



# Malaria Guideline for Healthcare Professionals

|                       |                                                                                                      |          |    |
|-----------------------|------------------------------------------------------------------------------------------------------|----------|----|
| Document Title:       | Malaria Guideline for Healthcare Professionals                                                       |          |    |
| Document Ref. Number: | DOH/GD/MGHP/ADPHC/V1/2024                                                                            | Version: | V1 |
| New / Revised:        | New                                                                                                  |          |    |
| Publication Date:     | May, 2024                                                                                            |          |    |
| Effective Date:       | August, 2024                                                                                         |          |    |
| Document Control:     | DoH Strategy Sector                                                                                  |          |    |
| Applies To:           | DoH licensed Healthcare Providers                                                                    |          |    |
| Owner:                | Abu Dhabi Public Health Center – Communicable Disease Department - Preparedness and Response Section |          |    |
| Revision Date:        | August, 2027                                                                                         |          |    |
| Revision Period:      | Three years from publication date                                                                    |          |    |
| Contact:              | <a href="mailto:ids@doh.gov.ae">ids@doh.gov.ae</a>                                                   |          |    |

## 1.Guideline Purpose and Brief

The purpose for this guideline is to standardize malaria case management including case definition, diagnosis, treatment, and prophylaxis. In addition to improve malaria surveillance in Emirates of Abu Dhabi. Malaria is considered a major public health issue globally. However, in United Arab Emirates malaria is an imported disease and associated with travel to other countries where malaria is endemic. Malaria is preventable and curable. It is one of the notifiable diseases in the United Arab Emirates.

## 2. Definitions and Abbreviations

| No.  | Term / Abbreviation | Definition                                   |
|------|---------------------|----------------------------------------------|
| 2.1  | ABGs                | Arterial Blood Gas                           |
| 2.2  | ACT                 | Artemisinin-Based Combination Therapy        |
| 2.3  | BID                 | Twice a Day                                  |
| 2.4  | CXR                 | Chest X-ray                                  |
| 2.5  | DEET                | N, N-Diethyl-meta-toluamide                  |
| 2.6  | ECG                 | Electrocardiogram                            |
| 2.7  | G6PD                | Glucose-6-phosphate dehydrogenase deficiency |
| 2.8  | GI                  | Gastrointestinal                             |
| 2.9  | HDU/ICU             | High Dependency Care / Intensive Care Unit   |
| 2.10 | HIV                 | Human Immunodeficiency Virus                 |
| 2.11 | ID                  | Infectious Diseases                          |
| 2.12 | IDN                 | Infectious Disease Notification System       |
| 2.13 | IM                  | Intramuscular Injection                      |
| 2.14 | IV                  | Intravenous Injection                        |
| 2.15 | P. falciparum       | Plasmodium falciparum                        |
| 2.16 | P. knowlesi         | Plasmodium Knowlesi                          |
| 2.17 | P. malariae         | Plasmodium malariae                          |
| 2.18 | P. ovale            | Plasmodium ovale                             |
| 2.19 | P. vivax            | Plasmodium vivax                             |
| 2.20 | PCR                 | Polymerase Chain Reaction                    |
| 2.21 | PO                  | Taken By Mouth, or Orally                    |
| 2.22 | PR                  | Per Rectum                                   |
| 2.23 | QD                  | Once a Day                                   |
| 2.24 | RBCs                | Red Blood Cells                              |
| 2.25 | SBET                | Standby Emergency Treatment                  |
| 2.26 | SKMC                | Sheikh Khalifa Medical City                  |
| 2.27 | SSMC                | Sheikh Shakhbout Medical City                |
| 2.28 | tab                 | Tablet                                       |
| 2.29 | TID                 | Three Times a Day                            |
| 2.30 | WHO                 | World Health Organization                    |

## Contents

|                                                                              |    |
|------------------------------------------------------------------------------|----|
| 1. <i>Introduction</i> .....                                                 | 4  |
| 1.1. About Malaria .....                                                     | 4  |
| 1.2. Causative Agent .....                                                   | 4  |
| 1.3. Transmission .....                                                      | 4  |
| 1.4. Notifying Malaria in Abu Dhabi .....                                    | 5  |
| 2. <i>Diagnosis, Case Definition and severity</i> .....                      | 5  |
| 2.1 Clinical description .....                                               | 5  |
| 2.2 Laboratory Criteria for Diagnosis .....                                  | 5  |
| 2.3 <i>Diagnostic Tests, Indications and Relevance</i> .....                 | 6  |
| 2.4 Case Definition .....                                                    | 6  |
| 2.5 Classification of Severity .....                                         | 7  |
| 2.5.1 Uncomplicated malaria .....                                            | 7  |
| 2.5.2 Severe or complicated malaria: .....                                   | 7  |
| 3 <i>Treatment Guidelines</i> .....                                          | 8  |
| 3.1 General Principles .....                                                 | 8  |
| 3.2 Drug resistance .....                                                    | 9  |
| 4. <i>Treatment</i> .....                                                    | 9  |
| 4.1 Falciparum Malaria or Species not identified.....                        | 9  |
| 4.1.1 Uncomplicated Falciparum Malaria .....                                 | 9  |
| 4.1.2 Severe or Complicated malaria:.....                                    | 10 |
| 4.2 Non-falciparum Malaria .....                                             | 12 |
| 4.2.1 Treatment of Acute Infection: .....                                    | 12 |
| 4.2.2 Prevention of Relapse in Vivax/Ovale Malaria: .....                    | 12 |
| 4.2.3 Treatment for Chloroquine-resistant P. vivax.....                      | 13 |
| 4.3 Malaria in Pregnancy .....                                               | 14 |
| 4.4 Follow up and Evaluation. ....                                           | 16 |
| 5. <i>Travelers Guidelines</i> .....                                         | 16 |
| 6. <i>Chemoprophylaxis</i> .....                                             | 17 |
| 6.1 Special Groups .....                                                     | 18 |
| 6.1.1 Pregnant Women .....                                                   | 18 |
| 6.1.2 Young Children .....                                                   | 18 |
| 6.1.3 Immunosuppressed Travelers .....                                       | 19 |
| Table 5: Dosages and Indications of antimalarial drugs for prophylaxis ..... | 20 |
| <i>References</i> .....                                                      | 24 |

## 1. Introduction

### 1.1. About Malaria

According to the latest World malaria report there were 249 million cases of malaria in 2022 compared to 244 million cases in 2021. The estimated number of malaria deaths was 608,000 in 2022 compared to 610,000 in 2021.

