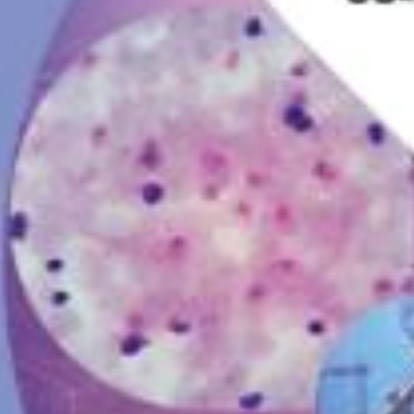




กรมการแพทย์
กรมโรคติดต่อป็นอันตราย

แนวทางเวชปฏิบัติ ในการรักษาผู้ป่วยโรคไข้มาลาเรีย

ประเทศไทย พ.ศ. 2564



กองโรคติดต่อทั่วไป กรมการแพทย์
กระทรวงสาธารณสุข

Guidelines for Clinical Management of Malaria

Thailand 2021

Division of Vector-borne Disease

Department of Disease Control, Ministry of Public Health

Guidelines for Clinical Management of Malaria 2021

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Order of the Department of Disease Control
The Committee on Malaria Drug Policy and Treatment Guidelines

Order of the Department of Disease Control

No. 192/2564

Establishment of the Committee on Malaria Drug Policy and Treatment Guidelines

Reference is made to the order of the Department of Disease Control No. 1387/2562 on establishment of the Malaria Drug Policy and Treatment Guidelines dated 11 October 2019 for providing technical support on malaria drug policy and treatment guidelines in Thailand. As some members of the former Committee have retired and there were reshuffles in administrative officers of the Department, to enable the committee to provide technical advice that are up-to date and standardized for the entire country, and to achieve the objectives and enhance collaboration and coordination among institutions effectively, therefore, the Director-General of the Department of Disease Control proposed the following commands:

1. Cancel the command No. 1387/2562 dated 11 October 2019.
2. Establish a new Committee on Malaria Drug Policy and Treatment Guidelines that consists of compositions, terms of reference and responsibilities as follows:

1. Composition of the Committee

1.1	Director-General, Department of Disease Control	Chair
1.2	Deputy Director-General, Department of Disease Control (that oversee DVBD)	Vice-chair
1.3	Mr Suwich Thamapalo, acting Senior Expert, DDC	Member
1.4	Ms Krongthong Thimasarn, Independent Consultant on Malaria	Member
1.5	Mr Wichai Satimai, Independent Consultant on malaria	Member
1.6	Mr Ronnatrai Rueangweerayut, Independent Consultant on Malaria	Member
1.7	Prof. Polrat Wilairattana, Faculty of Tropical Medicine, Mahidol University	Member
1.8	Prof. Srivicha Krudsood, Faculty of Tropical Medicine, Mahidol University	Member
1.9	Associate Prof. Pantip Chayakul, Faculty of Medicine, Songkhla University	Member
1.10	Assistant Prof. Cherdchai Sunthornpas, Faculty of Pharmacy, Khonkhaen University	Member

1.11	Assistant Prof. Damrongsak Pekthong, Faculty of Pharmacy, Naresuan University	Member
1.12	Representative, Drug Division, Food and Drug Administration (FDA)	Member
1.13	Representative, Government Pharmaceutical Organization (GPO)	Member
1.14	Representative, Siriraj Faculty of Medicine	Member
1.15	Representative, Phramongkutklao Faculty of Medicine	Member
1.16	Representative, Armed Forces Research Institute Medical Sciences (AFRIMS)	Member
1.17	Representative, the Royal College of Physicians of Thailand (RCPT)	Member
1.18	Representative, the Royal College of Pediatricians of Thailand (RC Ped T)	Member
1.19	Representative, the Royal Thai College of Obstetricians and Gynaecology (RTCOCG)	Member
1.20	Representative, Infectious Disease Association of Thailand	Member
1.21	Representative, Private Hospital Association of Thailand	Member
1.22	Representative, Thailand MOPH – U.S.CDC Collaboration on Health (TUC)	Member
1.23	World Health Organization Representative to Thailand (WR Thailand)	Member
1.24	Representative, Mahidol Oxford Tropical Medicine Research Unit (MORU)	Member
1.25	Director, Division of Vector-borne Disease, Department of Disease Control	Member and Secretariat
1.26	Deputy-Director, Division of Vector-borne Disease, Department of Disease Control	Member and Assistant Secretariat
1.27	Head, Malaria Cluster, Division of Vector-borne Disease, Department of Disease Control	Member and Assistant Secretariat

2. Terms of reference:

2.1 Formulate policy, guidelines for the use of antimalarial drugs including related drugs for treatment of malaria in the country.

2.2 Monitor, study and analyze situation and problems of antimalarial drug resistance.

2.3 Provide advice, recommendations on technical aspects related to treatment of malaria.

2.4 Other duties as assigned.

Effective from today onward

Dated 28 January 2021

(signature)

(Dr Opas Karnkawinpong)

(Director-General, Department of Disease Control)

Order of the Department of Disease Control

No. 1327/2564

Establishment of the Committee on Malaria Drug Policy and Treatment Guidelines (Amendment)

Reference is made to the order of the Department of Disease Control No. 192/2564 on establishment of the Malaria Drug Policy and Treatment Guidelines dated 28 January 2564 (2021). To enable the malaria treatment guidelines in Thailand to be in line with the current context and to standardize it for the whole country and to achieve the objectives and enhance collaboration and coordination among institutions effectively, and as per Article 32 of the State Administration Act, B.E. 2534 and its amendments (Edition 5 dated B.E. 2545) the Department of Disease Control appointed an additional member as follows:

1. Dr Krisada Jongsakul, Independent Consultant on Malaria as member of the Committee

Other issues remain unchanged.

Effective from 27 July 2021

(signature)

(Dr Opas Karnkawinpong)

Director-General, Department of Disease Control

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General knowledge and epidemiology of Malaria

Malaria

Malaria is an infectious disease caused by protozoa in Plasmodium group. Malaria is transmitted mainly by biting of Anopheles spp. mosquitoes. Besides, there have been reports on man-to-man transmission via blood transfusion, organ transplantation and from mother to fetus but this is very rare. Malaria is prevalent in tropical zone and during rainy season because Anopheles mosquitoes breed in natural water sources especially in warm climate. Mosquito larvae hatch from eggs in 2-3 days and they take 9-12 days in larval stages before becoming adult mosquitoes. Only female mosquitoes bite humans and animals so they can transmit malaria parasites. Persons who receive malaria parasites will develop symptoms after incubation period of some 10-14 days or longer depending on plasmodium species. Main symptoms are fever, chill, headache and muscle pain. Some severe cases may develop complications such as liver failure, renal failure, cerebral malaria which may lead to death if they do not receive proper treatment in time.

Life cycle of malaria parasites

There are 5 malaria parasites species that cause disease in human, i.e., *P. falciparum*, *P. vivax*, *P. malariae*, *P. ovale* and *P. knowlesi*. In Thailand, majority of parasites are *P. vivax* and *P. falciparum*. *P. knowlesi* is prevalent in Malaysia and Indonesia. However, Thailand has also reported *P. knowlesi* in several provinces.

Life cycle of Plasmodium consists of 2 stages as follows:

- 1) Sexual stage in vector (Sporogony)
- 2) Asexual stage in human (Schizogony), which is further divided into 2 stages:
 - Liver cell stage (Exo-erythrocytic schizogony)
 - Red blood cell stage (Erythrocytic schizogony)

In sexual life cycle in mosquito vectors, sporozoites in mosquito salivary gland are ready for transmitting the disease. When a malaria infected mosquito bites a human, sporozoites will enter to human blood stream and develop into asexual cycle in human.

