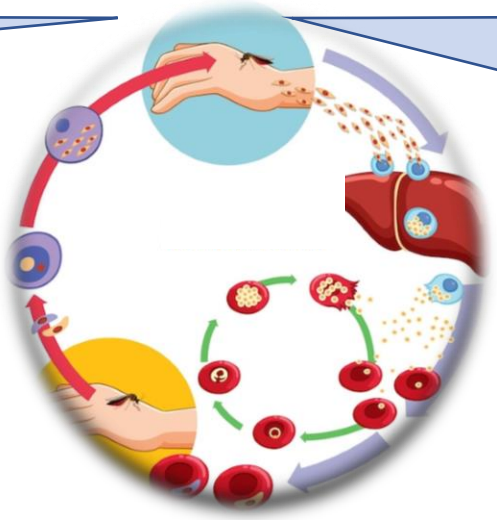
# National Guideline for Diagnosis and Treatment of Malaria in Bhutan

6th Edition, 2024



Vector Borne Disease Control Program

**DEPARTMENT OF PUBLIC HEALTH, | MINISTTRY OF HEALTH**

National guideline for the Diagnosis and Treatment of Malaria in Bhutan, 2024
Sixth Edition



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## Foreword

It is a great pleasure for me to present the 6th Edition of National Guideline for Diagnosis and Treatment of Malaria in Bhutan, 2024 which is reviewed and updated by the experts from the Ministry of Health and other allied agencies.

This revised guideline encompasses the latest WHO recommendations on malaria case management with the major changes being the 7-day short course standard dose primaquine treatment for *P.vivax* malaria from the previous standard 14-day regimen. The treatment regimen for the first trimester pregnant women has also been revised from the previous 7-day tablet quinine and tablet clindamycin to a 3-day ACT course aligned with the WHO recommendations and the local context. This is expected to enhance treatment adherence by the patients without compromising safety of the patients as well ease the patient follow up.

As Bhutan strives to realize the goal of malaria elimination, timely and effective case management is one of the key strategies and it is imperative that we keep ourselves abreast of evolving developments in this area.

Last but not the least, I take this opportunity to express my deepest gratitude and appreciation to all the members of the technical working group and the stakeholders involved in the revision of the 5th Edition of the malaria treatment guideline and coming up the 6th edition of the guideline. The Vector Borne Disease Control Program is duly acknowledged for the timely revision of the guideline. Good wishes for the successful implementation of the revised guideline throughout the country.

Director
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## Acknowledgement

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## Abbreviations and acronyms

| | |
|---|---|
| ABC | **Airway, Breathing and Circulation** |
| ACD | Active Case Detection |
| ACT | Artemisinin-based Combination Therapy |
| ART+L | Artemether + Lumifantrine |
| CDC | Centre for Disease Control |
| CRRH | Central Regional Referral Hospital |
| DHA/PPQ | Dihydroartemisinin + Piperaquine |
| DPHO | District Public Health Officer |
| DIC | Disseminated Intravascular Coagulation |
| DNA | Deoxyribonucleic Acid |
| DOT | Directly Observed Treatment |
| GDMO | General Duty Medical Officer |
| G6PD | Glucose 6-phosphate dehydrogenase |
| iDES | Integrated Drug Efficacy Studies |
| JDWNRH | Jigme Dorji Wangchuck National Referral Hospital |
| PCR | Polymerase Chain Reaction |
| PQ | Primaquine |
| PHC | Primary Health Centre |
| Pf | Plasmodium falciparum |
| RACD | Reactive Case Detection |
| RDT | Rapid Diagnostic Test |
| SOP | Standard Operating Procedures |
| VDCP | Vector-borne Diseases Control Program |
| VHW | Village Health Worker |
| WHO | World Health Organization |
| NMRL | National Malaria Reference Laboratory |
| PDC | Private Diagnostic Centre |

# 1.Introduction

## 1.1. Epidemiology

Since the launch of the first malaria eradication program in Bhutan in 1964, remarkable progress has been achieved in malaria control in the country. The malaria cases peaked at a historic high of 39,852 cases with 62 deaths in 1993-94. But with concerted efforts and evidence-based program interventions, the trend of malaria has decreased over the last many decades reaching to 436 cases in 2010 and just 18 cases in 2023 as shown in the **Fig.1.** Bhutan also sustained zero malaria death since 2013 except in 2017 and 2018 with one unfortunate death each.

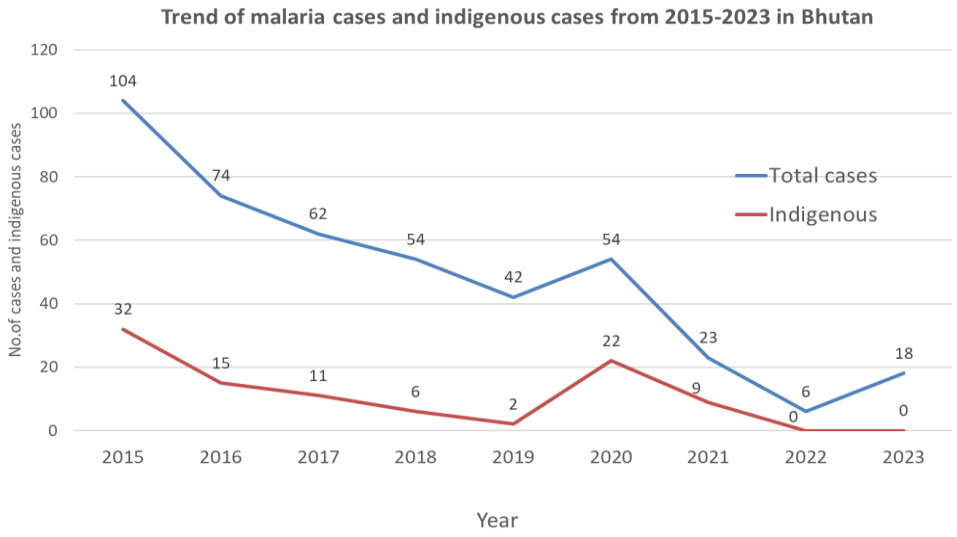


**Figure 1: Trend of malaria cases and deaths 2015-2023**

Although malaria is on the verge of elimination with the last indigenous cases reported in November, 2021, malaria still remains a public health priority disease in Bhutan. The current elimination efforts are guided by the National Strategic Plan for Elimination of Malaria and Prevention of Re-introduction in Bhutan 2020-2025 with a vision "Bhutan free of indigenous malaria". Quality assured malaria diagnosis and effective case management is one key strategy in the strategic framework for malaria elimination.

Out of 20 districts in Bhutan, 7 districts fall under low risk with API less than 1 per 1000 population, 8 districts under potential risk and 5 under no risk category as shown in **fig.2.**Bhutan is most receptive to malaria transmission from April to September during the warm monsoon period. The malaria transmission is seasonal following a two-peak pattern: the first peak occurs before the start of the monsoon season and the second one at the end. Malaria transmission occurs only at altitudes below 1700 meters, i.e., in the southern part of the country. Most of the malaria cases in the country are reported from seven southern districts of Bhutan bordering India. In the last five years from 2019-2023, all malaria active foci were confined in the district of Sarpang alone**.** Rest of the six districts have eliminated indigenous malaria and sustained the status till date.

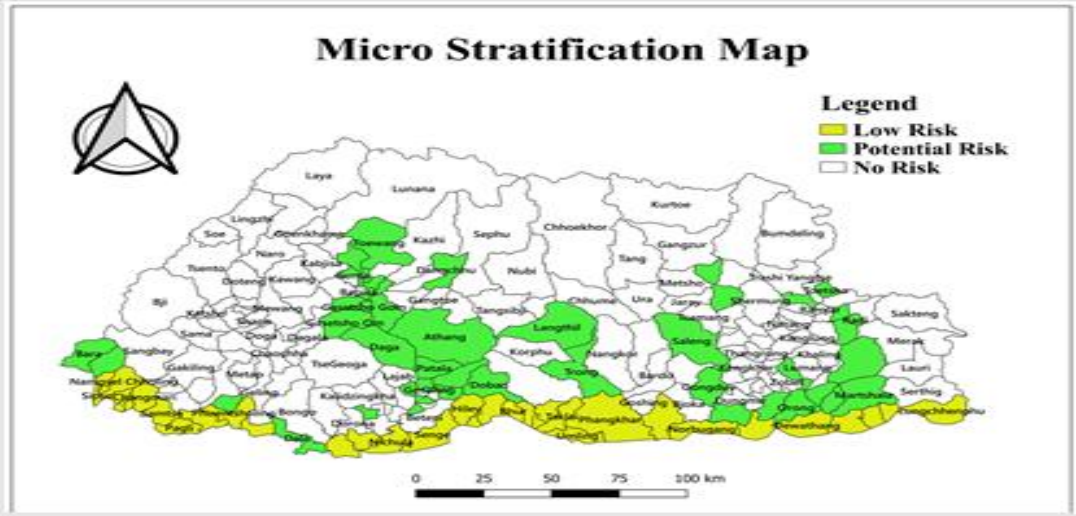


**Figure 2: Micro-stratification showing risk of malaria transmission in Bhutan**

Over the last five years period from 2019-2023, 45% of the malaria cases diagnosed in the country are imported. The proportion of the total malaria infection reported in 2023 was 44% *Plasmodium vivax* (Pv) and 56% *Plasmodium falciparum* (Pf) infection. However, the predominant malaria species in Bhutan is *P.vivax* as per the overall trend.

