline 7 days (Q7+T7) or
- ❖ Quinine 7 days + Doxycycline 7 days (Q7+D7) or
- ❖ Quinine 7 days + Clindamycin 7 days (Q7+C7)

(Tetracycline and Doxycycline are contraindicated in children younger than 8 years old and in pregnant and lactating women)

Tab Quinine is to be given at a dose of 10 mg/kg body weight 8 hourly for 7 days. The calculated dose for adults and children are given in the box.

	Body weight (kg)					
	3-9	10-19	20-29	30-39	40+	Duration
Quinine TDS Tab. 300 mg Sulphate	$\frac{1}{4}$	$\frac{1}{2}$	1	$1\frac{1}{2}$	2	Treatment for 7 days

- ❖ Teteracycline: 250 mg 6 hourly for 7 days
- ❖ Doxycycline: 100 mg once daily for 7 days
- ❖ Clindamycin: 10 mg/kg twice daily for 7 days

The Artemether + Lumefantrine (ACT) & Quinine + Tetracycline/ Doxycycline /Clindamycin can be alternatively used if there is failure of any regimen. So if a patient had received Artemether + Lumefantrine (ACT) and after completion of the course still have uncomplicated malaria (parasitaemia), he or she will be treated with Quinine + Tetracycline/Doxycycline/Clindamycin and if any patient had received Quinine + Tetracycline/Doxycycline/Clindamycin will be treated with ACT.

Reducing the transmissibility of *P. falciparum* infections:

Primaquine: 0.25 mg/kg single dose to be given on 1st day of ACT or Q7T7/Q7D7/Q7C7 treatment

Primaquine should not be given to:

- ❖ Pregnant women
- ❖ Infants < 6 months of age and
- ❖ Lactating women up to 6 months

Treating uncomplicated *P. faliparum* malaria in special risk groups:

Infants less than 5kg body weight-

Treat infants weighing <5 kg with uncomplicated *P. falciparum* malaria with an ACT at the same mg/kg bw target dose as for children weighing 5 kg.

Patients co-infected with HIV-

In people who have HIV/AIDS and uncomplicated *P. falciparum* malaria do not use artesunate + amodiaquine if they are also receiving efavirenz or zidovudine.

Non-immune travelers-

Treat travellers with uncomplicated *P. falciparum* malaria returning to nonendemic area with an ACT.

Uncomplicated hyperparasitaemia-

Persons with *P. falciparum* hyperparasitaemia (4 to 10 %) are at increased risk of treatment failure, severe malaria and death. They should receive 1st dose of ACT and immediately admitted in the nearest hospital for close monitoring and treatment.

Special issues:

Plasmodium knowlesi: Human infections with the monkey malaria parasite *P. knowlesi* are being reported from the forested regions of South-East Asia. No *P. knowlesi* has been reported from Bangladesh.

b. Severe Malaria (SM):

Severe malaria is a medical emergency and the patient should be treated in a hospital.

Objective of Treatment of Severe Malaria:

The main objective of the treatment of Severe Malaria is to prevent malarial death. Secondary objectives are prevention of disabilities and prevention of recrudescent infection. Managements of Severe Malaria comprises clinical assessment of the patient, specific antimalarial treatment, additional treatment and supportive care. Death from Severe Malaria often occurs within hours of admission to a hospital, so it is essential that a highly effective parental antimalarial drug to be given as soon as possible.

⇨ **Specific antimalarial treatment for SM:**

- ❖ IV Artesunate is the drug of choice.
- ❖ If for any reason IV Artesunate cannot be given, then IM Artesunate or IM Artemether will be given.
- ❖ IV Quinine drip/IM Quinine are alternative parenteral anti-malarial if IV/IM Artesunate/IM Artemether are not available. Loading dose of Quinine should be given.
- ❖ Parenteral treatment is either:
  - ◆ IV Artesunate- 2.4 mg/kg body weight at 0 hr, 12 hrs, 24 hrs and then 24 hourly until the patient can tolerate oral medication but not more than 5 days. At least three doses or upto 24 hrs treatment with IV Artesunate should be used.
  - ◆ IV Artesunate dose will be remain same for organ dysfunction (e.g-renal failure, hepatic failure etc.)

    or

- IM artemether 3.2 mg/kg stat followed by 1.6 mg/kg daily until the patient can tolerate oral medication but not more than 5 days.

  or

- Quinine dihydrochloride 20 mg salt/kg stat followed by 10 mg/kg/8 hourly. This may be given by slow intravenous infusion over 3 -5 hours, or by intramuscular injection to the anterior thigh diluted 1:1 in sterile fluid (the first 20 mg/kg dose is split into 10 mg/kg to each anterior thigh). After 6 doses (including loading dose) the quinine dose will be reduced to 15-20 mg salt/kg body wt/day until the patient can take oral medication

Follow on treatment:

- Full dose of ACT (6 dose: e.g. 24 tab for adults) should be given once the patient can tolerate oral medication for follow on treatment.
- If for any reason ACT cannot be given for follow on treatment after IV Artesunate/Quinine, then oral Quinine and Tetracycline/ Doxycycline/ Clindamycin for 7 days should be given (Quinine, 10 mg/kg/dose 8 hourly).