In asexual life cycle in human, malaria parasites undergo asexual cell division without mating of sexual cells. The cycle starts with liver stage when sporozoites enter human blood stream, they will enter liver cells and multiply several times until they reach schizont stage that contains thousands of merozoites which cause rupture of liver cells. It is approximately 6-16 days after human was infected, liver cells rupture and release merozoites that will mainly enter red blood cells.

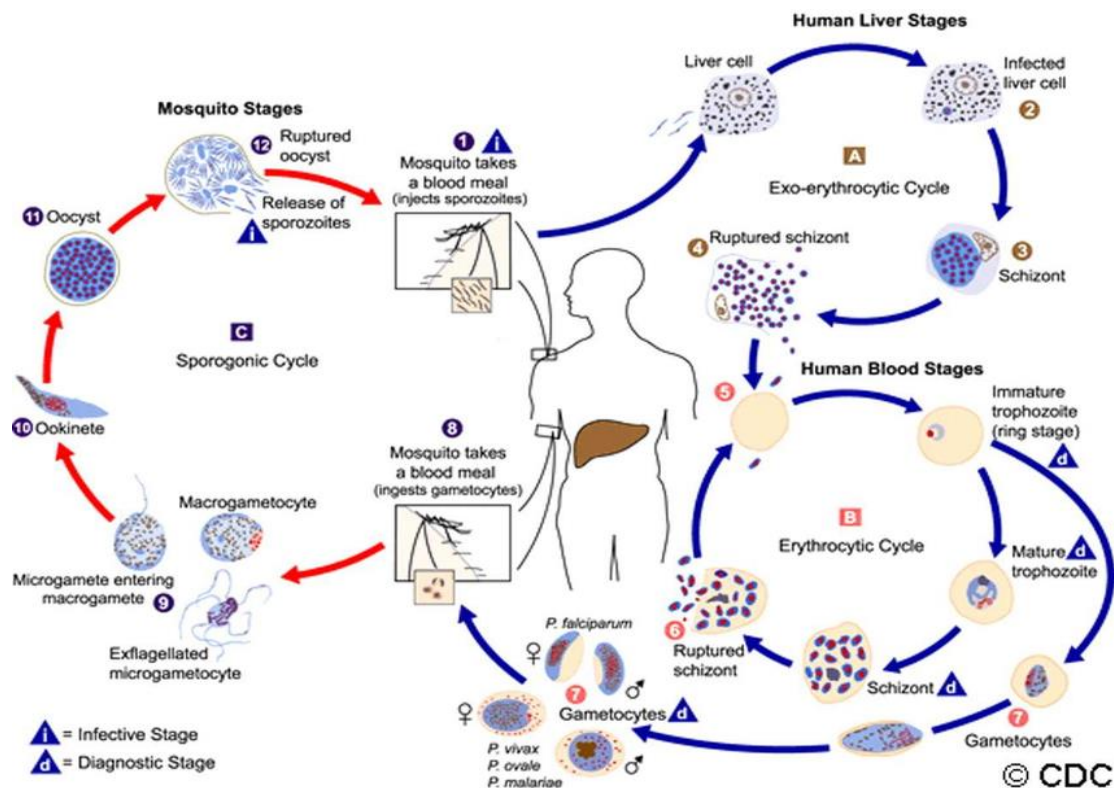
Some parasites of *P. vivax* and *P. ovale* in liver cells may persist quietly without any development or cell division for weeks or months or even years before they grow and multiply again and cause relapse. The resting stage of parasites in liver is called ‘hypnozoite’.

Merozoite stage in red blood cell will further develop into immature trophozoite (ring form) and mature trophozoite, respectively. After that it will enter schizont stage when its nucleus divides into numerous merozoites, until red blood cell rupture and release merozoites into blood circulation. These parasites will again invade new red blood cells and complete asexual life cycle in human red blood cells. This causes cycle of fever and chill due to rupturing of red blood cells. Cycle of fever varies depending on parasite species, as follows:

<i>P. falciparum</i> >>	approximately 36-48 hours
approximately 42-48 hours	<< <i>P. vivax</i>
<i>P. malariae</i> >>	approximately 72 hours
approximately 50 hours	<< <i>P. ovale</i>
<i>P. knowlesi</i> >>	approximately 24 hours, so it can cause rapid and severe symptoms because of short life cycle. Microscopic diagnosis is difficult. Therefore, if a patient is rapidly severe, <i>P. knowlesi</i> should be kept in mind. <i>P. knowlesi</i> is zoonotic malaria that parasites in monkey are transmitted to human through Anopheles mosquito bite.

After fever and chills for 3-15 days, some merozoites that invade red blood cells will change their forms to sexual stage, so-called ‘Gametocyte’ which consists of male and female

gametocytes. If an anopheles vector bites the human who harbors these sexual malaria parasites, they shall undergo life cycle in vector and cause further transmission (Figure 1). Sexual parasites do not cause any symptoms. If there is no mosquito to bite and take them, they will die and disappear from blood circulation within 1-2 months.

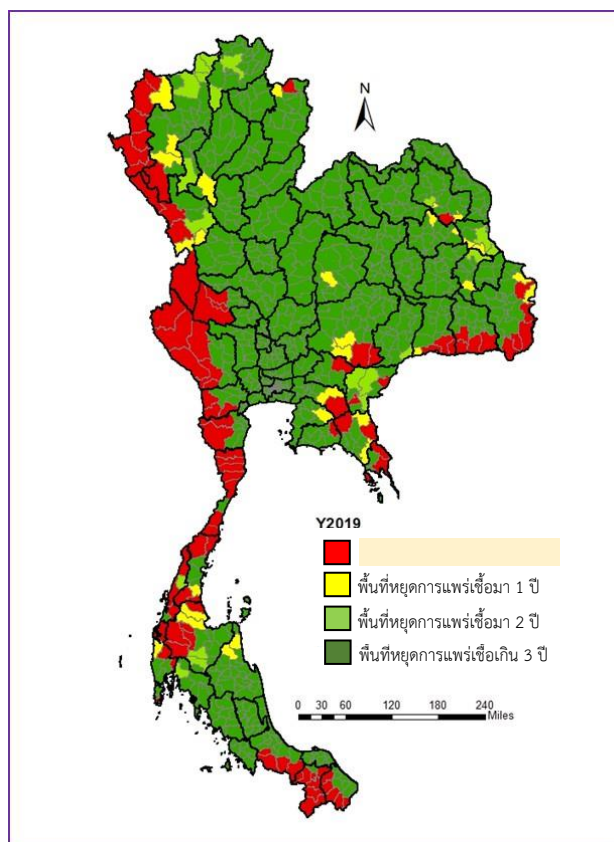


Source: www.cdc.gov/parasites/malaria/index.html

Figure 1 Life cycle of malaria parasites showing various stages.

Malaria situation in Thailand

At present, Thailand reports malaria patients less than 10,000 cases annually. Malarious areas are provinces near borders with neighboring countries where there are forests and mountains. Mosquito vectors can live in such areas. Therefore, border provinces and districts are vulnerable for malaria transmission (Figure 2). However, malaria cases can be found in all areas of the country. As malaria incidence has decreased significantly, population immunity also decreased. Thus, severe malaria patients are more common.



	Areas with transmission in the current year
	Areas where transmission ceased for 1 year
	Areas where transmission ceased for 2 years
	Areas where transmission ceased > 3 years

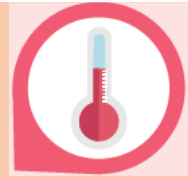
Source: <http://malaria.ddc.moph.go.th>

Figure 2: Areas in Thailand with various levels of malaria transmission.