## 1.2. Etiology and transmission

Malaria is caused by protozoa of the genus *Plasmodium*. Of the five species that cause human malaria (*P. falciparum, P. vivax, P. malariae, P. ovale and P. Knowlesi*) only two species, *Pf and Pv* are found in Bhutan. It is also not uncommon to find mixed infections with *Pf and Pv*. Almost all severe malaria and deaths are caused by *Pf*.

The protozoa are transmitted to humans by infected female mosquitoes of the genus Anopheles. Transmission can also occur rarely through transfusion of infected blood, contaminated needles and congenitally from mother to fetus. The natural hosts history of malaria parasites involves cyclical infection of humans and female Anopheles mosquitoes as shown in **Figure 3.**

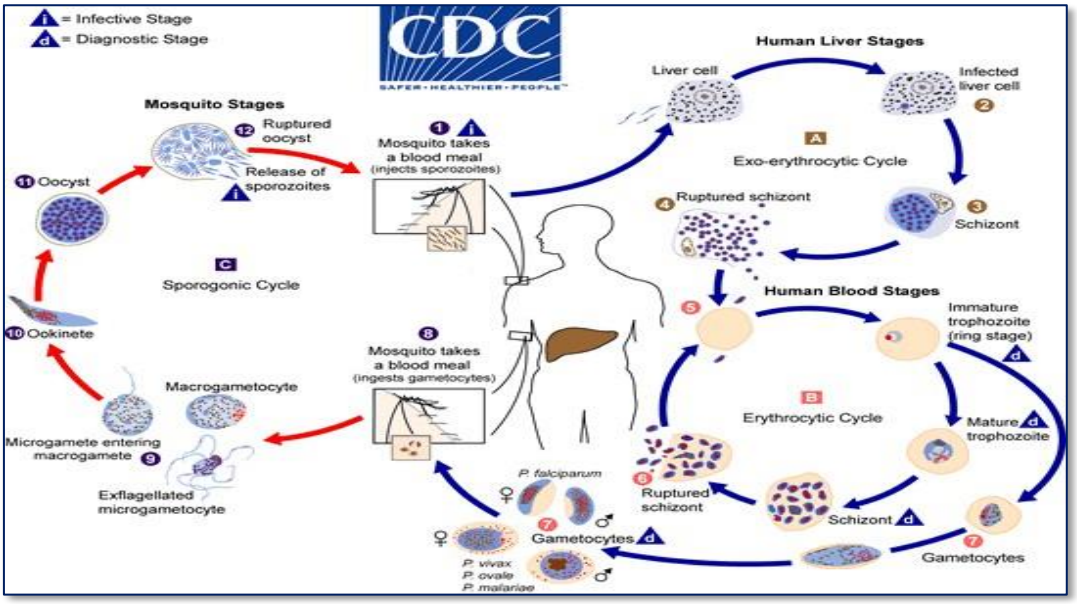


**Figure 3: Life cycle and transmission of malarial parasite (Source: CDC)**

## 1.3. Health care levels and malaria services

Bhutan has an integrated healthcare system with decentralized health healthcare service delivery that is achieved through a three-tier approach – Tertiary, secondary and primary level. Malaria diagnosis and case management is provided at all levels. The Primary Health Centers (PHCs) at primary level provide services for uncomplicated malaria with oral anti-malarial and pre-referral treatment of severe malaria patients while hospitals provide services for both uncomplicated and severe malaria patients. At the community, Community Action Groups (CAG) are involved to identify fever cases and referral for malaria diagnosis.

## 1.4. Objectives and core principles of malaria treatment guidelines

Early diagnosis and prompt case management remains a major strategy to achieve malaria elimination goals in the country. The main objective of this guideline is to provide health workers with evidence-based malaria treatment recommendations that are practical and safe. The recommendations are based on the following core principles:

- **Early diagnosis and prompt treatment of malaria**
  Uncomplicated falciparum malaria can progress rapidly to severe forms and prove fatal without treatment. Therefore, universal access to early diagnosis and prompt treatment within 24 hours of the diagnosis is crucial.
- **Rational use of antimalarial agents**
  The use of antimalarial drugs should be restricted to only patients with confirmed malaria and it should be given using DOTs with a monitoring system for full treatment course adherence.
- **Combination therapy**

  To help protect current and future antimalarial medicines resistance, all episodes of malaria should be treated with at least two effective antimalarial medicines with different mechanisms of action (combination therapy)

- **Appropriate weight/age-based dosing**
  Treatment should maximize the likelihood of rapid clinical and parasitological cure and minimize transmission from the treated infection by use of quality-assured antimalarial drugs at optimal dosages. To achieve this, dosage regimens should be based on the patient's weight/age and should provide effective concentrations of antimalarial drugs for a sufficient time to eliminate the infection in all target populations.

## 2. Diagnosis

The signs and symptoms of malaria are very non-specific (fever, chills, headache, nausea, vomiting and sometimes accompanied by diarrhea, body aches) and the clinical picture can resemble a flu-like illness or other systemic infection. This makes diagnosis of malaria quite difficult. Recent history of travel to malaria endemic areas is very important and should be always asked when the diagnosis of malaria is suspected. Other clinical features may include anemia, splenomegaly, thrombocytopenia and hypoglycemia. All confirmed malaria cases should be admitted at the hospital at least for 3 days for supervised treatment.

### 2.1. Case definitions

**A suspected malaria** case is one in which a resident or traveler from an endemic area presents with a fever (>37.5 ˚C) or a history of fever with no other obvious cause.

**Malaria case** is one that is parasitological based microscopically confirmed for the presence of malaria parasite by microscopy in the peripheral blood film or by quality assured a positive Rapid Diagnostic Test (RDT) or molecular diagnostic test (PCR).

### 2.2. Laboratory diagnosis of Malaria

For a definitive diagnosis of malaria, laboratory tests must demonstrate the malaria parasites or their components in the blood. During the malaria elimination phase, it is mandatory to screen all fever cases in endemic areas for malaria parasites in health centers with microscopy or RDT. Parasitological diagnosis by either microscopy or RDT is mandatory before initiation of treatment. The laboratory reports should be made available within one hour, after collection of blood and treatment should be started immediately as per the algorithms provided in Annexure 1. For microscopic and RDT standard procedure, refer to respective SOPs on RDT and microscope.

## 2.3. Microscopy

Microscopy is one of the standard methods for parasitological diagnosis of malaria. It is performed by examining a stained thick or thin blood smear for the presence of malaria parasites. Both thick and thin films are recommended. Parasite detection and quantification is performed in thick film to monitor response to treatment. Thin films are recommended for species identification. Additionally, the severity of malaria infection can be determined by parasitemia rate by performing parasite density count per microliter of blood. Microscopy can only be performed by well-trained microscopists. The accuracy of diagnosis is strongly dependent on the competence of the microscopists supported by a robust quality control system.

## 2.4. Rapid Diagnostic Tests

Rapid diagnostic tests are immuno-chromatographic tests. It is simple to perform and can be carried out by non-laboratory health staff after training. It detects specific parasite antigens (Histidine-rich protein 2 - HRP2 for Pf and Parasite- lactate dehydrogenase pLDH for Pv) in blood but cannot be used for follow-up of patients after the treatment. Quality of RDTs in both public health facilities and Private Diagnostic Centres (PDC) should be monitored by the National Malaria Reference Laboratory, RCDC through RDTs lot testing assessment and RDT panel testing.