Malaria is a life-threatening disease caused by parasites that are transmitted to people through the bites of infected female *Anopheles* mosquitoes. It is preventable and curable. Malaria symptoms usually appear within 10 to 15 days but can take up to one year to develop. The symptoms of malaria are nonspecific and may include fever with chills and a flu-like illness. However, fever is not always present. If left untreated, malaria can cause severe illness and death.

WHO's Africa Region continues to be disproportionately affected by the global malaria burden. In 2022, the African continent accounted for about 94% of all malaria cases and 95% of deaths. Children under the age of five account for about 78.1% of malaria deaths in Africa.

### 1.2. Causative Agent

There are 5 medically important species of malaria: *Plasmodium falciparum* (which is capable of invading a high proportion of red blood cells and rapidly leads to severe or life-threatening multiorgan disease), *P. vivax* (responsible for the majority of non-falciparum cases) and rarely other species: *P. ovale*, *P. malariae*, and *P. knowlesi*. *P. vivax* and *P. knowlesi* can also cause severe illness. These species differ in geographical distribution, microscopic appearance, clinical features, and potential to develop antimalarial drug resistance and relapses. However, the measures to prevent infection from all five species are similar.

### 1.3. Transmission

The malaria parasite is transmitted by female *Anopheles* mosquitoes that are active between dusk and dawn (night). Other modes of transmission include:

- Pregnant mother to baby (congenital malaria).
- Blood/organ transmission (survey is required before blood donation).
- Sharing needles contaminated with malaria-infected blood.

## 1.4. Notifying Malaria in Abu Dhabi

According to the Federal Law 14 of 2014, malaria is one of the notifiable diseases in the United Arab Emirates. UAE was certified as being malaria free since 2007. However, malaria remains a major public health problem in other countries in Asia, Africa, and the Middle East, including Afghanistan, Djibouti, India, Pakistan, Somalia, Sudan, and Yemen. Malaria is therefore considered an imported disease in the United Arab Emirates and is associated with travel to other countries where malaria is endemic. The majority of reported cases in the UAE are due to *P. vivax* and *falciparum*.

**All licensed healthcare facilities in Abu Dhabi must report any probable or confirmed case through the Infectious Disease Notification System (IDN).**

## 2. Diagnosis, Case Definition and severity

### 2.1 Clinical description

Patients with malaria usually presents with an acute and nonspecific illness associated with symptoms such as fever, chills and sweats, headaches, muscle pains, nausea and vomiting. However, fever may be absent. In severe malaria caused by *Plasmodium falciparum*, clinical findings like confusion, coma, neurologic focal signs, severe anemia, and respiratory difficulties are more striking and may increase the suspicion for malaria. Since the signs and symptoms of malaria are nonspecific, malaria should be suspected in any unwell patient with a history of travel to an endemic area, or other risk factors for transmission. Most cases of malaria occur within 6 months of travel to an endemic area however it can occur up to a year after travel. The absence of mosquito bites or not visiting a high-risk area within a country endemic for malaria should not be used to exclude the diagnosis of malaria.

### 2.2 Laboratory Criteria for Diagnosis

Early and accurate diagnosis is essential both for the effective management of malaria and to strengthen malaria surveillance. Prompt diagnosis of malaria before initiating treatment is crucial.

Laboratory diagnosis of malaria is usually based on the following tests:

- Detection of **malaria parasites in thick or thin peripheral blood films by microscopy**, (*Microscopic examination remains the “gold standard” for laboratory confirmation of malaria.* Tests to make a diagnosis of malaria should be performed immediately when ordered by a health-care provider.
- Rapid antigen tests are highly sensitive for *plasmodium falciparum* and *vivax* and should be routinely performed when malaria is suspected. However, these tests can also result in false positive results.

- Detection of **species-specific parasite DNA** in a sample of peripheral blood using a Polymerase Chain Reaction (PCR) test can also be used however malaria PCR is currently recommended to be used as a research tool rather than a clinical diagnostic tool.

### 2.3 Diagnostic Tests, Indications and Relevance

Blood film for malaria is the gold-standard investigation and should be requested urgently. The results of the blood film should be available within 2 hours.

All laboratories that offer blood film for malaria should also have an internal quality control assurance program.

If there is clinical suspicion of malaria but the initial film is negative, repeated films should be examined 12-24hrs later and again after another 24 hours (total 3 smears).

When the blood film is negative or parasitemia disproportionately low compared to the severity of illness, an alternative diagnosis should be considered.

Obtain blood cultures since secondary gram-negative infections (Salmonella bacteremia) can occur in patients with severe malaria.

Request G6PD levels for all patients diagnosed with non-falciparum malaria.

If there are any hemodynamic or respiratory problems, obtain baseline arterial blood gas (ABGs), electrocardiogram (ECG) and chest X-ray (CXR).

### 2.4 Case Definition

**Probable:** A clinically compatible case who has travelled to or lived in malaria endemic areas, OR Detection of Plasmodium species by rapid diagnostic antigen testing without confirmation by microscopy or nucleic acid testing in any person (symptomatic or asymptomatic).

**Confirmed:** A clinically compatible case that is laboratory confirmed by microscopy on blood film (Symptomatic or asymptomatic).

#### Considerations for Diagnosis and Reporting

- All probable cases must be confirmed with a confirmatory test (microscopy).
- A subsequent attack experienced by the same person but caused by a different Plasmodium species is counted as an additional case.
- A subsequent attack experienced by the same person and caused by the same species may indicate relapsing infection or treatment failure caused by drug resistance or a separate attack.
- **Recrudescence:** This is defined as recurrence of asexual parasitemia following treatment with the same genotypic characteristics of original infection due to incomplete clearance or failure of treatment.