In addition, Thailand has reported problems of drug resistant malaria for so long, especially *P. falciparum* with documented resistance to Chloroquine, Mefloquine and Artemisinin-based combination therapy. Therefore, the first line treatment for falciparum malaria has been changed to Dihydroartemisinin-Piperaquine plus Primaquine since 2015. However, in 2019 efficacy of Dihydroartemisinin-Piperaquine in Srisaket and Ubonratchathani Provinces reduced to lower than 90%. In addition, there have been evidences from biomolecular studies showing drug resistance in the same areas. Consequently, consensus of the National Committee

on Malaria Drug Policy and Treatment Guidelines proposed change of the first line treatment of falciparum malaria to the fixed-dose combination of Artesunate-Pyronaridine only in Srisaket and Ubonratchathani Provinces from 2019 onward. Therefore, drug resistance situation in the place of origin where patients contracted malaria should be considered whenever prescribing drugs.

Symptoms and types of patients



General symptoms

Following biting of malaria vectors, the most common symptom is fever. The incubation period (period between mosquito bite and onset of illness) varies depending on parasite species, as follows:

Parasite species	Incubation period
<i>P. falciparum</i>	9-14 days
<i>P. vivax</i>	12-17 days
<i>P. malariae</i>	18-40 days
<i>P. ovale</i>	16-18 days
<i>P. knowlesi</i>	9-12 days

Persons who get parasite infection as the first time, the initial illness is fever and timing of fever is irregular. Other symptoms are non-specific, such as headache, muscle pain, weakness, loss of appetite, during the first 2-3 days. After that, if patients do not receive treatment, fever will become regular and intermittent according to rupture of parasitized red blood cells.

Types of infections: Malaria morbidity consists of 4 types, as follows:

1. Primary attack:

There are signs and symptoms after receiving malaria parasites as the first time.

2. Relapse:

Malaria patients have recurring of fever. Malaria parasites are found in blood again after treatment without receiving new infection. The relapse of malaria can be found in *P. vivax* and *P. ovale* because these two species have dormant parasite liver stages (so-called hypnozoites) persisting in liver cells which can start growth and invade red

blood cells and cause relapse. Recurring fever is generally less severe than the first episode of fever.

3. **Recrudescence:**

Malaria patients have recurring of fever after treatment which is caused by remaining parasites in red blood cells that were not destroyed. This is because antimalarial drugs are not appropriate, or treatment is incomplete, or parasites resist to the antimalarial drugs. The remaining parasites can multiply and cause illness.

4. **Reinfection:**

Malaria patients have recurring of fever which is caused by new infections. It may be the same parasite species or different species from the previous infection.

Diagnosis and laboratory examination



History and symptoms suspected of malaria.

- Persons who live in, come from or have visited a malaria transmission area within the last 1 month.
- Persons who had malaria within the past 1 year.
- Having fever and/or non-specific symptoms like other viral infections, headache, fatigue, abdominal discomfort, muscle pain and joint pain, chill, sweating, loss of appetite, nausea and vomiting, children may be drowsy, take only little amount of food, or unable to eat, pale, enlarged liver and spleen.
- In severe malaria, consciousness is impaired or unconscious, very weak, convulsion, dyspnea, fast breathing, shock, yellowish sclera, jaundice, low urine output or anuria, dark urine and very pale (anaemia).

Laboratory examination.

Confirmation of malaria infections can be done through laboratory examination, as follows:

1. Microscopic diagnosis for malaria

Malaria microscopy is a standard method and malaria parasite species and stages can be identified and parasite density can be quantified. Both thick and thin blood films should be made because thick films provide high sensitivity in detecting malaria parasites, approximately 20-40 times higher than that of the thin films. Expert microscopists can detect as low as 5 parasites per 1 microlitre of blood. In average, they can detect 20-100 parasites per 1 microlitre of blood, depending on how good the blood films are prepared and skills of microscopists. Parasite species can be clearly determined in thin films. Making both thick and thin films on the same blood slide will comfort the microscopists and is easy for sending blood films for

confirmation. However, thick and thin films may be prepared separately on different blood slides but there should be a clear remark that they are from the same patient when sending blood films for confirmation of result.

2. Rapid Diagnostic Test

At present, there are rapid diagnostic tests that can differentiate between *P. falciparum* and non-*P. falciparum* and some brands can differentiate *P. vivax* and *P. ovale*. These tests are certified by WHO. It is recommended that RDTs be used in malaria posts, border malaria posts and sub-district health promoting hospitals where there are no microscopic facilities. However, at present, *P. knowlesi* cannot be diagnosed by RDT, such suspected cases blood samples must be sent for Polymerase Chain Reaction (PCR) diagnosis only.

Precaution: RDTs that detect *Plasmodium falciparum histidine-rich protein 2* (Pf HRP2) for *P. falciparum* will remain positive for several weeks after acute infection even if there are no viable parasites in blood circulation. Such RDTs can be used for diagnosis but not for post-treatment follow-up. In addition, negative results may be due to low parasitaemia.