**RDT is used in the following circumstances:**

- Active Case Detection (ACD)- Reactive Active Case Detection (RACD) and Proactive Case Detection (PACD).
- Where microscopy is not available, such as in a facility with no laboratory personnel.
- During emergencies, in delivering malaria results within 20 minutes
- All RDT positive should be subjected to microscopy to determine species, parasite stages & parasite density.

**Limitations of RDTs**

- Negative RDT test results do not rule out the possibility of infection with Pf & Pv malaria
- False negatives may also result from very low parasitemia i.e. parasite load <200 parasites/µl of blood or in malaria positive individual with HRP2 deletion
- False positives may occur, in patients who are positive for rheumatoid factor or other autoimmune markers.

**Note: Any patient with suspected malaria who initially tests negative and does not improve should be re-tested for malaria.**

### 2.5. Molecular diagnostic testing

PCR is a highly sensitive assay in detection of parasite DNA at low parasite density. PCR is used in clinical and therapeutic studies in making the distinction between recrudescence and re-infection, as well as in other specialized epidemiological investigations and to confirm discrepant results. whole blood or a dried blood spot (DBS) should be prepared for every malaria positive patient and 10% of reactive screening samples should be collected and shipped to RCDC within a week.

## 3. Integrated Drug Efficacy Surveillance (iDES)

As per WHO recommendations in the elimination stage, monitoring of anti-malarial drug efficacy is integrated into the routine surveillance system. Data are collected for all symptomatic and asymptomatic malaria infections for all species detected by both PCD and ACD surveillance system and are used to generate information about drug efficacy. This surveillance system requires:

- Good case detection
- Reporting on all diagnosed cases of malaria
- Ensuring that all patients receive supervised treatment using DOT
- Follow- up of all patients to confirm complete cure.

**Objectives**

- To monitor the efficacy of first- and second-line treatment including any newly registered treatment for which information is necessary.
- DOT treatment and patient follow-up to ensure treatment adherence and patient cure
- To assess efficacy of second-line treatment (only for patients with recrudescent infections after first-line treatment)
- To inform, review of anti-malaria treatment policy and ensure evidence-based recommendations

**The information required for iDES (Annexure 2)**

- Diagnosis and Patient classification
- Molecular analysis
- Responses to treatment
- Patient follow-up details
- Data interpretation and policy consideration

*Table 1: Mandatory and recommended activities for integrated surveillance of drug efficacy*

| Activity | Mandatory | Recommended |
|---|---|---|
| **Patient classification and diagnosis** | | |
| Patient classification | Imported, indigenous, induced, introduced, relapsing or recrudescent | |
| Diagnosis on day 0 | Identification of symptoms (uncomplicated, severe) Species identification by RDT or microscopy. | Parasitemia by microscopy. Gametocytemia by microscopy |
| Diagnosis on follow- up | Microscopy | PCR |
| G6PD | . | G6PD testing for vivax patients |
| **Molecular analysis** | | |
| Reinfection or recrudescence | | Blood collected on day 0 and day of failure |
| Markers of drug resistance | | Blood collected on day 0 for analysis of drug resistance. |
| **Treatment** | | |
| DOT | Ensure all treatments are given under direct supervision | Hospitalization of patients during treatment |
| Treatment failure | All cases of treatment failure must receive second-line treatment and be followed up for an additional full follow-up period | Hospitalization of patients during treatment. |
| **Patient follow-up** | | |
| Follow-up (Pf) | Day 2 & 28 days after start of treatment with a drug with a short half-life | Day 1,2, 28 after start of treatment |
| Follow-up (Pv) | Day 2, 28 and 3rd month (for relapses) | Day 1, 2, 7, 28, 3 month & Up to 1 year |
| Information collected on days of follow-up | Clinical symptoms, temperature & parasite density microscopy result | Follow-up visits. Alternatively, clinical symptoms only may be collected by telephone and additional follow-up visits made if necessary. |

**Note:** Any positive on the follow up days, blood sample should be sent to NMRL, RCDC for further investigation

## 4.Treatment regimens

Uncomplicated malaria is when a patient presents with symptoms of malaria and a positive test but with no features of severe 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 objectives of treatment are also to prevent onward transmission of the infection to others and to prevent the emergence and spread of resistance to antimalarial drugs.

### 4.1. Treatment regimen for *P.vivax* malaria

The objective of treating malaria caused by *P. vivax* is to cure both blood-stage and liver-stage infections (called radical cure), thereby preventing recrudescence and relapse, respectively. The anti-malaria treatment recommendation for uncomplicated Pv malaria is Chloroquine 250mg tablet (equivalent to 150mg base) and Primaquine 7.5mg base tablet. The dose of Primaquine is 0.5mg/kg body weight given for 7 days to ensure complete clearance of the hypnozoites from the liver and enhance treatment adherence. For chloroquine resistant Pv infection and when chloroquine is not available, treat with Artemisinin-based Combination Therapy (ACT).

**Protocol A: Treatment regimen for *P. vivax***

| Age group | Name of Drug | Day 0 | Day 1 | Day 2 | Day 3 to 7. |
|---|---|---|---|---|---|
| <1 year | Chloroquine | ½ tab (7.5ml syrup) | ½ tab (7.5ml syrup) | ¼ tab (3.75 ml syrup) | |
| | Primaquine ***(Only if >6 months old)*** | 0.5mg/kg | 0.5mg/kg | 0.5mg/kg | 0.5mg/kg |
| 1-4 years | Chloroquine | 1tab (15ml syrup) | 1tab (15ml syrup) | ½ tab (7.5ml syrup) | - |
| | Primaquine | 0.5mg /kg | 0.5mg/kg | 0.5mg/kg | 0.5mg/kg |
| 5-8 years | Chloroquine | 2 tabs. | 2 tabs. | 1 tab. | - |
| | Primaquine | 2 tab. | 2 tab. | 2 tab. | 2 tabs. each. |
| 9- 15 years | Chloroquine | 3 tabs. | 3 tabs. | 1 ½ tab. | - |
| | Primaquine | 3 tabs | 3 tabs. | 3 tabs. | 3 tabs |
| >15 years | Chloroquine | 4 tabs. | 4 tabs. | 2 tabs. | - |
| | Primaquine | 4 tabs. | 4 tabs. | 4 tabs. | 4 tabs each. |

***Note: If the patient vomits within 1hr. of taking the drug, the dose should be repeated***

### 4.2. G6PD testing prior to 7 days primaquine administration in Pv

Current WHO recommendations require G6PD testing prior to starting a patient on Primaquine treatment. Where feasible, all patients should be tested for G6PD deficiency before administering primaquine. **Where no G6PD test is available,** the decision to prescribe primaquine should be based on individual assessment of the risks and benefits. Patients who are prescribed primaquine should receive close medical supervision and patient counseling. Primaquine may cause hemolysis in G6PD deficient patients but it is mild and self-limiting in most cases. Nevertheless, patients should be advised to stop medication and come to the hospital if they develop dark colored urine, pallor, fatigue, shortness of breath and jaundice. Patients can be managed as per **Annexure 5.** Single dose primaquine given in uncomplicated P. falciparum malaria is well tolerated and prior testing for G6PD is not required. For the G6PD deficient patients with Pv, a primaquine 0.75/mg/kg/ bw should be provided once weekly for 8 weeks.

### 4.3. Treatment regimen for uncomplicated *P. falciparum* Malaria

Uncomplicated *P. falciparum* malaria is treated with ACT containing a combination of Artemether 20mg (ART) and Lumefantrine 120mg. All patients should be admitted for 3 days to ensure complete treatment. A single stat dose of primaquine at 0.5mg/kg body weight must be administered on Day 0 as an anti-gametocyte agent to stop transmission. Testing for G6PD is not required.

**Protocol B: Treatment regimen for uncomplicated *P. falciparum* malaria**

| Patient category | Drugs | Daily dose | No. of days of treatment |
|---|---|---|---|
| <15 kg | ART+ L (Coartem) | 1 tablet at 0, 8, 24, 36, 48 and 60 hours | 3 |
| | Primaquine | (0.5 mg/kg) body weight (**Do not give to infants < 6 months)** | Day 0 |
| 15 - 24kg | ART+ L (Coartem) | 2 tablets at 0, 8, 24, 36, 48 and 60 hours | 3 |
| | Primaquine | Single dose (0.5 mg/kg) body weight | Day 0 |
| 25 –34kg | ART+ L (Coartem) | 3 tablets at 0, 8, 24, 36, 48 and 60 hours | 3 |
| | Primaquine | Single dose (0.5 mg/ kg) body weight | Day 0 |
| ≥34 kg | ART+ L (Coartem) | 4 tablets at 0, 8, 24, 36, 48 and 60 hours | 3 |
| | Primaquine | Single dose (0.5 mg /kg) body weight | Day 0 |

### 4.4. Patients co-infected with HIV and TB

In people who have HIV/AIDS and uncomplicated P. falciparum malaria, artesunate + SP is not recommended if they are being treated with co-trimoxazole, efavirenz or zidovudine. and artesunate + amodiaquine is not recommended if they are being treated with efavirenz or zidovudine. Patients co-infected with HIV and TB should be monitored closely as they are at increased risk of severe malaria and malaria deaths. In addition, they are at higher risk of recrudescent infection.