## 2.5 Classification of Severity

### 2.5.1 Uncomplicated malaria

Uncomplicated malaria is defined as symptomatic parasitemia without signs of severity OR evidence of organ dysfunction. Patients with uncomplicated malaria may present with a combination of the following symptoms:

- Fever
- Chills
- Sweats
- Headaches
- Nausea and vomiting
- Body aches
- General malaise

Additional laboratory findings may include mild anemia, mild decrease in blood platelets (thrombocytopenia), elevation of bilirubin, and elevation of aminotransferases.

### 2.5.2 Severe or complicated malaria:

Severe or complicated malaria is defined as symptomatic parasitemia with signs of severity OR evidence of organ dysfunction.

The groups at risk of severe or complicated malaria include:

- Children <5 years of age.
- Pregnant women.
- Immunosuppression such as HIV positive patients and patients who have had a splenectomy.

The features of severe or complicated malaria include any of the following:

- *P. falciparum* parasitemia >10 percent (>500,000/mcL).
- Impaired consciousness – Glasgow Coma Score <11 in adults or Blantyre Coma Score <3 in children.
- Prostration – Generalized weakness so that a person is unable to sit, stand, or walk without assistance.
- Multiple convulsions – More than two episodes within 24 hours.
- 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. Clinical indicators of acidosis include rapid, deep, labored breathing.
- Hypoglycemia – Blood or plasma glucose <40 mg/dL (<2.2 mmol/L).

- Severe malarial anemia – Hemoglobin concentration  $\leq 5$  g/dL or hematocrit  $\leq 15$  percent in children  $<12$  years of age ( $<7$  g/dL and  $<20$  percent, respectively, in adults) with parasite count  $>10,000/\text{mCL}$ .
- Renal impairment – Plasma or serum creatinine  $>3$  mg/dL (265  $\mu\text{mol/L}$ ) or blood urea  $>20$  mmol/L.
- Jaundice – Plasma or serum bilirubin  $>50$   $\mu\text{mol/L}$  (3 mg/dL) with a parasite count  $>100,000/\text{mCL}$  (approximately 2 percent).
- Pulmonary edema – Radiographically confirmed or oxygen saturation  $<92$  percent on room air with respiratory rate  $>30/\text{min}$ , often with chest indrawing and crepitation on auscultation.
- Significant bleeding – Including recurrent or prolonged bleeding from the nose, gums, or venipuncture sites, hematemesis, or melena.
- Shock – Compensated shock is defined as capillary refill  $\geq 3$  seconds or temperature gradient on leg (mid to proximal limb) but no hypotension. Decompensated shock is defined as systolic blood pressure  $<70$  mmHg in children or  $<80$  mmHg in adults, with evidence of impaired perfusion (cool peripheries or prolonged capillary refill).

### *3. Treatment Guidelines*

#### **3.1 General Principles**

- Determine disease severity (uncomplicated vs complicated), parasite species and previous use of antimalarial treatment in order to decide on choice of treatment. Also use the geographic region of infection to assess the likelihood of drug resistance.
- All cases of falciparum malaria should be initially admitted for a minimum of 24 hours observation and treated in hospital to ensure they are tolerating treatment and given the risk of deterioration.
- If the private hospital needs to refer the patient for the treatment, they should refer them to an emergency department in a facility with ID services – not outpatient clinics.
- Facilities that cannot provide malaria treatment should refer non-severe *P. vivax* cases to the Diseases Prevention and Screening Center for treatment.
- All severe malaria cases irrespective of species and *P. falciparum* cases should be referred to an appropriate secondary care facility for treatment.
- Seek specialist infectious diseases (ID) advice if there are any doubts.

**For Treatment Recommendations Seek Specialist Advice from The Following**

- SSMC Hospital: ID oncall
- SKMC Hospital: ID oncall
- Tawam ID hospital: ID oncall
- For pediatric patients, contact SKMC or Tawam ID oncall

### 3.2 Drug resistance

Resistance is defined as a delay in the clearance of parasites from the bloodstream after effective treatment with artemisinin-based combination therapy (ACT). This resistance mechanism is limited to the ring stage and is also referred to as "partial resistance." In the absence of additional partner drug resistance, partial resistance rarely leads to treatment failure.

Persistent parasitemia on Day 3 of ACT therapy is suggestive of artemisinin resistance and requires specialist ID consultation.

## 4. *Treatment*

### 4.1 Falciparum Malaria or Species not identified.

- All patients with severe malaria should be admitted to hospital and treated as an inpatient due to the risk of deterioration.
- Treatment should not be delayed in patients with suspected malaria.
- Urgent appropriate parenteral therapy is indicated for:
  - All patients with severe/complicated malaria.
  - Patients at high risk of developing severe disease (parasitaemia >2%, pregnant women).
  - Patients who are unable to swallow oral tablets because of vomiting.

### 4.1.1 Uncomplicated Falciparum Malaria

Table 1-a: Uncomplicated Falciparum Malaria Treatment

| Drug                                                                                                                                                                                  | Recommended Adult Regimens                                                                                                                                                                                                                                                                                                               | Comments                                                                                                                                                                                                   |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b><u>1<sup>st</sup> line:</u>Artemether-lumefantrine (Riamet®)</b><br>(1 oral tab: 20 mg artemether and 120mg lumefantrine)                                                          | Three-days course:<br><br><b>Adults (&gt;35 kg):</b> <ul style="list-style-type: none"> <li>Day 1: 4tabs Initial dose then 4 tabs second dose 8 hours later</li> <li>Days 2 and 3: 4 tabs PO BID</li> </ul> <b>Adults (5-15kg):</b> 1 tab per dose<br><b>Adults (15-25kg):</b> 2 tab per dose<br><b>Adults (25kg-35):</b> 3 tab per dose | It must always be given with fatty food or milk to maximize absorption.<br><br>Pregnancy: contraindicated in the first trimester, but is the preferred first line treatment in second and third trimesters |
| <b><u>2<sup>nd</sup> line:</u></b> should only be used if Arthemether-lumefantane cannot be obtained AND the patient cannot be urgently referred to an appropriate treating facility. |                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                            |
| <b>A. Atovaquone - Proguanil (Malarone ®)</b><br>(Adult tab: 250mg Atovaquone - 100mg Proguanil)                                                                                      | 4 tablets daily for 3 days                                                                                                                                                                                                                                                                                                               | Contraindicated in pregnancy.                                                                                                                                                                              |
| <b>B. Quinine plus Oral Doxycycline</b><br><b>OR</b><br><b>C. Quinine plus Oral Clindamycin</b>                                                                                       | <ul style="list-style-type: none"> <li>Oral Quinine sulphate 600mg every 8 hours plus oral Doxycycline 200mg daily for 7 days</li> <li>Oral Quinine sulphate 600mg 8 hourly plus Oral Clindamycin 450mg 8 hourly for 7 days can be safely used in all trimesters.</li> </ul>                                                             |                                                                                                                                                                                                            |