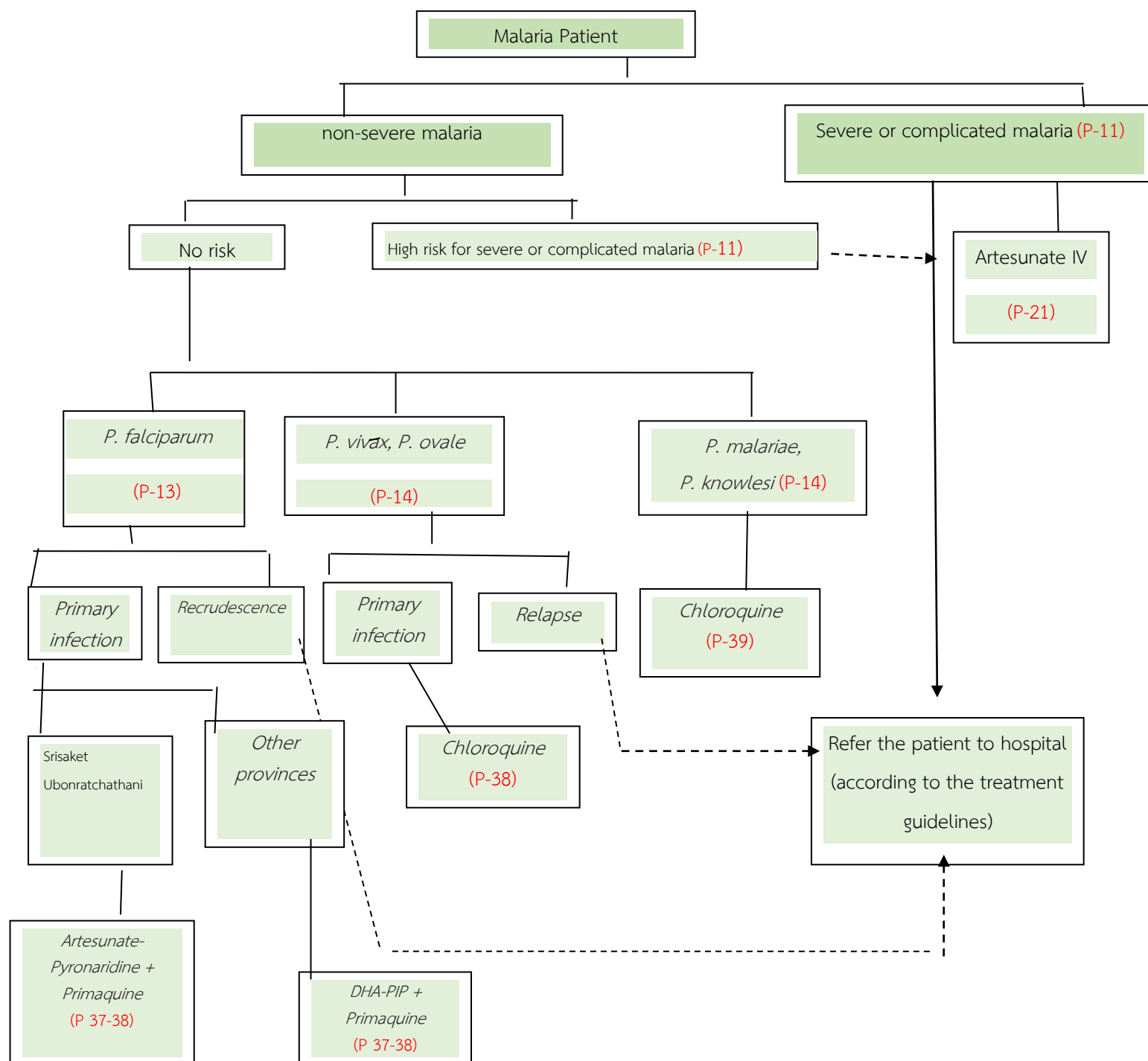
3. Bio-molecular test

Such as detection of genes by polymerase chain reaction (PCR) method to diagnose and confirm malaria species. Blood samples should be taken and sent to health facilities that can conduct the tests, for the following patients:

- 1) Patients with microscopic diagnosis suspected of *P. knowlesi* or *P. malariae*.
- 2) Patients suspected of malaria, but other tests are negative.
- 3) Patients with severe malaria (suspected)
- 4) Patients who die of malaria (suspected)

Clinical management of malaria patients

Diagram 1: Summary of drugs for treatment of malaria according to the policy on malaria diagnosis and treatment under the National Malaria Elimination Strategy, 2017-2026.



To prescribe antimalarial drugs to patients with laboratory-confirmed malaria parasites as soon as possible. To follow-up patients to ensure complete drug intake and no severe drug side effects and cure from the illness including negative repeat blood examination.

A. Malaria patients with complications or severe malaria.

- Impaired consciousness or unconsciousness.
- Very weak until cannot sit, walk and stand on his own.
- Convulsions
- Dyspnea, rapid breathing.
- Jaundice, yellowish sclera, high blood bilirubin with parasite density higher than 100,000 parasites/ μ l blood.
- Anaemia with parasite density higher than 100,000 parasites/ μ l blood.
- Shock.
- Low urine output or no urine at all over 4 hours or renal failure.
- Abnormal bleeding, hematemesis (vomiting blood), and melena (bloody stool).
- Hypoglycaemia.
- Acidosis, high level lactate or low bicarbonate.
- Dark urine (Hemoglobinuria).
- Pulmonary edema.

B. High risk group of complications or severe malaria

- Children below 1 year or body weight lower than 11 kg
- Children below 5 years who have fever, temperature higher than 39 degrees Celsius.
- Pregnant women or lack of menstruation and suspected pregnancy.
- Patients with G6PD deficiency
- Suspected *P. knowlesi* infection
- Patients with underlying diseases, such as obesity, alcoholism, liver disease, renal disease, diabetic mellitus, hypertension, blood disorder, abnormal immunity, etc.
- Patients who cannot ingest oral drug or vomit after taking drug or repeated vomiting within one hour after taking new tablet.
- Patients with history of allergy to antimalarial drug.
- Patients with malaria parasite density higher than 2500 parasites per 200 WBC or 100,000 parasites/ μ l blood in thick film, or schizont stage is found.

The must do list for patient care:

- Adjust drug dosage according to patient body weight based on ideal body weight (not more than 80 kg.)
- Conduct G6PD test (to check if G-6-PD deficiency) or take history of black urine of all *P. vivax* and *P. ovale* patients before prescribing Primaquine.
 - In case of mild G6PD deficiency, if quantitative G6PD test (annex) is conducted, or if the patient has history of black urine, consider prescribing Primaquine 45 mg. in adults (0.75mg/kg) once a week for 8 weeks and follow-up on Day 3, 5 and 7 after treatment to check if there is hemolysis. If this condition is found, stop the drug immediately.
 - In case there is no G6PD test at health facility and health facility cannot send blood sample to check G6PD status such as in remote community hospital, consider prescribing Primaquine 0.25mg/kg/day for 14 days. Advise the patient to check if there is dark or black urine or the patient becomes weak, has yellowish sclera, jaundice, stop Primaquine immediately and go to see doctor at hospital.
- In pregnant women, strictly do not prescribe Primaquine.
- Monitor treatment outcome by follow-up as scheduled visits, by taking thick and thin blood films in the same slide for checking parasites in all follow-up visits.
 - *P. falciparum*, *P. malariae* and *P. knowlesi* cases: to appoint patient for checking symptoms and blood on Day 3, 7, 28 and 42 after the beginning of treatment.
 - *P. vivax* and *P. ovale* cases: to appoint patient for checking symptoms and blood on Day 14, 28, 60 and 90 after the beginning of treatment.
- Diagnosis and treatment of uncomplicated malaria in high-risk groups of complications and severe malaria should be done at community hospital or higher level.
- Diagnosis and treatment of severe or complicated malaria should be done at community hospital with adequate facilities or general hospital or regional hospital.
- Provide patient cards for all patients to monitor treatment outcome continuously.
- Do not recommend chemoprophylaxis in Thailand as there is drug resistance until there is no suitable drug that completely protects against malaria. Recommend personal protection against mosquito bite instead.



If there is any question or need advice on drug use, contact the Hot Line of the Department of Disease Control at 1422.

Treatment of uncomplicated malaria patients

Treatment of uncomplicated malaria can be done at malaria clinic, malaria post, border malaria post and sub-district health promoting hospital and higher level.

Uncomplicated malaria in high-risk groups of complications and severe malaria should be referred to community hospital or higher level.

1. Uncomplicated falciparum malaria

1.1. In area where resistance to Dihydroartemisinin-Piperaquine (DHA-PIP) has not been reported

Drug used: Dihydroartemisinin-Piperaquine (Fixed-Dose Combination) and Primaquine

Drug administration: Oral dose of Dihydroartemisinin-Piperaquine 3 days and Primaquine 1 day as follows:

Day from the day treatment starts	Day 0 (first day)	Day 1	Day 2
Dihydroartemisinin-Piperaquine (DHA-PIP) Drugs should be taken at the same time of the day, every day.	1 time	1 time	1 time
Primaquine	1 time only on any day by considering patient's symptoms to see when he can take oral drug without vomiting.		

1.2. In area where resistance to Dihydroartemisinin-Piperaquine has been found

(data as of September 2019, *P. falciparum* resisted to DHA-PIP only in Srisaket and Ubonratchathani provinces)

Drug used: Artesunate-Pyronaridine (Fixed-dose combination) and Primaquine.

Drug administration: Oral dose of Artesunate-Pyronaridine 3 days and Primaquine 1 day as follows:

Day from the day treatment starts	Day 0 (first day)	Day 1	Day 2
Artesunate-Pyronaridine by taking the drug at the same time of the day, every day.	1 time	1 time	1 time
Primaquine	1 time only on any day by considering patient's symptoms to see when he can take oral drug without vomiting.		

2. Uncomplicated vivax and ovale malaria

Drug used: Chloroquine and Primaquine.

Drug administration: Chloroquine 3 days and Primaquine 14 days as follows:

Day from the day treatment starts	Day 0 (first day)	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13
Chloroquine	1 time	1 time	1 time	-	-	-	-	-	-	-	-	-	-	-
Primaquine	1 time	1 time	1 time	1 time	1 time	1 time	1 time	1 time	1 time	1 time	1 time	1 time	1 time	1 time

3. Uncomplicated malariae and knowlesi malaria

Drug used: Chloroquine.