### 4.5. Artemisinin-resistant falciparum malaria

Artemisinin resistance in P. falciparum is now prevalent in parts of Cambodia, the Lao People's Democratic Republic, Myanmar, Thailand and Viet Nam. Malaria patients with travel history to those countries and not responding to standard treatment, consider a longer course (5-7 days) of ACT or new fixed combination drugs (eg.artesunate + pyronaridine)

### 4.6. Treatment regimen for mixed malaria

Treatment regimen for mixed malaria is protocol C. The treatment consists of ACT and primaquine.

**Protocol C: Treatment regimen for mixed malaria**

| Patient category | Drugs | Daily dose | No. of days of treatment |
|---|---|---|---|
| <15 kg | ART+ L (Coartem) | 1 tablet at 0, 8, 24, 36, 48 and 60 hours | 3 |
| | Primaquine | 0.5mg/kg body weight daily **(Do not give to infants < 6 months)** | 7 |
| 15 – 24 kg | ART+ L (Coartem) | 2 tablets at 0, 8, 24, 36, 48 and 60 hours | 3 |
| | Primaquine | 0.5mg/kg body weight daily | 7 |
| 25 – 34kg | ART+ L (Coartem) | 3 tablets at 0, 8, 24, 36, 48 and 60 hours | 3 |
| | Primaquine | 0.5mg/kg body weight daily | 7 |
| >35 kg | ART+ L (Coartem) | 4 tablets at 0, 8, 24, 36, 48 and 60 hours | 3 |
| | Primaquine | 0.5mg/kg body weight daily | 7 |

### 4.7. Second line anti-malarial treatment

The recommended second line anti-malarial in case of treatment failure to first line ACT is (fixed combination) Dihydroartemisinin + Piperaquine (DHA/PPQ). It should be made available at the national and regional referral hospitals. It is programmatically suitable for both P. vivax and P. falciparum malaria. The longer half-life of PPQ has an advantage over Lumefantrine in treatment of vivax malaria. A second line antimalarial (DHA/PPQ) should be used in the following situations:

- Where the patient does not tolerate or has adverse reactions to the first line medicine
- Recrudescence (Treatment failure) - reappearance of symptoms and parasitemia within 28 days following initial antimalarial treatment with first line antimalarial drug.

Dihydroartemisinin (DHA) /Piperaquine (PPQ) is given over three days at a dose of **DHA 4 mg/kg per day and PPQ 18 mg /kg per day PPQ once a day for 3 days for adults and children weighting more than 25 kgs. C**hildren weighing less than 25 kgs should receive 4 mg kg of DHA and 24 mg /kg of PPQ.

**Regimen for second line antimalarial Dihydroartemisinin Piperaquine**

| Body weight in kg | Dihydroartemisinin (DHA) /Piperaquine (PPQ) 40mg/320 mg base tablets |
|---|---|
| 5 to 7 | ½ tablet |
| 8 to 10 | ¾ tablet |
| 11 to 16 | 1 tablet |
| 17 to 24 | 1 ¼ tablet |
| 25 to 35 | 2 tablets |
| 36 to 59 | 3 tablets |
| 60 to 79 | 4 tablets |
| 80 and above | 5 Tablets |

### 4.8. Treatment regimen for malaria during pregnancy

Malaria is associated with low-birth-weight infants, increased anemia and, in low transmission settings, increased risk for severe malaria, pregnancy loss and death. There is insufficient information on the safety, efficacy and pharmacokinetics of most antimalarial agents in pregnancy, particularly during the first trimester. It is important to exclude pregnancy in all women of child bearing age prior to treatment with antimalarial drugs.

P. vivax malaria in pregnancy should be treated with Chloroquine. However, use of primaquine is contraindicated throughout the duration of pregnancy and in lactating mothers. The recommended treatment regimen for pregnant women and lactating mothers is as below (Protocol D).

**Protocol D: Treatment Regimen for Malaria during pregnancy**

| Patient category | Drugs | Duration of treatment | No. of days of treatment |
|---|---|---|---|
| P.vivax | Chloroquine | 4 tabs on Day 0<br>4 tabs on Day 1<br>2 tabs on Day 2<br>***Continue Chloroquine 2 tabs weekly till baby is 6 months old*** | |
| | Primaquine<br>**(Contra-indicated during pregnancy and lactating mothers with infants less than 6 months of age)** | 4 tabs daily<br>**(<u>After baby is 6 months old)</u>** | 7 Days |
| P.falciparum (Uncomplicated) | ART + L (Coartem) | 4 tabs at 0, 8, 24, 36, 48 & 60hrs | 3 |
| **Severe malaria** | **REFER PROTOCOL "E"** | | |

## 5. Management of severe malaria

Severe malaria is defined as one or more of the following manifestations that occur without any alternative cause and in presence of a positive test (usually for Pf malaria). Severe malaria may present with impaired consciousness/coma, seizures, jaundice, severe anemia (Hb< 7gm/dl), acute respiratory distress, acidosis, acute renal failure, hypoglycemia, abnormal bleeding or DIC and shock. The most important manifestations of severe malaria are cerebral malaria and severe anemia. The above severe manifestations may develop and can occur as single or more commonly, in combination in the same patient**.** Severe malaria is mainly caused by P. falciparum and is a medical emergency. The main objective is to prevent mortality as the case fatality is 100% in untreated cases but falls to 10-20% with antimalarial treatment.

**Patients with severe malaria should be referred to the nearest district hospital as soon as possible.**

**History Taking:** The following details are very essential for all malaria patients:

- Area of residence or history of travel to endemic districts/countries
- Recent or past history of convulsions
- Urine output in the last 8-12 hours

**Clinical Assessment:**

- Maintain airway, breathing, and circulation (ABC of critical care in Annexure)
- Monitor vital signs every 2-4 hours.
- Catheterize unconscious patients or those with reduced urine output.

In addition, the following complications should be assessed and managed:

- Convulsions
- High fever
- Hypoglycemia
- Anemia

### 5.1. Treatment regimen for severe malaria

The overall management of severe malaria is specific antimalarial drugs, adjunctive therapy and supportive care. First antimalarial drug of choice for treatment of severe malaria is **IV /IM Artesunate** for all ages. If artesunate is not available, artemether or quinine can be used in order of preference. The parenteral antimalarial drugs should be given for a minimum of 24 hrs once started (**irrespective of the patient's ability to tolerate oral medication earlier**) or until the patient can tolerate orally. Thereafter, complete treatment by giving a full course (3 days) of ACT.

**Protocol E: Treatment Regimen options for severe malaria**

| Drug | Route | Schedule |
|---|---|---|
| 1.Artesunate | IM/IV | 1.Adults and older children > 20 kg: 2.4mg/kg body weight<br>2.Children <20 kg: 3.0 mg/kg body weight and<br>Give at 0, 12, 24hrs and thereafter every 24hours until the patient is able to take orally. This should be followed by 3 days of ACT. (Refer Annex 3). |
| 2. Artemether | IM | 3.2mg/kg body weight IM given on admission. Then 1.6mg/kg IM once a day followed by a full course of combination therapy as soon as the patient can swallow. |
| 3. Quinine | IV | *Loading dose* of 20mg/kg body weight of quinine dihydrochloride salt given over a 4-hour period in IV fluid (glucose 5% preferred to prevent hypoglycemia) then give *maintenance dose* of 10 mg/kg after 8 hours and repeated 8-hourly until the patient is able to take Quinine tablet orally. The oral dose of quinine is 10mg/kg body weight given every eight hours. The total duration of treatment is 7 days including both IV and oral treatment. The infusion<br>rate should not exceed 5mg/kg body weight per hour. Quinine can be given by IM injections in the same dosage if IV infusion is not possible. It should be diluted in normal saline to a concentration of 60-100 mg/ml salt, the dose divided equally and administered on the two anterior thighs (not on the buttock). |

**To be noted:**

1. Anti-malarial drugs should be given parenteral for a minimum of 24 hours and replaced by oral medications as soon as it can be tolerated.