#### 4.1.2 Severe or Complicated malaria:

- Assessment of severe malaria should include careful clinical evaluation and review of investigations for the features of severe malaria detailed above.
- Intravenous Artesunate is the treatment of choice for severe malaria based on severity classification and irrespective of species.
- Patients at risk of developing severe or complicated falciparum malaria who also require parenteral therapy as in patients with severe malaria include:
  - hyperparasitemia (>2%).
  - Pregnant women (treatment requires discussion with an ID specialist).
  - Patients unable to swallow/retain tablets.

Table 1-b: Severe or Complicated malaria requires parenteral therapy with IV Artesunate.

| Drug                                                                      | Recommended Adult Regimens                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Comments                                                                                                                                                                                                                                                               |
|---------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <u>1st line:</u> <b>Artesunate</b>                                        | <p>Intravenous Artesunate 2.4 mg/kg given at 0 hours, 12 hours, 24 hours, and 48 hours for a total of 4 doses.</p> <ul style="list-style-type: none"> <li>• Continue above regimen until patient is improving (minimum 24 hours/maximum 5 days) and can reliably swallow, then switch to complete a full course of oral antimalarial chemotherapy (ACT)</li> </ul>                                                                                                                                                                                              | <p>If IV Artesunate is not available do not delay treatment, give 2nd line treatment.</p> <p>Artesunate can cause delayed hemolysis 7-21 days after completing treatment - follow up hemoglobin measurement is required</p>                                            |
| <u>2nd line:</u> <b>IV Quinine plus either doxycycline or clindamycin</b> | <p><b>IV Quinine dose:</b></p> <p><u>Loading dose:</u> 20 mg/kg quinine dihydrochloride followed by</p> <p><u>Maintenance dose:</u> 10 mg/kg every 8 hours for the first 48 hours (start 8 hours after the loading dose).</p> <ul style="list-style-type: none"> <li>▪ If there is no improvement in the patient's condition within 48 hours, the dose should be reduced by 1/3. Consult an ID Specialist</li> <li>▪ Continue until the patient can swallow, then switch to oral quinine plus doxycycline or clindamycin to complete a total 7-days.</li> </ul> | <p>IV quinine must be administered as a slow infusion (e.g. over 4 hours)</p> <p>The infusion rate should not exceed 5 mg/kg per hour. Fast infusion can result in severe hypotension. Patients should be closely monitored: ECG changes and blood glucose levels.</p> |

#### 4.1.2.1 Supportive care for severe malaria:

- Patients with severe or complicated malaria should be managed in High dependency unit HDU/ICU.
- Careful fluid balance is important to avoid over-filling, which can exacerbate the increased pulmonary capillary permeability that occurs in severe malaria.
- Blood glucose should be checked routinely every 4hr and at any time that reduced consciousness occurs.
- Some patients may develop shock which may be secondary to complicating bacteremia, treat patients with signs of septic shock with broad spectrum antibiotics (Ceftriaxone)
- There is no role for the following:
  - Platelet transfusion unless there is active bleeding.
  - Routine prophylaxis for seizures.
  - Mannitol for raised Intracranial pressure.
  - Exchange transfusion.

#### 4.2 Non-falciparum Malaria

- Most non-falciparum malaria cases can be treated in an outpatient setting.
- *P. vivax* and *P. ovale* may develop liver hypnozoites, or dormant forms, that can result in relapsing infection. Treatment needs to be targeted at both the acute infection and prevention of relapse in these species.
- Non-falciparum species can cause severe malaria – these cases should be treated as for severe falciparum malaria with parenteral artesunate or oral ACT.

##### 4.2.1 Treatment of Acute Infection:

Table 2.a. Treatment of Acute Infection in Non-Falciparum Malaria

| Drug                                   | Recommended Adult Regimens                                                                                        | Comments                                                                                                     |
|----------------------------------------|-------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------|
| <b>Chloroquine-sensitive</b>           | Chloroquine 1 g on day 1, followed by 500 mg at 6 hours, 24 hours and 48 hours after first dose.                  |                                                                                                              |
| <b>OR</b><br><b>Hydroxychloroquine</b> | Hydroxychloroquine 800mg once, followed by 400 mg at 6 hours, 24 hours and 48 hours after first dose (total 2 g). | NB: Chloroquine-resistant <i>P. vivax</i> have been reported in India, Indonesia, central and south America. |

#### 4.2.2 Prevention of Relapse in Vivax/Ovale Malaria:

Table 2.b. Treatment of Prevention of Relapse in Vivax/Ovale Malaria Summary

| Drug                                                                                        | Dosage                                                                                                                           | Comments                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|---------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p><b>Primaquine</b></p> <p>It is the drug of choice for the elimination of hypnozoites</p> | <ul style="list-style-type: none"> <li>30mg/day for 14 days for P. vivax.</li> <li>15mg/day for 14 days for P. ovale.</li> </ul> | <ul style="list-style-type: none"> <li>Patients should be screened for G6PD deficiency before primaquine treatment, as primaquine may precipitate hemolysis in G6PD deficient individuals.</li> <li>Consult ID Specialist if the patient has G6PD Deficiency</li> <li>The primaquine course <b>MUST</b> overlap with treatment for acute infection.</li> <li>For malaria caused by P. vivax or P. ovale, once G6PD deficiency has been excluded, start Primaquine as soon as possible and with the course of Chloroquine – it increases the efficacy of anti-relapse therapy</li> </ul> |