Drug administration: Oral drug for 3 days

4. Treatment of uncomplicated mixed infections malaria

4.1. Patient with falciparum and vivax or ovale malaria

Drug used: Dihydroartemisinin-Piperaquine and Primaquine

Drug administration: Oral dose of Dihydroartemisinin-Piperaquine once a day for 3 days (Day 0 - 2) and Primaquine 14 days (Day 0 - 13)

4.2. Patient with falciparum and malariae malaria

Drug used: Dihydroartemisinin-Piperaquine and Primaquine

Drug administration: Same as falciparum malaria

Treatment of uncomplicated malaria patients who are at high risk of developing complications or severe malaria

Uncomplicated malaria patients who are at high risk of developing complications or severe malaria should be hospitalized to closely monitor symptoms.

1. Children aged lower than 1 year or body weight lower than 11 kg

Drug used: Dihydroartemisinin-Piperaquine

Drug administration: Oral dose of Dihydroartemisinin-Piperaquine once daily for 3 days, as follows:

Body weight (kg.)	Dihydroartemisinin-piperaquine (mg/day)	Dihydroartemisinin-piperaquine (tablet/day)
< 8 kg	20/160	1/2
8 to lower than 11 kg	30/240	3/4

Remark: 1 tablet of Dihydroartemisinin-piperaquine consists of Dihydroartemisinin 40 mg and Piperaquine 320 mg.

2. Pregnant women are at high-risk in developing severe malaria that has impact on fetus.

2.1. Pregnant women with uncomplicated falciparum malaria

2.1.1. First trimester of pregnancy

Drug used: Quinine sulfate and Clindamycin.

Drug administration: Oral Quinine Sulfate (300mg) 2 tablet 3 times per day (every 8 hours) and Clindamycin (300 mg) 1 capsule twice daily (every 12 hours) for 7 days; **and strictly do not prescribe Primaquine**, as follows:

Day from the day treatment starts.	Day 0 (First day)	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Quinine 300 mg/tab.	3 times 2 tablets	3 times 2 tablets	3 times 2 tablets	3 times 2 tablets	3 times 2 tablets	3 times 2 tablets	3 times 2 tablets
Clindamycin 300 mg/capsule.	2 times 1 capsule	2 times 1 capsule	2 times 1 capsule	2 times 1 capsule	2 times 1 capsule	2 times 1 capsule	2 times 1 capsule

Remark* Be careful of hypoglycemia in patients receiving Quinine Sulfate.

2.1.2. Second and third trimesters

Drug used: Dihydroartemisinin-Piperaquine.

Drug administration: oral drug once daily for 3 days and **strictly do not prescribe Primaquine.**

2.2. Vivax or ovale or malariae or knowlesi malaria in pregnancy of all trimesters.

Drug used: Chloroquine.

Drug Administration: Oral Chloroquine for 3 days and **strictly do not prescribe Primaquine.**

3. Lactating mother

Drug used: Prescribe drugs according to parasite species, like uncomplicated malaria.

Drug administration: Prescribe drugs according to parasite species but do not prescribe Primaquine, except in the cases that both mother and baby do not have G6PD deficiency so Primaquine can be given to the mother.

4. Patients with history of black urine or having G6PD deficiency.

Drug used: Prescribe drugs according to parasite species, like uncomplicated malaria, except primaquine.

Drug Administration:

- Administer drugs according to parasite species, like uncomplicated malaria **but**
- Prescribe Primaquine 0.75 mg/kg (not more than 45 mg) once weekly for 8 weeks in vivax or ovale malaria patients.
- May not prescribe Primaquine for falciparum malaria patients if the patients have severe G6PD deficiency. This is because the objective of prescribing primaquine is to reduce malaria transmission and not for treatment purpose.

5. Uncomplicated malaria with suspected *P. knowlesi*

Drug used: Chloroquine.

Drug administration: Chloroquine for 3 days.

6. Patient who cannot ingest oral drug or take the pills and vomit. When repeat another dosage, vomit again within 1 hour.

Drug used: Inject intravenous Artesunate 2.4 mg/kg, followed by 2.4 mg/kg at 12 and 24 hours (In patient BW lower than 20 kg inject Artesunate 3 mg/kg), then inject intravenous Artesunate once daily until the patient can take oral drugs, change to oral tablet for each parasite species by counting the first day of oral drug as Day 0 and continue until completing the full regimen. Follow-up the patient according to the schedule of each malaria species.

7. Patient allergic to antimalarial drug.

Drug used: use drug in other groups that the patient does not have history of allergy to, and consult experts by contacting through hotline of the Department of Disease Control -1422 round the clock

8. Falciparum malaria patient with parasite density higher than 100,000 parasites per microliter (or app. 2,500 parasites per 200 WBC in thick blood film, or 25 parasites per 1,000 RBC in thick blood film), or Schizont stage is found, indicating high parasite density that may lead to complications.

Drug used: To hospitalize the patient and treat as if he is a severe malaria case to prevent complications.

Treatment of complicated or severe malaria

Management of severe and complicated malaria should be done in hospitals with ready facilities, such as provision of blood components, and/or hemodialysis or peritoneal dialysis, etc. If there is a need to refer the patient, should inject bolus Artesunate or intravenously drip loading dose of Quinine hydrochloride prior to referral, or prescribe oral Dihydroartemisinin-Piperaquine or Artesunate-Pyronaridine if there is no injectable drug and the patient can take oral drug.

Diagram 2 Treatment of severe malaria.