Pre referral treatment:

Pre referral treatment saves life.

- Artesunate suppository should be used in all patients under 6 years of age during referral to hospital. Dose: 10 mg/kg body weight
- For above 6 years: IM Artesunate/IM Artemether/IM Quinine should be given. Dose of Quinine dihydrochloride is 20 mg salt/kg stat IM will be given half in each thigh.
- Hospitalization is must for complete treatment

2. Vivax Malaria (VM):

Objectives of Treatment of VM:

The clinical objectives of treating vivax malaria are to cure the infection as rapidly as possible and to prevent relapse. The public health objectives of treatment are to prevent onward transmission of the infection to others and to prevent the emergence and spread of resistance to antimalarial drugs.

If BSE and /or RDT is positive for *P. vivax* then it will be labeled as VM.

Treatment of Vivax Malaria (VM):

Chloroquine 3 days + Primaquine 14 days (CQ3+PQ14)

Dose Schedule:

- Chloroquine (CQ):
  - 1st day: 10 mg/kg (4 tabs for adult)
  - 2nd day: 10 mg/kg (4 tabs for adult)
  - 3rd day: 5 mg/kg (2 tabs for adult)
- Primaquine (PQ):
  - To be given along with choloroquine from first day.
  - 0.25 mg/kg for 14 days

Precaution:

G6PD deficient patient can develop severe haemolysis after getting primaquine, which can manifest by anaemia, jaundice, yellow colour of urine,vomiting and haemoglobinuria. If any one of these develops, then the drug should he stopped and patient should be hospitalized for blood transfusion and supportive management.

Patient receiving 14 days' Primaquine should have follow up information (Pharmacovigillance).

3. Mixed Infection:

Objectives of treatment of Mixed Infection:

The clinical objectives of treatment of Mixed Infection are to treat *P. falciparum* infection as wall as *P. vivax* infection to cure and to prevent onwards transmission/relapse.

- **ACT for 3 days + Primaquine for 14 days**

◆ Malaria in pregnant women

❖ **Falciparum Malaria (FM)**

a. Uncomplicated Malaria (UM):

Like non-pregnant woman with ACT in all trimester of pregnancy.

Alternate treatment will be 7 days of Quinine + Clindamycin (Q7+ C7)

b. Severe Malaria (SM):

- ❖ IV Artesunate is preferred antimalarials for SM in all trimester of pregnancy
- ❖ IM Artemether can be given in all trimester if for any reason IV Artesunate can not be given.
- ❖ In absence of parenteral Artemisinin derivative, IVQ/IMQ (Alternatively) should be given. Loading dose of Quinine should be given
- ❖ Oral follow on treatment will be ACT full dose after IV Artesunate/IM Artemethar/IV Quinine treatment

❖ **Vivax Malaria (VM):**

- ◆ Chloroquine 3 days (CQ3)

Chloroquine is safe in all trimester of pregnancy.

If the patient developed recurrent attack of vivax malaria, Chloroquine can be given in every episode of illness. Chloroquine is still highly sensitive and effective in vivax malaria.

Primaquine is contraindicated in any trimester of pregnancy and lactation upto 6 months. Radical cure can be done by primaquine during postpartum period preferably after 6 month if mother is nursing with breast feeding.

Chemoprophylaxis for malaria:-

May be used for special risk group or Children and short time travellers but discouraged.

Bangladesh is a multi-drug resistant area for Falciparum Malaria. Chloroquine, SP have very high failure rates. Quinine and Artemisinine derivatives are not suitable for prophylaxis.

So, recommendations are:

- ❖ To use personal preventive measures (bed net, mosquito repellents, protective wears etc.)
- ❖ All febrile episodes (up to 4 weeks following visit) should be investigated for malaria by RDT/ BSE and treatment with ACT if positive. If cannot be tested for Malaria, should be treated with ACT on suspicion.
- ❖ Mefloquine (250mg weekly for adult) may be used: to be started 2 weeks before and 4 weeks following visit.