2. A loading dose of quinine can be given at recommended doses even in acute renal failure (ARF) or severe jaundice up to 48 hours. Subsequent doses should be reduced to half. In such cases, the volume of intravenous fluid for quinine administration can be reduced to half (Quinine dihydrochloride 10 mg salt/ kg body weight diluted in 5% Dextrose, 5 ml/kg body weight every 12 hours).

3. A loading dose of quinine should NOT be given if the patient has received quinine, within the preceding 12 hrs, or the previous history of drug intake cannot be ascertained. If these conditions exist then, patients should be treated with a maintenance dose of quinine only. The maximum dose in adults should not exceed 2000mg/day and 1800mg/day or 600mg/dose in children.

4. Monitor pulse and blood pressure at least every 2hrs while the patient is on quinine infusion. Avoid standing and sitting postures of the acutely sick patient during quinine

therapy to prevent severe postural hypotension. Fatal hypotension may occur if severe malaria patients receiving IV quinine are allowed to walk or stand for a longer time.

5. Quinine, if given rapidly through IV route (intravenous push) may cause serious cardiovascular complications and even may lead to death. IV bolus injection may lead to fatal hypotension. Intramuscular quinine may cause severe local reaction and is therefore given only when IV access is not available.

## 5.2. Management of complications of severe malaria

| Complications | Immediate management |
|---|---|
| Coma (cerebral malaria) | Maintain airway, place patient on his/her side, exclude other treatable causes of coma (Eg. Hypoglycemia, bacterial meningitis),avoid harmful ancillary treatments, intubate if necessary |
| Convulsions | Maintain airway: treat promptly with IV or rectal Diazepam, Lorazepam, Midazolam. Check blood glucose |
| Hypoglycemia | Check blood glucose, correct hypoglycemia and maintain with glucose containing infusion.<br>Hypoglycemia is defined as blood glucose < 54mg/dl for children<5 yrs and<br><40mg/dl for older children and adults |
| Severe anemia | Transfuse with screened fresh whole blood (Hb <7gm/dl) |
| Acute pulmonary edema | Keep in propped up position, give O2, Diuretics, stop IVF, intubate and add positive end-expiratory pressure or continuous positive airway pressure in life threatening hypoxemia |
| Acute kidney injury | Exclude pre-renal causes, check fluid balance and urinary sodium, hemodialysis/peritoneal dialysis in established renal failure |
| Spontaneous bleeding and coagulopathy | Transfuse with screened fresh whole blood (cryoprecipitate, fresh frozen plasma and platelets, if available), give Inj. Vit K. |
| Metabolic acidosis | Exclude or treat hypoglycemia, hypovolemia, and septicemia. If severe hemodialysis or hemofiltration. |
| Shock | Suspect septicemia, take blood for culture; give parenteral broad spectrum antimicrobials, correct hemodynamic disturbances |

### 5.3. Referral of patients with severe malaria

Severe malaria is a medical emergency and early management is crucial. Pre-referral treatment should be provided with a single dose of IM/IV artesunate and referred to a higherto higher level health facility. IM artemether or IVM quinine can be given if artesunate is not available.

## 6.Malaria death

A malaria death refers to a fatal outcome caused by the malaria infection. Malaria is a life-threatening disease caused by parasites (most commonly Plasmodium falciparum) transmitted through the bites of infected female Anopheles mosquitoes. A death from malaria typically occurs when the infection leads to severe complications such as:

- Cerebral malaria (brain involvement)
- Severe anemia
- Acute respiratory distress syndrome (ARDS)
- Organ failure (such as kidney or liver)
- Severe hypoglycemia
- Metabolic acidosis

Malaria death should be thoroughly investigated as per the form (annexure 8) and the investigating team should comprise of the following officials:

1. Program Officer from VDCP (team leader)
2. Chief Medical Officer/Medical Officer from other health centre,
3. District Public Health Officer.
4. Laboratory Officer

## 7. Directly Observed Treatment (DOT)

Administration of supervised antimalarial drugs is mandatory in the treatment of both Pf and Pv malaria patients as per the WHO and national treatment protocol during malaria elimination phase. All confirmed malaria patients should be admitted during the first three days of treatment. Subsequent doses of primaquine in Pv cases should be provided and monitored as per information provided in **Annexure 4.**

### 7.1. Roles and Responsibilities (for DOT implementation)

- **District Public Health Officer (DPHO)** – The DHO should ensure to brief VHWs during annual VHW training on DOT for malaria and its importance during malaria elimination phase.

- **Clinician (Doctors/ACOs/HA)** – The clinicians should inform the patient about the follow-up visits and inform the focal persons (Malaria/Lab.personnel) about the case. The focal person should then identify DOT provider as per convenience of patient and explain about DOT strategy of treatment for the remaining duration of treatment.

- **Malaria Technician / Laboratory personnel** – He is the primary focal point at district and health facility level for promoting and monitoring of DOT activities. The following are some of the DOTs activities that need to be implemented.

    - ✓ Arrange and properly handover patient and remaining days of primaquine to the identified DOT provider during discharge of the patient

    - ✓ Explain on daily dosage and need to advise to bring back patient to the health center in case of any dark colored urine, pallor, fatigue, shortness of breath and jaundice as per checklist list for counseling patient on PQ **Annexure 5**.

    - ✓ Case follow-up on day 28 for Pf and 7, 28, 3 months and 1 year for Pv to check for drug adherence and parasite clearance (Refer **Annexure 2 & 4**)

    - ✓ Check whether DOT has been ensured and sign on the form during every visit to verify that DOT is followed both by the DOT Provider and the patient

    - ✓ Submit verified DOT completion form to VDCP and retain a copy in the laboratory (**Annexure 4)**

**DOT Provider** – The potential DOT providers can be VHWs, School Health coordinator, office colleague, family member or hospital staff. As a DOT provider, he/she should be responsible for the following:

- ✓ Administer DOT as per the instructions from hospital clinician for the patient till completion of the recommended primaquine regimen
- ✓ Inform the diagnosing and accepting health center if the patient leaves to other location before completion of DOT
- ✓ Refer patient to the health center if patient develop pallor, fatigue, shortness in breathing, jaundice or passes dark colored urine during primaquine DOT

**CMO/In-charges**

- ✓ Verify that DOT has been implemented and complete documents are submitted to the program as per guidelines
- ✓ Provide feedback immediately to the health center if there are incomplete documents.

## 8.Supply Management

The drugs and supplies related to malaria services at the health facilities should be ensured through regular supervision and monitoring visits.

| Mandatory stock at hospitals | Mandatory stock at PHCs |
|---|---|
| • RDT kit<br>• Malaria Microscope<br>• Tablet Chloroquine<br>• Tablet Primaquine<br>• Tablet Coartem (ACT)<br>• Inj. Artesunate/Artemether<br>• Inj. Quinine<br>• Dihydroartemisinin (DHA)+ Piperaquine (PPQ) (at national and regional referral hospitals)<br>• G6PD test kits in endemic areas and referral hospitals | • RDT kit<br>• Malaria Microscope in endemic areas<br>• Tablet Chloroquine<br>• Tablet Primaquine<br>• Tablet Coartem (ACT)<br>• Injection Artesunate /Artemether<br>• Inj Quinine |

## 9.Malaria Chemoprophylaxis

Malaria prophylaxis is not necessary for in-country travel within Bhutan. It is always necessary to be reminded that chemoprophylaxis is not 100% protective. People from non-endemic areas (Malaria free districts) traveling to endemic areas (Southern low risk malaria districts) may seek prophylactic antimalarial drugs from health centers. However, other than personal protective measures and use of nets, prophylactic drugs are not recommended. Where chemoprophylaxis is used, it is important to remember that it should be combined with other measures to prevent mosquito bites.

## 10. References


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2. WHO Guidelines for the treatment of malaria, 3rd Edition 2015

3. National Malaria Treatment Protocol 2019, Epidemiology and Disease Control Division Department of Health Services, Nepal.
4. WHO, Global malaria control and elimination: report of a technical review, 2008.