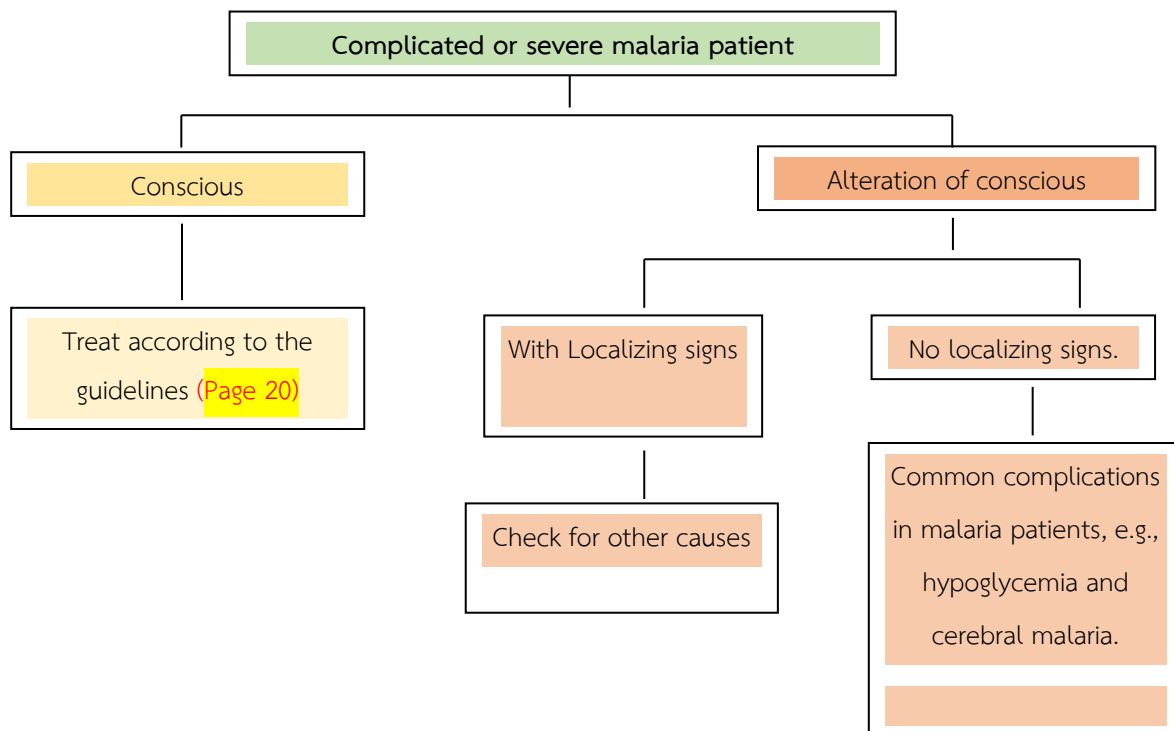
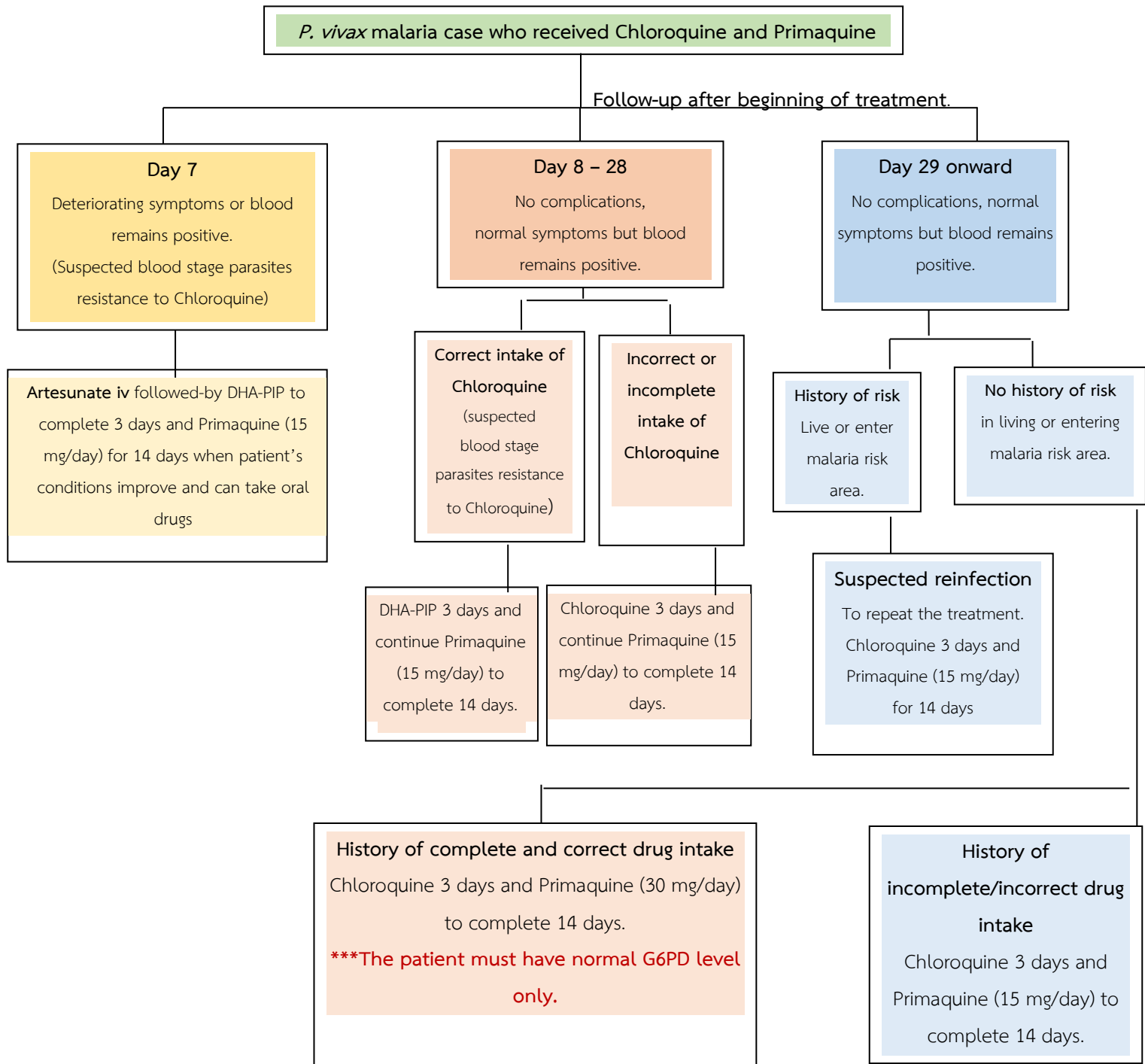


Diagram 3 Treatment of vivax malaria patients with treatment failure.



Specific treatment

1. Inject intravenous Artesunate as the first drug by:
 - Give interval injection at least in the first 24 hours.
 - Inject bolus drug, **do not give infusion or continuous drip**.
 - Artesunate ampule that was open for use, even if there is left over, must discard, do not keep it for further use because it has poor stability.
 - When patient's conditions improve and he can eat, change to oral Dihydroartemisinin-Piperaquine or Artesunate-Pyronaridine for 3 days plus Primaquine (if no contraindication)
2. If injectable Artesunate is not available, give intravenous Quinine Hydrochloride drip instead.
 - Give the drug at interval at least in the first 24 hours.
 - Quinine Hydrochloride must be given as infusion in 2-4 hours and **do not give bolus injection** because it may cause cardiotoxic effects, such as cardiac arrhythmia and must be careful of hypoglycemia.
 - When the patient is better and can eat, change to oral Dihydroartemisinin-Piperaquine or Artesunate-Pyronaridine for 3 days plus Primaquine (if no contraindication)

Drug dosage for severe malaria patients

- **It is recommended to choose Artesunate injection rather than Quinine injection,** because Artesunate can reduce mortality rate in severe malaria patients more than that of Quinine.
- **First line drug:** Artesunate 2.4 mg/kg bolus intravenous injection immediately, followed by 2.4 mg/kg at 12 and 24 hr. (in patients BW lower than 20 kg give Artesunate 3 mg/kg). Then give injection once daily until the patient can take oral drug, change to oral Artemisinin-based Combination Therapy (ACT) over 3 days
- **Second line drug: (if Artesunate injection is not available):** Quinine Dihydrochloride 20 mg/kg intravenous infusion drip in 4 hours, followed by 10 mg/kg intravenous drip in 2-4 hours every 8 hours. When the patient can take oral drug, change to oral Artemisinin-based Combination Therapy (ACT) over 3 days **or** Quinine sulphate and Doxycycline **or** Quinine sulphate and Clindamycin **or** oral Artesunate and Doxycycline **or** oral Artesunate and Clindamycin for 7 days.

Remark: Artemisinin-based Combination Therapy (ACT) is a combination that consists of a drug in Artemisinin group and other antimalarial drugs.

- In patients with abnormal liver function or renal failure or deterioration of general condition:
 - It is not essential to reduce dosage of Artesunate.
 - If Quinine Dihydrochloride is given, to reduce its dosage on Day 3 to 2/3 or half of the maintenance dose.
- Do not prescribe Doxycycline in pregnant women, lactating women, and children below 8 years old.
- Giving drugs to a patient during high fever, the patient may vomit and will not receive adequate dose, so should provide antipyretics prior to the antimalarial drugs, such as paracetamol, or provide tepid sponge.
- Should diagnose other common causes or co-infections if there is an indication.

Treatment of Malaria Treatment Failure Cases

Treatment failure means that after treatment with any drug regimen and one of the following conditions is found:

1. Deterioration of clinical symptoms on any day and the same parasite species is found in blood film.
2. There is recurring sign/symptom, but symptoms are not severe.
3. No sign/symptom but the same parasite species is found in blood film within 28 days after treatment started.

To prescribe the second line treatment for treatment failure case and the health personnel will refer such patient to hospital.