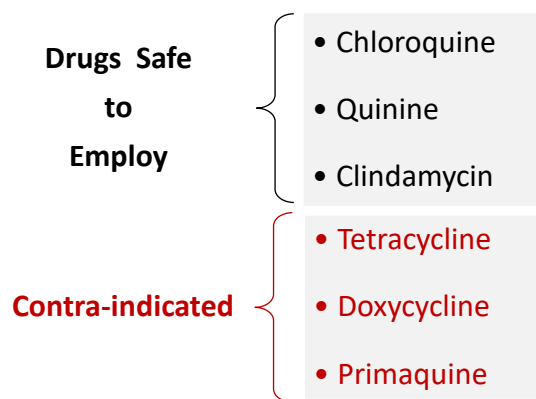
#### 4.2.3 Treatment for Chloroquine-resistant *P. vivax*

Table 2.c. Treatment Chloroquine-resistant *P. vivax* Summary

| Drug                                                                                                                            | Recommended Adult Regimens                                                                                                                                                                                                                                                                                                                                                                                    | Comments                                                 |
|---------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|
| <b>Artemether-lumefantrine (Riamet®)</b><br>(1 oral tab: 20 mg artemether and 120mg lumefantrine)<br><br><b>Plus Primaquine</b> | Three-days course:<br><b>Adults (&gt;35 kg):</b> <ul style="list-style-type: none"> <li>Day 1: 4tabs Initial dose then 4 tabs second dose 8 hours later</li> <li>Days 2 and 3: 4 tabs PO BID</li> </ul> <b>Adults (5-15kg):</b> 1 tab per dose<br><b>Adults (15-25kg):</b> 2 tab per dose<br><b>Adults (25kg-35):</b> 3 tab per dose<br><br><b>primaquine</b> 15mg/day for 14 days<br>OR 30mg/day for 14 days | Consult ID Specialist if the patient has G6PD Deficiency |
| <b>OR</b><br><b>Quinine plus doxycycline plus primaquine</b>                                                                    | <ul style="list-style-type: none"> <li><b>Quinine sulfate:</b> 542 mg base (650 mg salt) PO TID x 3 days</li> <li><b>Doxycycline:</b> 100 mg po BID x 7 days</li> <li><b>primaquine</b> 15mg/day for 14 days<br/>OR 30mg/day for 14 days</li> </ul>                                                                                                                                                           | Consult ID Specialist if the patient has G6PD Deficiency |
| <b>OR</b><br><b>atovaquone/proguanil (Malarone®) plus primaquine</b>                                                            | <ul style="list-style-type: none"> <li>Adult tab: 250 mg atovaquone and 100 mg proguanil) 4 adult tabs PO QD x 3 days</li> <li><b>primaquine</b> 15mg/day PO for 14 days</li> <li>OR 30mg/day PO for 14 days</li> </ul>                                                                                                                                                                                       | Consult ID Specialist if the patient has G6PD Deficiency |
| <b>OR</b><br><b>mefloquine plus primaquine</b>                                                                                  | <ul style="list-style-type: none"> <li><b>Mefloquine</b> 15 Dose 1: 684 mg base (750 mg salt) PO Dose 2 at 6 to 12 h: 456 mg base (500 mg salt) PO</li> <li><b>primaquine</b> 15mg/day PO for 14 days</li> <li>OR 30mg/day PO for 14 days</li> </ul>                                                                                                                                                          | Consult ID Specialist if the patient has G6PD Deficiency |

### 4.3 Malaria in Pregnancy

- Malaria in pregnancy causes major maternal and fetal complications.
- Severe falciparum malaria in non-immune women in late-stage pregnancy has a high mortality rate (~50%).
- In areas with high intensity of malaria transmission, the background immunity among pregnant women may be high and *P. falciparum* infection is usually asymptomatic.
- Placental malaria occurs when infected RBCs sequester in the placenta and disrupt nutritional exchange between mother and fetus, and is associated with low birth weight, preterm birth, stillbirth, and maternal anemia.
- Greater severity of illness is related to the frequency of hypoglycemia and pulmonary compromise due to relative immunosuppression and parasite sequestration. *P. falciparum* malaria in the setting of pregnancy may be considered as criterion for IV therapy.



- Mefloquine: changed from pregnancy category C to category B. Considered safe during all trimesters of pregnancy.
- Artemisinin-based combination therapies (ACT):
  - Artemether-lumefantrine is recommended for uncomplicated *P. Falciparum* malaria in the second and third trimesters of pregnancy and during the first trimester when other options are unavailable. Quinine in addition to Clindamycin can be used during the first trimester. Please consult ID Specialists.
- Atovaquone/Proguanil (malarnoe) is not indicated for use in pregnant women as data are lacking, yet in uncomplicated malaria caused by chloroquine-resistant *P. falciparum* infection, atovaquone-proguanil may be used if other treatment options are not available.