Rationale for use/not to use of other drugs available in the market:

Chloroquine: Treatment Failure rate is high, so it should not be used in falciparum cases.

Sulphadoxine+Pyremethamine (Fansidar) : Failure rate is high.

Quinine Monotherapy: Effective but not recommended

Metloquine Monotherapy: Effective but not recommended

A**rtesunate Monotherapy:** Effective but not recommended

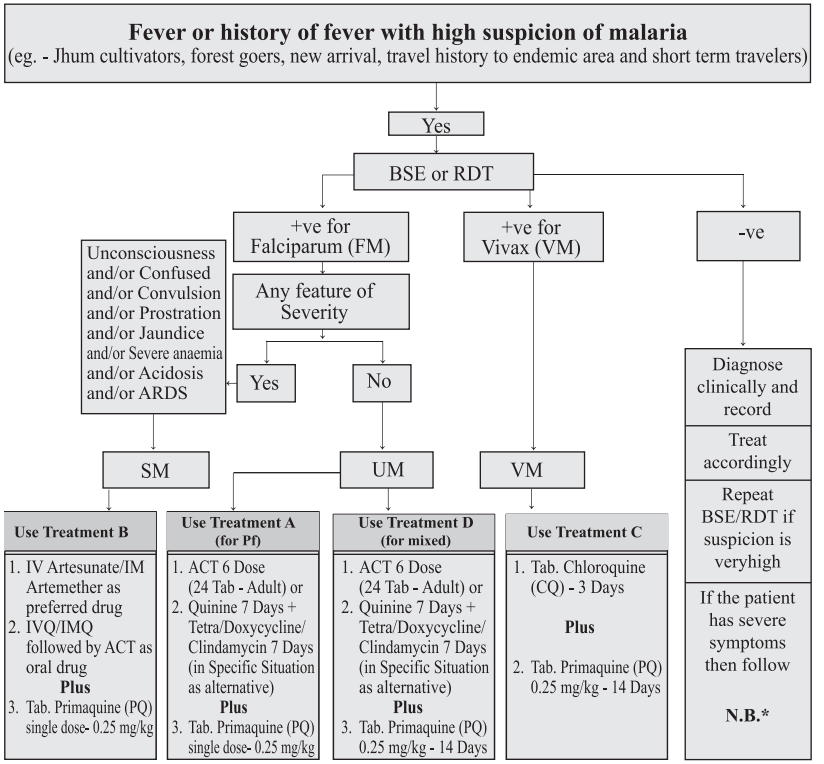
**Monotherapy is less effective and leads to early development of resistance and not recommended.

Implementation of treatment guideline

1. All health care providers should be trained on National Guideline.
2. Parasitological diagnosis of Malaria and drugs should be made available at all level.
3. RDT should be the method of choice for parasitological diagnosis at the community level.
4. Static health services should use microscopy or RDT for parasi -tological diagnosis
5. Use RDT for patients presenting in odd hours or in private health setting.
6. Provision of drugs for pre referral treatment at the community.
7. Education of the patient/attendant regarding completion of treatment should be emphasized.

MALARIA

DIAGNOSIS AND MANAGEMENT CHART



1. This chart is prepared for P.falciparum and mvax endemic zone.
2. Drug history is important as BSE may be negative despite malaria disease. RDT would become more important in those cases.BSE is more important for SM cases for diagnosing and monitoring in treatment
3. UM: uncomplicated malaria; 1/M : Vivax malaria; SM : Severe malaria
   BSE: blood slide examination; RDT: rapid diagnostic test, ACT: Artemesinin based combination therapy (e.g- Artemether+Lumifantrine)

N.B.*: If the patient is very sick and BSE/RDT are not available with very high suspicion of malaria, then parenteral treatment should be started immediately. RDT is preferred over BSE in urgent situation.

Treatment –A (UM)

1. Artemether +Lumefantrin combination (ACT)

Drug	Day	No of Dose	Time hrs	5- <15 kg	15- <25 kg	25-<35 kg	>35- kg
Tab. ACT	Day-1	1st	0	1	2	3	4
		2nd	8	1	2	3	4
	Day-2	3rd	24	1	2	3	4
		4th	36	1	2	3	4
	Day-3	5th	48	1	2	3	4
		6th	60	1	2	3	4

2. Q7+T7 or Q7+D7 or Q7+C7 may be alternative(s) [Q7 = Quinine for 7days]
Tetracycline: Adult (250 mg 6 hourly), Children above 8yrs (4mg/kg 6 hourly) Doxycycline: Adult (100 mg once daily), Children (3mg/kg once daily) Clindamycin: 10 mg/kg twice daily for 7 days