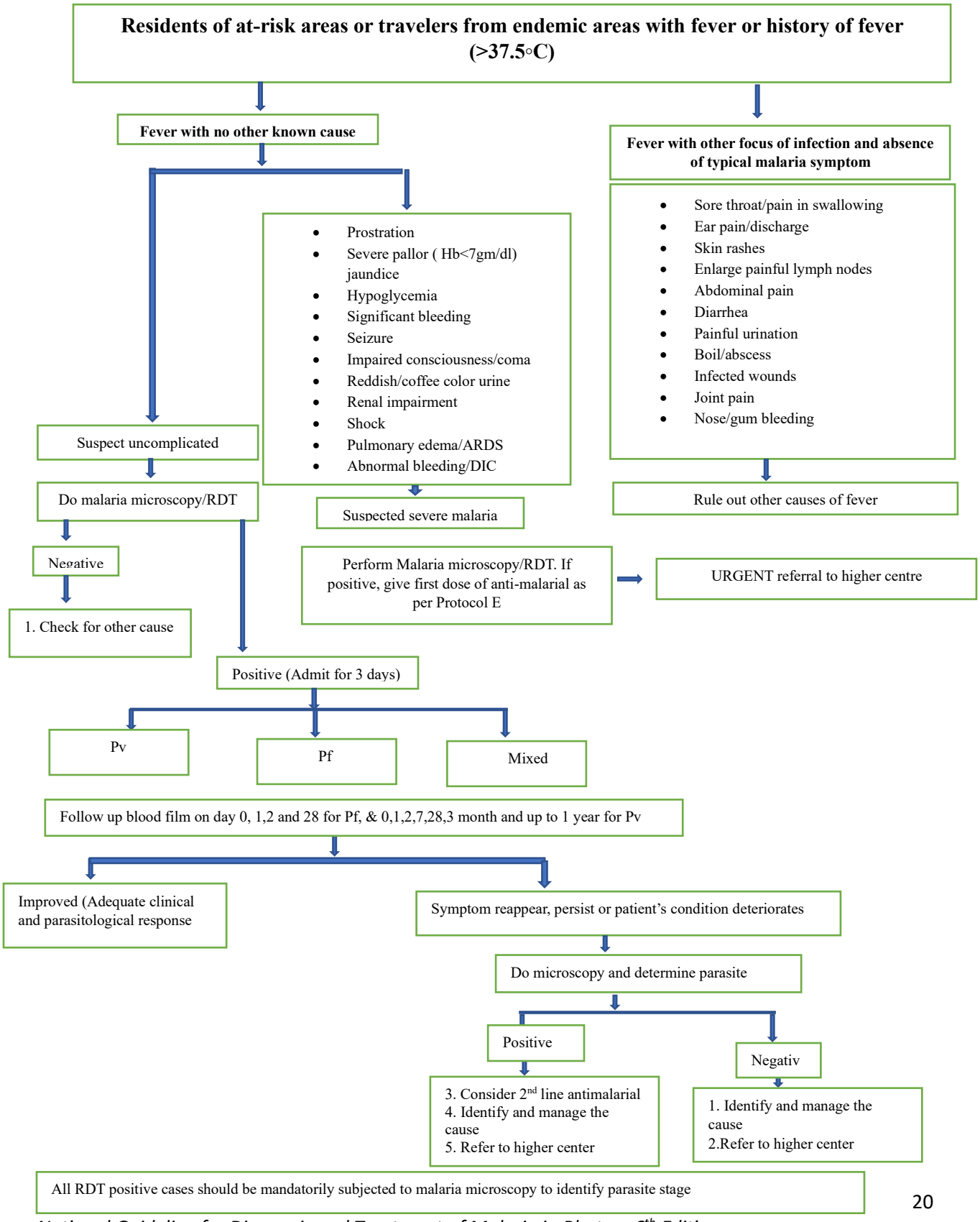
5. World Health Organization (2000), severe falciparum malaria. Transactions of the Royal Society of Tropical Medicine and Hygiene, 94: Supplement 1.

6. World Health Organization Regional Office for the Western Pacific, Malaria Rapid Diagnosis Making it Work , Meeting Report (20-23 January 2003)

7. World Health Organization South East –Asia Regional Office (2003), Regional Guidelines on the management of severe falciparum malaria in Level I and Level II hospitals

8. WHO Guidelines for malaria, 2023

# Annexure 1: Malaria Diagnosis and Treatment Algorithm



## Annexure 2: integrated Drug Efficacy Surveillance (IDES) follow-up form

**INTEGRATED DRUG EFFICACY SURVEILLANCE FORM**

Name of health center: ..…… Dzongkhag:…… BTC No: ……
Unique code:……..
Name of patient:……Age/sex…… Pregnant: Yes [ ] No [ ]
Nationality:…… Occupation: ……..…… Mobile/Telephone No:…….

| Due dates | D0 …../...../… | D1 …./..../… | D2 …../…./… | D7 .../..../… | D28 ../..../… | 3 months ../..../… | 1 year ..../…./.. | Remarks |
|---|---|---|---|---|---|---|---|---|
| Actual visit date | | | | | | | | |
| Temperature (ºC) | | | | | | | | |
| Species Pf(+ve/-ve) | | | | Not required | | Not required | | |
| Parasite count | | | | | | | | |
| DOT treatment-Pf | ACT+PQ * | ACT | ACT | | | | | |
| | Yes / No | Yes / No | Yes / No | | | | | |
| Species *Pv*(+ve/-ve) | | | | | | | | |
| Parasite count | | | | | | | | |
| *DOT treatment-Pv | CQ+PQ | CQ+PQ | CQ+PQ | PQ | | | | |
| | Yes / No | Yes / No | Yes / No | Yes / No | | | | |
| Vomiting within 30 mins of drug intake | Yes / No | Yes / No | Yes / No | | | | | |
| Other drugs (Specify) | | | | | | | | |
| Follow up visits by | | | | | | | | |
| DBS taken or not? | Yes/No | | | | | | | |

****Note: DBS should be taken before initiation of treatment**
***PQ DOT Day3 to 13 to be reported in separate DOT form by DOT provider.**

**Name & Signature**
**In-charge of Laboratory unit**

**Name & signature of CMO**

## Annexure 3: SOP for the preparation and administration of injection Injectable Artesunate

- Weigh the patient
- Determine the no. of vials needed according to body weight (refer protocol E)
- Reconstitute
  - Artesunate powder + 1 ml 5% sodium bicarbonate ampoule (immediately before use)
- Calculate the Artesunate solution according to route of administration:
  - Reconstituted Artesunate + saline solution or 5% dextrose (5ml for IV and 2ml for IM)
- Administer:
  - IV slow bolus 3-4ml/min
  - IM: Inject slowly, spread the doses if more than 2ml over different sites for babies and 5ml for adults
  - The solution should be prepared freshly for each administration and should not be stored.

## Annexure 4: Directly Observed Treatment (DOT) form

**DIRECTLY OBSERVED TREATMENT (DOT) FORM**
**MINISTRY OF HEALTH**
**VECTOR BORNE DISEASE CONTROL PROGRAMME**

| | | | | | | |
|---|---|---|---|---|---|---|
| **A** | **Details of the Patient** | | | | | |
| **A.1** | Name: | | | **A.2** | Age/sex | |
| **A.3** | Village: | | | **A.4** | Chiwog: | |
| **A.5** | Gewog: | | | **A.6** | Dzongkhag: | |
| **A.7** | Contact Number: | | | | | |
| | | | | | | |
| **B** | **Details of treating health center** | | | | | |
| **B.1** | Name of health center : | | | **B.2** | Dzongkhag: | |
| **B.3** | Phone number: | | | | | |
| **B.4** | Three Days Admission: Completed [ ] Not completed [ ] | | | | | |
| **B.5** | Primaquine as per the age of patient handed to DOT provider: Yes [ ] No [ ] | | | | | |
| | | | | | | |
| **C** | **DOT Provider details and proof of DOT** | | | | | |
| **C.1** | **Days** | **Date of DOT** | **Time for DOT** | **Signature of DOT Provider** | **Monitoring** | |
| | Day 3 | | | | Verified by Malaria Technician / Lab Technician By Name & Signature Date…….. | |
| | Day 4 | | | | | |
| | Day 5 | | | | | |
| | Day 6 | | | | | |
| | Day 7 | | | | | |
| C.2 | Name of DOT provider: | | | C.3 | Village/School/Town/Residence: | |
| C.4 | Contact Number: | | | C.5 | Gewog: | |
| C.6 | Chiwog: | | | C.7 | Dzongkhag: | |

We have successfully completed DOT with primaquine as advised by the clinician without dark colored urine, pallor, fatigue shortness of breath and jaundice.