Table 3: Malaria Treatment in Pregnancy

| Drug                           | Recommendation                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|--------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Artemether/lumefantrine</b> | (Coartem) A fixed-dose combination tablet is an alternative first-line treatment of uncomplicated malaria. The intravenous formulation of artesunate is available to treat severe malaria. Artemisinin derivatives, i.e., artesunate, artemisinin, and artemether, appear equally effective and can be administered PO, IM, IV or PR. Avoid monotherapy to limit drug resistance. It is recommended in 2nd and 3rd trimesters, and during 1st trimester when other options unavailable. |
| <b>Atovaquone/proguanil</b>    | (Malarone) A fixed antibiotic combination is effective at treating chloroquine-resistant <i>P. falciparum</i> . It is also approved for malaria prophylaxis. Prophylaxis can be started the day of arriving in a malaria-endemic region and stopped seven days after leaving the endemic region. The drug is well tolerated. Data lacking in pregnancy.                                                                                                                                 |
| <b>Chloroquine</b>             | Although this agent was once the mainstay of prophylaxis and treatment for malaria, areas without chloroquine-resistant <i>P. falciparum</i> are limited, e.g., central America, west of the Panama Canal. <i>P. falciparum</i> malaria should be considered resistant to chloroquine. Chloroquine-resistant <i>P. vivax</i> malaria has been reported from Indonesia, Papua New Guinea, Myanmar, India, Central and South America.                                                     |
| <b>Doxycycline</b>             | Doxycycline is useful for malaria prophylaxis in multi-drug resistant <i>P. falciparum</i> -endemic regions, in particular, Southeast Asia such as along the Thai-Burmese border. It is also used in combination with other drugs particularly quinine/quinidine in the treatment of severe malaria. Equally beneficial IV or PO, as long as GI absorption is reliable. Concerns regarding use include photosensitivity and vaginal candidiasis.                                        |
| <b>Mefloquine</b>              | Mefloquine changed from pregnancy category C to category B. It may cause neurotoxicity at treatment doses. Considered safe in all trimesters of pregnancy.                                                                                                                                                                                                                                                                                                                              |
| <b>Primaquine</b>              | Primarily used to eradicate dormant liver forms of <i>P. vivax</i> and <i>P. ovale</i> . Screen for G6PD deficiency prior to treatment to avoid hemolytic anemia.                                                                                                                                                                                                                                                                                                                       |
| <b>Quinine</b>                 | Drug of choice for the treatment of severe malaria where chloroquine resistance is possible. Quinidine is used as an interchangeable substitute. Often results in cinchonism (reversible tinnitus and reversible high tone hearing loss).<br>Used in combination with doxycycline, tetracycline or clindamycin.                                                                                                                                                                         |
| <b>Tetracycline</b>            | Same utility as doxycycline, but less preferable due to problems with absorption and pharmacokinetics.                                                                                                                                                                                                                                                                                                                                                                                  |

#### 4.4 Follow up and Evaluation.

All patients diagnosed with malaria should be given an appointment on discharge, preferably with an ID clinic on discharge from hospital. They should be referred to SSMC Tropical and ID Division, SKMC or Tawam Hospital infectious disease department. For pediatric patients, contact SKMC or Tawam ID Departments.

### *5.Travelers Guidelines*

#### Preventive Measures for Travelers:

- Be aware of the risk, the incubation period, and the main symptoms. The longer the stay in endemic areas, the higher the risk of contracting malaria.
- Avoid being bitten by mosquitoes, especially between dusk and dawn, although some species of mosquito which can transmit dengue fever bite during the day also.
- An impregnated bed net should be used unless the accommodation is fitted with functioning air conditioning and windows and doors are adequately screened to prevent mosquito entry.
- Backpackers staying in budget accommodation and those engaged in outdoor activities have a higher risk of being bitten compared to tourists staying in air-conditioned hotels.
- Cover exposed body parts with DEET-based (N, N-diethyl-m-toluamide) insect repellents. If DEET is not tolerated (or is not available), an alternative preparation can be used (citronella creams for example), but few preparations are as effective as DEET. Duration of protection with DEET is 1 to 3 hours for 20%, up to 6 hours for 30% and up to 12 hours for 50% DEET. The interval between applications depends on this as well as the DEET formulation and concentration used. When both sunscreen and DEET are required, DEET should be applied afterwards. DEET reduces the efficacy of sun block; however, sunscreens do not reduce the effectiveness of DEET.
  - DEET is not recommended for infants below the age of 2 months.
  - Use of 20% DEET in the second and third trimesters of pregnancy was not associated with adverse effects on infants from those pregnancies followed for up to 12 months after birth.
  - Given the seriousness of malaria in pregnancy, the use of DEET at a concentration of up to 50% as part of the malaria prevention regimen is not contraindicated for pregnant women, including those in the first trimester.
  - DEET may be used at a concentration of up to 50% while breastfeeding and for infants and children aged over 2 months.

- Don't apply insect repellent around eyes and mouth or on hands of children and don't put it on wounds or broken skin.
- Wear appropriate clothes to minimize exposed skin.
- Take antimalarial drugs (Chemoprophylaxis) to prevent infection when appropriate.
- Immediately seek diagnosis and treatment if a fever develops one week or more after entering an area where there is malaria risk, and up to 3 months after departure.

## 6. Chemoprophylaxis

Nearly half of the world's population is at risk of malaria. In areas with high malaria transmission, young children and pregnant women are particularly vulnerable to malaria infection and death. The use of preventive chemotherapies has had a major impact in reducing the global burden of this disease.

The most appropriate chemoprophylactic antimalarial drugs for the destination(s) should be prescribed in the correct doses.

- Travelers and their doctors should be aware that no antimalarial prophylactic regimen can give complete protection against malaria infection. Risk avoidance as described above is still necessary.
- Adverse reactions attributed to malaria chemoprophylaxis are common, but most are minor and do not affect the activities of the traveler. Retinal toxicity is a concern especially when a cumulative dose of 100 g of chloroquine is reached. Data does not indicate an increased risk of serious side effects with long term use of mefloquine if the drug is tolerated in the short-term. Available data on long-term chemoprophylaxis with doxycycline (i.e., more than 12 months) is limited but reassuring.
- Seek specialist advice if the client has severe hepatic or renal impairment.
- Some countries have areas where *P. vivax* is the predominant species and *P. falciparum* is the predominant species in others. In this case, consider prophylactic treatment should cover *P. falciparum* due to the relatively higher clinical severity of its infection and potential complications.
- Depending on the type of malaria destination, travelers should be advised about the possibility of late-onset *P. vivax* and *P. ovale* infections.
- The possibility of interactions between malaria prophylaxis and other medications should always be considered as well as other medical contraindications like drug allergies.

## 6.1 Special Groups

Some group of travelers, especially young children, pregnant women and immunosuppressed travelers are at particular risk of serious consequences if they become infected with malaria. Recommendations for these groups are difficult to formulate because safety data are limited.