1. Treatment of falciparum treatment failure case.

1.1. Patients with deterioration of symptoms on any day and the same parasites are found in blood films.

To treat such case as a severe malaria case, when the condition is better and the patient can take food, then change to oral drugs in one of the following regimens, which is different from the first line treatment:

- A. Artesunate-Pyronaridine
- B. Artemether-Lumefantrine
- C. Quinine Sulfate and Clindamycin or Doxycycline or Tetracycline
- D. Atovaquone-proguanil

A. The second line treatment - Artesunate-Pyronaridine

Drug used: Artesunate-Pyronaridine and Primaquine

Drug administration: Oral Artesunate-Pyronaridine for 3 days and Primaquine for 1 day as follows:

Day from the day treatment starts	Day 0 (First day)	Day 1	Day 2
Artesunate-Pyronaridine by taking the drugs at the same time, every day.	1 time	1 time	1 time

Primaquine	1 time on any day by considering patient's symptom if he can take oral drug without vomiting.
------------	---

B. The second line treatment - Artemether-Lumefantrine

Drug administration: Oral dose twice daily for 3 days and Primaquine for 1 day.

C. The second line treatment - Quinine Sulfate and Clindamycin or Doxycycline or Tetracycline

Drug administration: Quinine Sulfate 600 mg (8.3 mg base/kg) 3 times per day and Clindamycin 10 mg/kg twice daily for 7 days or Doxycycline 3 mg/kg once daily (or twice daily) for 7 days or Tetracycline 4 mg/kg 4 times per day for 7 days and Primaquine for 1 day.

D. The second line treatment - Atovaquone-Proguanil

Drug administration: Oral dose once daily for 3 days and Primaquine for 1 day.

1.2. Patients with recurring sign/symptom but symptoms are not severe

To assess completeness of the patient's drug intake (drug compliance) of the first line treatment. If the patient took drugs correctly and completely, prescribe the second line treatment. If the patient did not take full dosage or he is not sure, repeat the first line treatment.

1.3. Patients without recurring sign/symptom but the same parasites are found in blood film within 28 days after treatment started.

To assess completeness of the patient's drug intake (drug compliance) of the first line treatment. If the patient took drugs correctly and completely, prescribe the second line treatment. If the patient did not take full dosage or he is not sure, repeat the first line treatment.

2. Treatment of vivax malaria treatment failure case (Diagram 3)

2.1. Deterioration of symptoms on any day and the same parasites are found in blood film.

To treat as if he is a severe malaria case and followed by the following regimen:

Drug used: Dihydroartemisinin-Piperaquine and Primaquine which is the second line regimen for vivax treatment failure.

Drug administration: Oral drug once daily for 3 days by regarding the first day of treatment as Day 0 and give drug continuously to complete 3 days (Day 0-2) and Primaquine when the patient's condition improves to complete 14 day-course.

2.2. Patients with recurring sign/symptom but symptoms are not severe.

To assess completeness of the patient's intake of the first line treatment (Drug compliance). If the patient took drugs completely, prescribe the second line treatment. If the patient did not take full course or he is not sure, repeat the first line treatment again.

2.3. Patients without sign/symptom, but blood film is positive within 28 days after the first day of treatment.

To assess completeness of the patient's intake of the first line treatment (Drug compliance). If the patient took drugs completely, prescribe the second line treatment. If the patient did not take full course or he is not sure, repeat the first line treatment again.

3. Treatment of *P. knowlesi* and *P. malariae* treatment failure cases.

To treat as vivax malaria treatment failure case but do not prescribe Primaquine.

Post – treatment follow-up



Post-treatment follow-up in all malaria cases is essential to ensure that the patients received full medication according to the prescribed regimen, and there are no serious side effects from the drugs, the patients recover from the illness and repeated blood examination is negative. It indicates that the patients are cured and will not transmit the disease to community. The guidelines on follow-up are as follows:

The first day the patient is seen (Day 0)

1. Take blood samples and prepare thin and thin blood films on the same slide for checking malaria parasites by microscopy. Collect blood spots in filter paper and send for PCR test to confirm parasite species and for monitoring of drug resistance.
2. Health staff should let the patients take the medication immediately in front of them, by prescribing drugs according to the guidelines for treatment of malaria. Observe the patients for at least 30 minutes. If the patients vomit within 30 minutes after drug intake, health staff must give the same drugs and same dosage again. If the patients vomit again within 30 minutes after the second dose, should hospitalize the patient.
3. Educate patients, relatives or care takers about taking drugs in front of them and at home, the patients should continue to take full medication according to the malaria treatment guidelines.

Follow-up appointment to monitor treatment outcome

- *P. falciparum*, *P. malariae* and *P. knowlesi*: To follow-up for checking symptoms and blood on Day 3, 7, 28, 42.
- *P. vivax* and *P. ovale*: To follow-up for checking symptoms and blood on Day 14, 28, 60, 90.

To ask the patients about symptoms and take blood samples by making thick and thin blood films on the same slide and examine malaria parasites using microscope for all follow-up visits. Collect blood spots in filter paper and send for PCR test in case of positive blood film.

- If blood film remains positive on Day 3 and symptoms deteriorate, to regard this case as a treatment failure case, to hospitalize the case and treat as a severe malaria case.
- If blood film remains positive on Day 3 (in *P. falciparum*, *P. malariae*, and *P. knowlesi* case) without any signs and symptoms, to continue follow-up closely.
- If parasites are found from Day 7 onward (in *P. falciparum*, *P. malariae* and *P. knowlesi*) to regard this case as a treatment failure case, to change to the second line treatment regimen.
- If parasites remain on Day 14 (in *P. vivax* and *P. ovale*) to regard this case as a treatment failure case, to change to the second line treatment regimen.

Patients having the following symptoms should be advised to return to see the doctor immediately without waiting for the appointment date.

High fever, very exhausted		Jaundice
Cannot take food/water, vomit a lot.		Low urine output.
Take drug and then vomit.		Dark or black urine
Dyspnea, fast breathing.		Alteration of consciousness

New antimalarial drug under feasibility study in Thailand



Tafenoquine

Tafenoquine is a drug in 8-aminoquinoline group that has long action because its half-life is approximately 2 weeks. The drug can act on all stages of malaria parasites including dormant liver stage (hypnozoite). The drug has been registered in USA and Australia, and in Thailand in December 2019 for use in patients 16 years or over for treatment of *P. vivax* and *P. ovale*, to replace Primaquine by prescribing together with Chloroquine. The objective is to eliminate hypnozoites. As the drug has long action, it can be used in single dose so there is no problem of patient compliance compared with Primaquine that must be taken for 14 days.

Administration of Tafenoquine

The drug can be given to *P. vivax* and *P. ovale* malaria patients **of 16 years or over only**. The dosage is 300 mg, single dose and to be prescribed with Chloroquine, as follows:

Day from the first day of treatment	Day 0 (start)	Day 1	Day 2
Chloroquine	1 time (600 mg)	1 time (600 mg)	1 time (300 mg)
Tafenoquine	1 time (300 mg)	-	-

Remark: Tafenoquine is strictly contraindicated in pregnant women.

Important side effects

Like Primaquine, Tafenoquine causes acute hemolytic anaemia in G6PD deficient patients because Tafenoquine has a long action, so **it is strictly contraindicated to prescribe the drug in G6PD deficient patients**. Before doctors prescribe the drug must check G6PD deficiency status by using G6PD quantitative test to know the exact level of G6PD enzyme. To prescribe the drug must consider the following conditions:

G6PD enzyme level > 6 U/gHb (>70% of normal level), to prescribe Tafenoquine single dose of 300 mg.
G6PD enzyme level between 4-6 U/gHb (30% - 70% of normal level), to prescribe Primaquine 15 mg once daily for 14 days.
G6PD enzyme level < 4 U/gHb (<30% of normal level), to prescribe Primaquine 45 mg once weekly for 8 weeks.