DOT Provider's signature Signature of In-charge/CMO/MS

# Annexure 5: Checklist for patient counseling, detection and management of primaquine- induced hemolysis

## 1.Patient counseling

- G6PD activity is genetically inherited from one's parents
- Explain the reason and benefit of PQ administration
    - We are testing you for G6PD deficiency.
    - We will collect a small sample of blood and test it to determine the levels of G6PD enzyme activity in your blood.
    - We are conducting this test today as a routine part of your care for malaria.
    - This is a rapid test – the results will be delivered within 30 seconds to 3 minutes (depending on the diagnostic tool used).
    - If you would like to know your test results, they can be provided to you during this clinic session. Your treatment provider needs to know if you have G6PD deficiency before prescribing certain medications, such as primaquine, to treat malaria.
    - It will be helpful for you to know if you have G6PD deficiency because if you are G6PD deficient, you may need to avoid specific foods and medications that may cause illness.
- Inquire the patient of any medical history of hemolysis and bleedings
- Inform patient of possible risk of acute hemolytic anemia when taking PQ. Some forms of G6PD deficiency can cause serious illness and others only cause mild symptoms.
- The most serious effect of G6PD deficiency is called haemolysis. Haemolysis is caused by damage to your red blood cells. The red blood cells of people with G6PD deficiency are vulnerable to damage from certain types of foods and medications.

**Symptoms of acute haemolytic anaemia**

- Includes back pain, fever, shortness of breath, jaundice, dizziness, paleness, dark colored urine
- If you experience any of these symptoms, you should notify your health care provider immediately.
- Instruct the patient to monitor her urine color or abnormal menstrual bleedings
- Instruct patient to stop primaquine if his/her urine becomes dark and SEEK IMMEDIATE MEDICAL ATTENTION at the nearest health centre

**2. Management of side effects**

Primaquine is rapidly eliminated from the body (3.5-8hrs) and therefore hemolysis is self-limiting once drug administration is stopped.

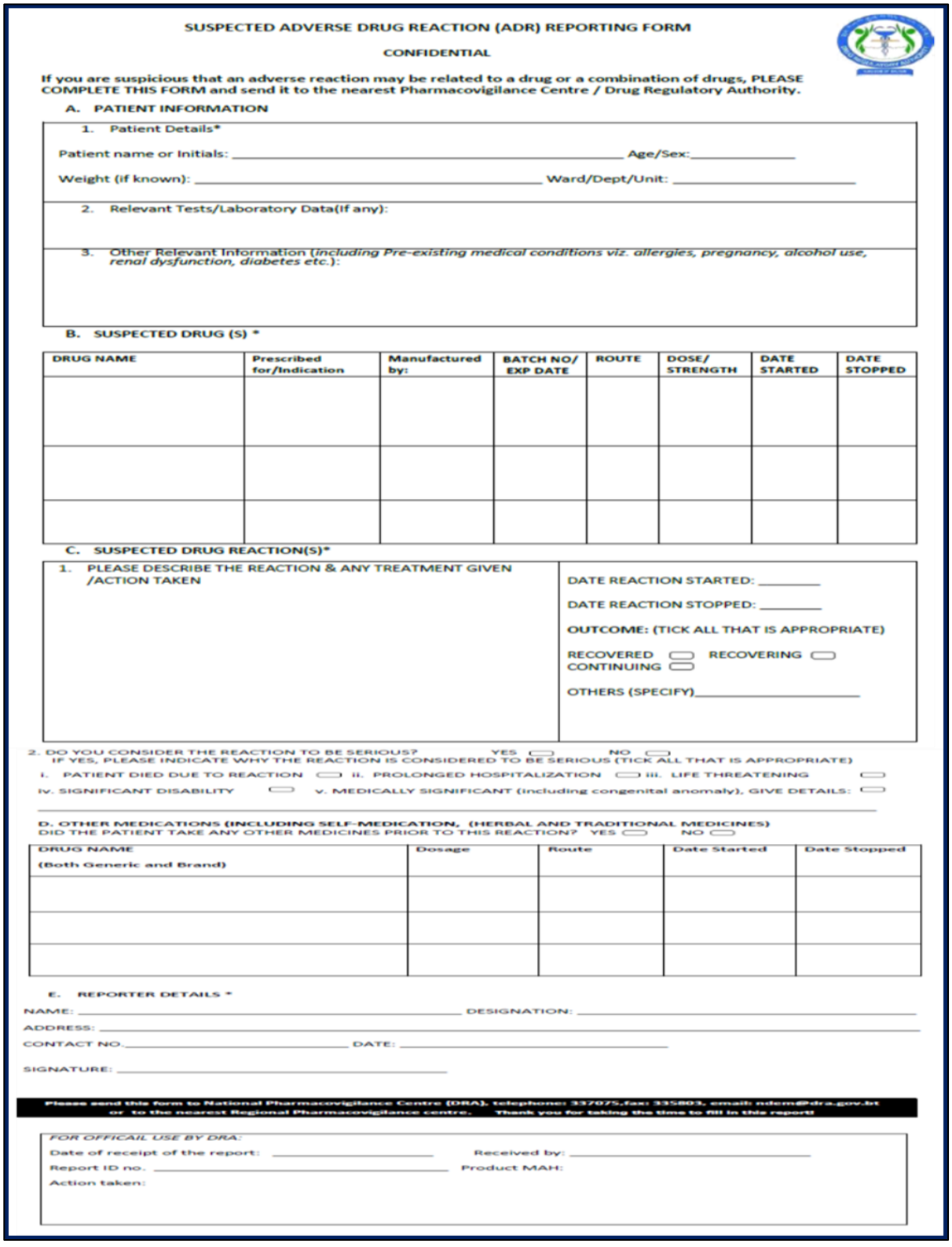
- Provide oral hydration
- Consider admission
- Check hemoglobin or hematocrit
- Check serum creatinine or blood urea
- Arrange blood transfusion if necessary
    - Haemoglobin <7g/dl. give blood transfusion
    - Haemoglobin <9g/dl with ongoing haemolysis, give transfusion
    - Haemoglobin 7-9g/dl with no on-going haemolysis, careful fluid management with monitoring of urine color.

## Annexure 6: Adverse effects and contraindications of antimalarial Drugs

| Sl No | Name of Drug | Adverse Effects | Contraindications |
|---|---|---|---|
| 1 | Chloroquine | Pruritus, Headache, hepatitis, elevated liver enzymes, nausea, vomiting, diarrhea, skin rashes and rarely convulsions and mental changes. | Known hypersensitivity to chloroquine or any aminoquinolone compounds. |
| 2 | Primaquine | Nausea, vomiting, anorexia and abdominal pain. Rarely, it can cause hypertension and cardiac arrhythmia. It can result in hemolysis in G6PD deficiency cases. | Known hypersensitivity to primaquine, in G6PD deficiency pregnancy, breast feeding and infants less than 6 months. |
| 3 | Coartem (Artemether + Lumefanthrine) | Nausea, dizziness and headache | Known hypersensitivity to either artemether or lumefantrine |
| 4 | Artemether | Hypersensitivity reactions gastrointestinal disturbances, dizziness, reticulocytopenia, neutropenia and elevated liver enzymes. | Known hypersensitivity to any a artemisinin derivatives |
| 5 | Artesunate | Hypersensitivity reactions gastrointestinal disturbances, cough, rash, arthralgia, dizziness and delayed hemolysis. Dose dependent neutropenia was observed in some cases. | Known hypersensitivity to artesunate or artemisinin derivatives |
| 6 | Quinine | Cinchonism (tinnitus, headache, blurred vision, hearing change, nausea and diarrhea) Deafness, blindness, postural hypotension and hypoglycemia are other some of the serious adverse effects. | Quinine is contraindicated in patients with known hypersensitivity to quinine or any of the cinchona alkaloids. |

# Annexure 7: Serious adverse drug event reporting form

(can be reported online: https://dra.gov.bt/?page_id=2117)



**SUSPECTED ADVERSE DRUG REACTION (ADR) REPORTING FORM**

**CONFIDENTIAL**

**If you are suspicious that an adverse reaction may be related to a drug or a combination of drugs, PLEASE COMPLETE THIS FORM and send it to the nearest Pharmacovigilance Centre / Drug Regulatory Authority.**

**A. PATIENT INFORMATION**

1. Patient Details*

Patient name or Initials: _____ Age/Sex:_____

Weight (if known): _____ Ward/Dept/Unit: _____

2. Relevant Tests/Laboratory Data(If any):

3. Other Relevant Information (*including Pre-existing medical conditions viz. allergies, pregnancy, alcohol use, renal dysfunction, diabetes etc.*):

**B. SUSPECTED DRUG (S) ***

| DRUG NAME | Prescribed for/Indication | Manufactured by: | BATCH NO/ EXP DATE | ROUTE | DOSE/ STRENGTH | DATE STARTED | DATE STOPPED |
|---|---|---|---|---|---|---|---|
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |

**C. SUSPECTED DRUG REACTION(S)***

1. PLEASE DESCRIBE THE REACTION & ANY TREATMENT GIVEN /ACTION TAKEN

DATE REACTION STARTED: _____

DATE REACTION STOPPED: _____

**OUTCOME:** (TICK ALL THAT IS APPROPRIATE)

RECOVERED ☐ RECOVERING ☐
CONTINUING ☐

OTHERS (SPECIFY)_____

2. DO YOU CONSIDER THE REACTION TO BE SERIOUS? YES ☐ NO ☐
IF YES, PLEASE INDICATE WHY THE REACTION IS CONSIDERED TO BE SERIOUS (TICK ALL THAT IS APPROPRIATE)

i. PATIENT DIED DUE TO REACTION ☐ ii. PROLONGED HOSPITALIZATION ☐ iii. LIFE THREATENING ☐

iv. SIGNIFICANT DISABILITY ☐ v. MEDICALLY SIGNIFICANT (including congenital anomaly), GIVE DETAILS: ☐

_____

**D. OTHER MEDICATIONS (INCLUDING SELF-MEDICATION, (HERBAL AND TRADITIONAL MEDICINES)**
DID THE PATIENT TAKE ANY OTHER MEDICINES PRIOR TO THIS REACTION? YES ☐ NO ☐

| DRUG NAME (Both Generic and Brand) | Dosage | Route | Date Started | Date Stopped |
|---|---|---|---|---|
| | | | | |
| | | | | |
| | | | | |

**E. REPORTER DETAILS ***

NAME: _____ DESIGNATION: _____

ADDRESS: _____

CONTACT NO._____ DATE: _____

SIGNATURE: _____

**Please send this form to National Pharmacovigilance Centre (DRA), telephone: 337075,fax: 335803, email: ndem@dra.gov.bt or to the nearest Regional Pharmacovigilance centre. Thank you for taking the time to fill in this report!**

*FOR OFFICAIL USE BY DRA:*

Date of receipt of the report: _____ Received by: _____

Report ID no. _____ Product MAH:

Action taken:

## Annexure 8: Malaria death Investigation form

**Malaria Death Investigation Form**

Record No……. Name of Health Center…….

District ……

Name ……Age ……. Sex :……

Name of guardian……

Address ……

Contact No……

1. **Duration of illness before admission to referral hospital**

**1.1 History**

| **Signs and Symptoms** | **Duration (hrs/Days)** |
|---|---|
| Fever | |
| Not able to drink and or eat | |
| Repeated vomiting | |
| Unable to stand and sit | |
| Unconsciousness | |
| Convulsion | |
| Severe jaundice | |
| History of treatment taken | |

**Note:** Write number of days or hours if known: (-) if not known: (X) if absent

**1.2.Clinical examination at primary health center (PHC/hospitals)**

| **Signs and symptom** | **Date** | **Date** | **Date** |
|---|---|---|---|
| Temperature | | | |
| Jaundice | Present/Absent | Present/Absent | Present/Absent |
| Sensorium (with grading) | Coma grade/1/2/3/4/5 | Coma grade/1/2/3/4/5 | Coma grade/1/2/3/4/5 |
| Dehydration | Mild/moderate/severe | Mild/moderate/severe | Mild/moderate/severe |
| Pulmonary oedema | Present/Absent | Present/Absent | Present/Absent |
| Spontaneous bleeding | Present/Absent | Present/Absent | Present/Absent |
| Shock/hypertension | Present/Absent | Present/Absent | Present/Absent |
| Convulsions | Present/Absent | Present/Absent | Present/Absent |
| Hypoglycemia | Present/Absent | Present/Absent | Present/Absent |

| | | | |
|---|---|---|---|
| ( blood sugar <40mg/dl | …… ml | …… ml | …… ml |
| Urine output( in ml/24hrs Parasitaemia at admission | …… ……./µl | …… ……./µl | …… ……./µl |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Hematocrit | | | | | | | | |
| S.Bilirubin | | | | | | | | |
| S.creatinine | | | | | | | | |
| S.Electrolyte | | | | | | | | |
| RBC/mm3 | | | | | | | | |
| Platelets/mm3 | | | | | | | | |
| **Note: Put (X) if not done** | | | | | | | | |

**2. Clinical presentation at admission (Referral Hospital)**

| **Signs and symptom** | **Date** | **Date** | **Date** |
|---|---|---|---|
| Temperature | | | |
| Jaundice | Present/Absent | Present/Absent | Present/Absent |
| Sensorium (with grading) | Coma grade/1/2/3/4/5 | Coma grade/1/2/3/4/5 | Coma grade/1/2/3/4/5 |
| Dehydration | Mild/moderate/severe | Mild/moderate/severe | Mild/moderate/severe |
| Pulmonary oedema | Present/Absent | Present/Absent | Present/Absent |
| Spontaneous bleeding | Present/Absent | Present/Absent | Present/Absent |
| Shock/hypertension | Present/Absent | Present/Absent | Present/Absent |
| Convulsions | Present/Absent | Present/Absent | Present/Absent |
| Hypoglycemia | Present/Absent | Present/Absent | Present/Absent |
| ( blood sugar <40mg/dl | ……ml | ……ml | ……ml |
| Urine output (in ml/24hrs Parasitaemia at admission | ……/µl | ……./µl | ……./µl |

**3. Response to treatment**

| Parameter | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 |
|---|---|---|---|---|---|---|
| 1.Parasitological ( Counts/µl of blood if available | | | | | | |
| 2.Clinical highest temperature in ◦C | | | | | | |
| Jaundice | P/A | P/A | P/A | P/A | P/A | P/A |
| Sensorium ( write grade if in comma) | C/- | | C/- | C/- | C/- | C/- |
| Dehydration | M/Mod/S | M/Mod/S | M/Mod/S | M/Mod/S | M/Mod/S | M/Mod/S |
| Pulmonary odema | | | | | | |
| Central venous pressure | | | | | | |
| Respiratory insufficiency | P/A | P/A | P/A | P/A | P/A | P/A |
| Spontaneous bleeding | P/A | P/A | P/A | P/A | P/A | P/A |
| Shock | P/A | P/A | P/A | P/A | P/A | P/A |
| Convulsion | P/A | P/A | P/A | P/A | P/A | P/A |
| Acidosis | P/A | P/A | P/A | P/A | P/A | P/A |
| Hypog;yaemia(blood sugar <40mg/dl | P/A | P/A | P/A | P/A | P/A | P/A |
| Fluid intake/output in ml/24hrs | MI | MI | MI | MI | MI | MI |
| Sepsis | P/A | P/A | P/A | P/A | P/A | P/A |
| **Note:**<br>**Present/Absent: P/A**<br>**Mild/moderate/severe: M/Mod/S**<br>**Conscious/coma grade : C/-** | | | | | | |

**4. Investigation**

| Laboratory result | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Day 8 |
|---|---|---|---|---|---|---|---|---|
| Blood sugar | | | | | | | | |
| Hematocrit | | | | | | | | |
| S.Bilirubin | | | | | | | | |
| S.creatinine | | | | | | | | |
| S.Electrolyte | | | | | | | | |
| RBC/mm3 | | | | | | | | |
| Platelets/mm3 | | | | | | | | |
| **Note:** Put (X) if not done | | | | | | | | |

**5.Treatment given (with dose)**

| |
|---|
| |

**6. Tolerance to the drugs**

| Time in hours | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Day 8 |
|---|---|---|---|---|---|---|---|---|
| Cardiac site effects | | | | | | | | |
| Arrhythmia | | | | | | | | |
| Hypotension | | | | | | | | |
| Hypoglycemia | | | | | | | | |
| Hemmorage | | | | | | | | |
| Any other (specify) | | | | | | | | |

7. **Cause of death**

Specify according to format used for HMIS

Comments/ inference

Most probable cause of death in your opinion was

| | |
|---|---|
| a. Delay in diagnosis and treatment | Yes ( ) No ( ) |
| b. Lack of awareness | Yes ( ) No ( ) |
| c. Inaccessibility of the health center | Yes ( ) No ( ) |
| d. Treatment failure | Yes ( ) No ( ) |
| e. Drug intolerance | Yes ( ) No ( ) |
| f. Secondary complications | Yes ( ) No ( ) |
| If yes specify: | |

Any other Yes/No

**Investigation team**

| Sl.no | Name | Designation | Signature |
|---|---|---|---|
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## Annexure 9: Flowchart for G6PD test