### 6.1.1 Pregnant Women

- Malaria in pregnant women increases the risk of maternal death, miscarriage, stillbirth, and low birth with associated risk of neonatal death.
- Pregnant women should be advised to avoid travel to areas where malaria transmission occurs.
- Effective malaria prevention measures should be taken.
- Pregnant women are particularly susceptible to mosquito bites and should therefore be vigilant in using protection measures, including insect repellents and insecticide –treated mosquito nets.
- In light of danger of malaria to mother and fetus, experts increasingly agree that travel to a *P. falciparum* area during the first trimester of pregnancy should be avoided or delayed at all costs; if this is truly impossible, good preventive measures should be taken, including prophylaxis with mefloquine where this indicated.
- **Doxycycline is Contraindicated during pregnancy.**

### 6.1.2 Young Children

- Parents should be advised not to take babies or young children to areas with risk of *falciparum* malaria.
- If travel cannot be avoided, children must be very carefully protected against mosquito bites and be given an appropriate chemoprophylactic drug.
- Babies should be kept under insecticide- treated mosquito nets as much as possible between dusk and dawn.
- Chloroquine, proguanil and mefloquine are considered compatible with breastfeeding.
- Dosage in children should be based on body weight, and tablets should be crushed and grounded as necessary.

**Falciparum Malaria in Young Children Is a Medical Emergency.** It may be rapidly fatal. Early symptoms are atypical and difficult to recognize, and life-threatening complications can occur within hours of the initial symptoms.

### 6.1.3 Immunosuppressed Travelers

- Immunosuppressed travelers are at increased risk of malaria.
- Individual pre-travel advice should be carefully sought.

Table 4: Malaria Risk and Recommended Prophylaxis Summary

|               | Malaria Risk                                                                                     | Type of Prevention                                                                                                                                                                                                            |
|---------------|--------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Type A</b> | Very limited risk of malaria transmission                                                        | Mosquito bite prevention only.                                                                                                                                                                                                |
| <b>Type B</b> | Risk of <i>P. vivax</i> malaria only.                                                            | Mosquito bite prevention plus chloroquine, OR doxycycline or atovaquone-proguanil or mefloquine.<br><br>chemoprophylaxis (select according to parasite sensitivity, reported side-effects and contraindications) <sup>a</sup> |
| <b>Type C</b> | Risk of <i>P. falciparum</i> with reported chloroquine and sulfadoxine-pyrimethamine resistance. | Mosquito bite prevention plus malaria, atovaquone-proguanil or doxycycline or mefloquine<br><br>chemoprophylaxis (select according to reported side effects and contraindications) <sup>a</sup>                               |
| <b>Type D</b> | Risk of <i>P. falciparum</i> malaria in combination with reported multidrug resistance.          | Mosquito bite prevention plus atovaquone-proguanil or doxycycline or mefloquine chemoprophylaxis.<br><br>(Select according to reported drug-resistance pattern, side-effects and contraindications)<br><sup>a,b</sup>         |

a. Alternatively, for travel to rural areas with low risk of malaria infection, mosquito bite prevention can be combined with Standby Emergency Treatment (SBET).

b. In certain areas with multidrug-resistant malaria, mefloquine chemoprophylaxis is no longer recommended. At present these areas include Cambodia, south-eastern Myanmar, and Thailand.

Table 5: Dosages and Indications of antimalarial drugs for prophylaxis

| Drug                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Indications                                                                                                                                                                                                                                                                                                                                                                                                                                                | Usage restrictions                                                                                                                                                                                                                                                                                                                                                                                 |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>ATOVAQUONE/PROGUANIL</b><br><b>(Malarone)</b><br><b>ADULTS</b> <ul style="list-style-type: none"> <li>1 Adult tablet daily.</li> </ul> <b>CHILDREN</b> <ul style="list-style-type: none"> <li>5-8 Kg: ½ pediatric tablet daily.</li> <li>8-10 kg: ½ pediatric tablet daily.</li> <li>10-20 Kg: 1 pediatric tablet daily.</li> <li>20-30 kg: 2 pediatric tablets daily.</li> <li>30-40 Kg: 3 pediatric tablets daily.</li> <li>40 Kg and over: 1 adult tablet daily.</li> </ul> <p>Begin 1-2 days before travel, daily during travel, and for 7 days after leaving.</p> | <p>Good for last-minute travelers because the drug is started 1-2 days before traveling to an area where malaria transmission occurs.</p> <p>Some people prefer to take daily medicine.</p> <p>Good choice for shorter trips because you only have to take the medicine for 7 days after traveling rather than 4 weeks.</p> <p>Very well tolerated medicine – side effects uncommon.</p> <p>Pediatric tablets are available and may be more convenient</p> | <p>Cannot be used by women who are pregnant or breastfeeding a child less than 5 kg.</p> <p>Cannot be taken by people with severe renal impairment. (Especially for trips of long duration).</p> <p>Some people (including children) would rather not take a medicine every day.</p>                                                                                                               |
| <b>CHLOROQUINE</b><br><b>ADULTS</b> <ul style="list-style-type: none"> <li>300 mg base (500 mg salt), once/week.</li> </ul> <b>CHILDREN</b> <ul style="list-style-type: none"> <li>mg/kg base (8.3 mg/kg salt) (maximum adult dose), once/week.</li> </ul> <p>Begin 1-2 weeks before travel, once/week during travel, and for 4 weeks after leaving.</p>                                                                                                                                                                                                                  | <p>Some people would rather take medicine weekly.</p> <p>Good choice for long trips because it is taken only weekly.</p> <p>Some people are already taking hydroxychloroquine chronically for rheumatologic conditions. In those instances, they may not have to take additional medicine.</p> <p>Can be used in all trimesters of pregnancy.</p>                                                                                                          | <p>Cannot be used in areas with chloroquine or mefloquine resistance.</p> <p>May exacerbate psoriasis.</p> <p>Some people would rather not take a weekly medication.</p> <p>For trips of short duration, some people would rather not take medication for 4 weeks after travel.</p> <p>Not a good choice for last-minute travelers because drug needs to be started 1-2 weeks prior to travel.</p> |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p><b>DOXYCYCLINE</b></p> <p>ADULTS:</p> <ul style="list-style-type: none"> <li>• 100 mg daily.</li> </ul> <p>CHILDREN</p> <ul style="list-style-type: none"> <li>• ≥8 years old: 2.2 mg/kg (maximum adult dose) daily.</li> </ul> <p>Begin 1-2 days before travel, daily during travel, and for 4 weeks after leaving.</p>                                                                                                                                                                          | <p>Appropriate for people who prefer to take medication daily.</p> <p>Good for last-minute travelers because the drug is started 1-2 days before traveling to an area where malaria transmission occurs.</p> <p>People who are already taking doxycycline long term for other reasons in those circumstance, they do not have to take an additional medicine.</p> | <p>Cannot be used by pregnant women and children &lt;8 years old.</p> <p>Some people would rather not take medication every day.</p> <p>For trips of short duration, some people would rather not take medication for 4 weeks after travel.</p> <p>Women prone to getting vaginal yeast infections when taking antibiotics may prefer taking a different medicine.</p> <p>Persons planning on considerable sun exposure may want to avoid the increased risk of sun sensitivity.</p> <p>Some people are concerned about the potential of getting an upset stomach from doxycycline.</p> |
| <p><b>MEFLOQUINE</b></p> <p>ADULTS:</p> <ul style="list-style-type: none"> <li>• 228 mg base (250 mg salt), weekly.</li> </ul> <p>CHILDREN</p> <ul style="list-style-type: none"> <li>• ≤9 kg: 4.6 mg/kg base (5 mg/kg salt), weekly.</li> <li>• 10-19 kg: ¼ tablet weekly.</li> <li>• 20-30 kg: ½ tablet weekly.</li> <li>• 31-45 kg: ¾ tablet weekly.</li> <li>• &gt;45 kg: 1 tablet weekly.</li> </ul> <p>Begin 1-2 weeks before travel, weekly during travel, and for 4 weeks after leaving.</p> | <p>People who prefer to take medication weekly.</p> <p>Good choice for long trips because it is taken only weekly.</p> <p>Can be used during pregnancy.</p>                                                                                                                                                                                                       | <p>Cannot be used in areas with mefloquine resistance.</p> <p>Cannot be used in patients with certain psychiatric conditions.</p> <p>Cannot be used in patients with a seizure disorder.</p> <p>Not recommended for people with cardiac conduction abnormalities.</p> <p>Not a good choice for last-minute travelers because drug needs to be started at least 2 weeks prior to travel.</p>                                                                                                                                                                                             |