3. Alternative Regimen:

(a) Artesunate plus Amodiaquine

Body weight (kg)	Artesunate + amodiaquine dose (mg) given daily for 3 days
4.5 to < 9	25 + 67.5
9 to<18	50 + 135
18 to<36	100 + 270
> 36	200 + 540

(b) Artesunate plus Mefloquine

This is currently available as separate scored tablet containing 50 mg of Artesunate and 500 mg base of Mefloquine, respectively

Age	Dose in mg (no. of tablets)					
	Artesunate			Mefloquine		
	Day-1	Day-2	Day-3	Day-1	Day-2	Day-3
5-11 Months	25(½)	25	25	--	125 (¼)	--
1-6 years	50 (1)	50	50	--	205(½)	--
7-13 years	100(2)	100	100	--	500(1)	250(½)
>13years	200(4)	200	200	--	1000(2)	500(1)

►► In Specific & special situation

Drug	Dose (Weight in Kg)					
	3-9	10-19	20-29	30-39	40+	Duration
Tab. Quinine (300 mg)	¼ tab	½ tab	1 tab	1 ½ tab	2 tab	3 times daily for 7 days

Treatment B (SM)

Artemesinin derivatives: (First Line treatment)

Artesunate: 2.4 mg/kg IV stat and followed by 2.4 mg/kg at 0, 12 and 24 hours, then 2.4 mg/kg daily maximum 5 days, if the patient is able to swallow, the daily dose of ACT can be given orally.

Artemether: 3.2 mg/kg (loading dose) IM followed by 1.6 mg/kg daily for 5 days. If the patient can swallow, the daily dose of ACT can be given orally.

Oral follow on treatment:

ACT [Oral Artemether+Lumefantrine]: (After IV Artesunate/ IM artemether only). Dose- 6 doses

N.B.:

- Patient of less than 20 kg IV Artesunate should be started with dose of 3mg/kg stat.
- IV Artesunate dose will be remain same for organ dysfunction (e.g. renal failure, hepatic failure etc)
- ACT should be taken immediately after food or a fat containing drink (e g milk)

Quinine: (If Artemesinin are not available)

Loading dose: Quinine dihydrochloride 20 mg salt/kg of body weight (loading dose) by infusion over 4 hours in 5% dextrose saline (5-10 ml/kg of body weight depending on the patients overall fluid balance).

Maintenance dose: 8 to 12 hours after the start of the loading dose, give a maintenance dose of Quinine 10 mg salt/kg of body weight in dextrose saline diluted as above over 4 hours. This maintenance dose should be repeated every 8-12 hours, calculated from the beginning of the previous infusion until the patient can take oral medication (e.g. 08 hrs, 16 hrs, 24 hrs).

Oral Quinine: Quinine sulphate 10mg salt/kg, 8 hourly to complete a 7 days course of treatment (IV+Oral) with additional Tetracycline/ Doxycycline/ Clindamycin during oral follow on treatment.

Weight kg 8-12 Hourly	Quinine IV/IM (60mg/ ml) 3 times daily	Tab. Quinine Oral
3	½ m1	¼ tab
4-9	1 ml	¼ tab
6-9	1 ½ ml	¼ tab
10-14	2 ml	½ tab
1 5-19	3 ml	½ tab
20-24	4 ml	1 tab
25-29	5 ml	1 tab
30-39	6 ml	1 ½ tab
40-49	7.5 ml	1 ½ tah
50+	10 ml	2 tab

N.B.:

ACT is preferable during follow on treatment than Q+T/D/C even after IV quinine therapy in SM. If ACT is not available then only Q+T/D/C should be chosen for follow on treatment.

Treatment –C (VM)

Drug	Day	Dose (Weight in Kg)						
		3-5	6-9	10-19	20-29	30-39	40-49	50+
Tab. Chloroquine (150mg)	Day-1	¼	½	1	1 ½	2	3	4
	Day-2	¼	½	1	1 ½	2	3	4
Plus	Day-3	¼	½	1	1 ½	2	3	4
Tab. Primaquine (PQ)	0.25 mg/kg – 14 Days							

Treatment –D (Mixed Infection)

Drug	Dose
Tab. ACT **Plus**	6 doses for 3 days
Tab. Primaquine (PQ)	0.25 mg/kg for 14 Days
If ACT not available (Q7+T7) or (Q7+D7) or (Q7+C7) will be given as alternative treatment.	

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