|                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | <p>Some people prefer not to take medication weekly.</p> <p>For trips of short duration, some people would prefer not take medication for 4 weeks after travel.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| <p><b>PRIMAQUINE</b></p> <p><b>ADULTS</b></p> <ul style="list-style-type: none"> <li>• 30mg base, daily</li> </ul> <p><b>CHILDREN</b></p> <ul style="list-style-type: none"> <li>• 0.5 mg/kg base up to adult dose daily.</li> </ul> <p>Begin 1-2 days prior to travel, daily during travel, and for 7 days after leaving.</p> | <p>It is one of the most effective medicines for preventing <i>P. vivax</i> and so it is a good choice for travel to places with &gt; 90% <i>P. vivax</i>.</p> <p>Good choice for shorter trips because you only have to take the medicine for 7 days after traveling rather than 4 weeks.</p> <p>Good for last-minute travelers because the drug is started 1-2 days before traveling to an area where malaria transmission occurs.</p> <p>For people who prefer to take medication daily.</p> | <p>Cannot be used in patients with glucose-6-phosphatase dehydrogenase (G6PD) deficiency.</p> <p>Cannot be used in patients who have not been tested for G6PD deficiency.</p> <p>There are costs and delays associated with getting a G6PD test done; however, it only has to be done once. Once a normal G6PD level is verified and documented, the test does not have to be repeated the next time primaquine is considered.</p> <p>Cannot be used by pregnant women.</p> <p>Cannot be used by women who are breastfeeding unless the infant has also been tested for G6PD deficiency.</p> <p>Some people (including children) would prefer to avoid taking medication every day.</p> <p>Some people are concerned about the potential of getting an upset stomach from primaquine.</p> |

| 4.Relevant References Documents |                 |                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                   |
|---------------------------------|-----------------|---------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| No.                             | Reference Date  | Reference Name                                                | Relation Explanation / Coding / Publication Links                                                                                                                                                                                                                                                                                                                                                                 |
| 1                               | 4 December 2023 | Malaria, WHO                                                  | <a href="https://www.who.int/news-room/fact-sheets/detail/malaria">https://www.who.int/news-room/fact-sheets/detail/malaria</a>                                                                                                                                                                                                                                                                                   |
| 2                               | 18 August 2023  | CDC – Parasite - Malaria                                      | <a href="https://www.cdc.gov/parasites/malaria/index.html">https://www.cdc.gov/parasites/malaria/index.html</a>                                                                                                                                                                                                                                                                                                   |
| 3                               | 1 February 2023 | CDC – Malaria – Travelers -Choosing a Drug to Prevent Malaria | <a href="https://www.cdc.gov/malaria/travelers/drugs.html">https://www.cdc.gov/malaria/travelers/drugs.html</a>                                                                                                                                                                                                                                                                                                   |
| 4                               |                 | Global Malaria Programme                                      | <a href="https://www.who.int/teams/global-malaria-programme/case-management/diagnosis/rapid-diagnostic-tests/how-malaria-rdts-work#:~:text=Malaria%20RDTs%20detect%20specific%20antigens,falciparum%2C%20P">https://www.who.int/teams/global-malaria-programme/case-management/diagnosis/rapid-diagnostic-tests/how-malaria-rdts-work#:~:text=Malaria%20RDTs%20detect%20specific%20antigens,falciparum%2C%20P</a> |
| 5                               | 2014            | Federal Law No. 14                                            | <a href="https://mohap.gov.ae/app_content/legislations/php-law-en-35/mobile/index.html#p=1">https://mohap.gov.ae/app_content/legislations/php-law-en-35/mobile/index.html#p=1</a>                                                                                                                                                                                                                                 |