Remark: If health facilities cannot check quantitative G6PD enzyme level, Tafenoquine is strictly contraindicated.

Annex

Counting malaria parasite density

1. Counting malaria parasite in thick blood film (according to the standard operating procedure on malaria microscopy and quality control: MM-SOP-11)

Malaria parasite density is information for assessing severity of infection and response to treatment. Counting malaria parasite is conducted by counting only asexual blood stage but reporting of result in *P. falciparum* cases must also report sexual stage (if any). In case of mixed infections (more than one species), all parasite species must be reported. However, parasites of all species must be counted collectively. Measuring malaria parasite density is conducted by calculating number of parasites in 1 μL of thick blood film. The parasites are counted against 200 white blood cells (WBC). In addition, number of WBC in 1 μL of blood must be known, if do not know the hemogram, should assume that the patient has 8000 WBC. Before counting parasites, thick blood film must be examined and at least 100 oil fields must be examined under 1000 X magnification.

Only asexual form (trophozoites and schizonts) should be counted. In mixed infections with more than 1 parasite species, asexual forms of all species are counted together and to report all species found.

Parasite count should be stopped using the following criteria:

- When 100 parasites or more per 200 WBC are counted, then stop and report result as number of parasites per 200 WBC.
- If less than 100 parasites per 200 WBC are counted, to continue counting until 500 WBC are found.

Count all malaria parasites and WBC in the last oil field although the total WBC may be higher than 200 or 500. For instances, when counting till the last oil field the total WBC is 210, use 210 for calculation as the following formula.

$$\text{Malaria parasites per } 1\mu\text{L blood} = \frac{\text{Number of observed parasites} \times \text{No. of WBC}/\mu\text{L}^*}{\text{No. of counted WBC}}$$

Remark: If actual WBC count is not known, use the average WBC count of 8000 per 1µL blood.

Example: If total WBC is 210 and parasite count is 105 and actual WBC count in 1µL blood is not known the parasite density is calculated as follows:

$$\text{Malaria parasites per 1}\mu\text{L blood} = \frac{105 \times 8,000}{210} = 4,000$$

2. Counting malaria parasite in thin blood film (Number of parasites/µL of blood [thin film])

Move blood slide toward the end of blood film and choose area that red blood cells (RBC) line up evenly but some RBC may overlap. There should be some 250 RBC in one oil field. Count only parasitized RBC, then move blood film to count it continuously by avoiding counting in the same oil field. Take at least 20 oil fields and when 20 oil fields are counted there should be some 5000 RBC, then stop counting parasites. Record number of parasitized RBC and calculate parasite density as follows:

$$\text{Malaria parasites per 1}\mu\text{L blood} = \frac{\text{Number of parasitized RBC} \times \text{No. of RBC per 1 1}\mu\text{L blood}}{\text{No. of oil field} \times 250}$$

Remark: If RBC count is not known, use an average value of 5,000,000 RBC per 1 1µL blood.

G6PD enzyme test at health facilities (at point of care)

G6PD deficiency is caused by mutation of G6PD gene on the X chromosome. The gene expression may vary, from normal enzyme function or no symptom at all to acute and severe hemolysis when the patient receives free radicals or some certain drugs and the most important drugs for malaria treatment are primaquine and other drugs in the same group.

As *P. vivax* or *P. ovale* malaria patients must receive Primaquine (or Tafenoquine if the drug is introduced to Thailand in future) to eliminate the parasite stage hiding in the liver (Hypnozoite) to prevent relapse and interrupt malaria transmission in community.

However, Primaquine must be taken continuously for 14 days. Tafenoquine has a property of long action (half-life is 14-28 days) even if it is taken in single dose. It may cause a side effect in G6PD deficient patients that is RBC breakdown (hemolysis) which may be fatal. Therefore, checking G6PD enzyme level must be conducted before the patients be given with

the drugs, especially in case of Tafenoquine it is essential to check quantitative G6PD enzyme level precisely.

G6PD enzyme test should be conducted at the malaria diagnosis and treatment point of care, to help determining G6PD deficiency status before prescribing the drug to the patient. At present there are test kits that can be conducted rapidly at the point of care, as follows:

1. Qualitative G6PD enzyme test.

This test kit can be used for quick screening of the G6PD deficiency status. The color on the test kit indicates the result; if the patient is G6PD deficient there will be no color on the test kit (Figure 3).

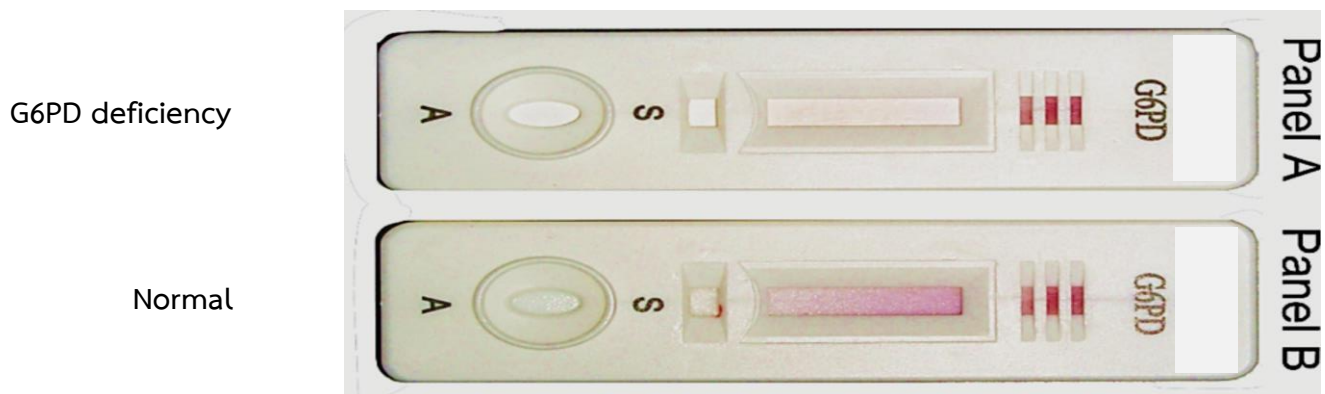


Figure 3 Results of qualitative G6PD enzyme test.

However, the test has a limitation, i.e., reading the color on the test kit by visual reading may result in a discrepancy in readings, especially in mild G6PD deficient patients. Therefore, the display may be ambiguous.

2. Quantitative G6PD enzyme test.

G6PD quantitative biosensor test (Point-of-care STANDARD™) is a new screening test for G6PD deficiency that can detect G6PD activity and measure hemoglobin level and calculate G6PD activity in U/gHb. Blood for the screening test can be drawn from finger prick and venous blood. The test is suitable for the case that numeric enzyme level is required, especially for the patients who will receive Tafenoquine that quantitative G6PD enzyme level is required. The result of test will be enzyme level on the G6PD analyzer as shown in the Figure 4.



Figure 4 Quantitative G6PD test. The analyzer displays G6PD enzyme level in U/gHb on the screen

The principle of G6PD test: Glucose-6-phosphate dehydrogenase (G6PD) is a catalyst for oxidation of glucose-6-phosphate (G6P) that changes it to 6-phosphogluconate and reduced nicotinamide adenine dinucleotide phosphate (NADP) and to reduced form of nicotinamide adenine dinucleotide phosphate (NADPH). When it interacts with 5-bromo-4-chloro-3-indolyl-phosphate (BCIP) and nitro blue tetrazolium (NBT) by diaphorase reaction and causes purple color. Intensity of color is direct proportional to G6PD activity. SD Biosensor STANDARD G6PD test was designed for measuring intensity of purple color quantitatively and corresponding with amount of hemoglobin (Hb). The result is displayed in G6PD enzymatic activity per 1 gm Hb (U/gHb) as shown in Figure 5.

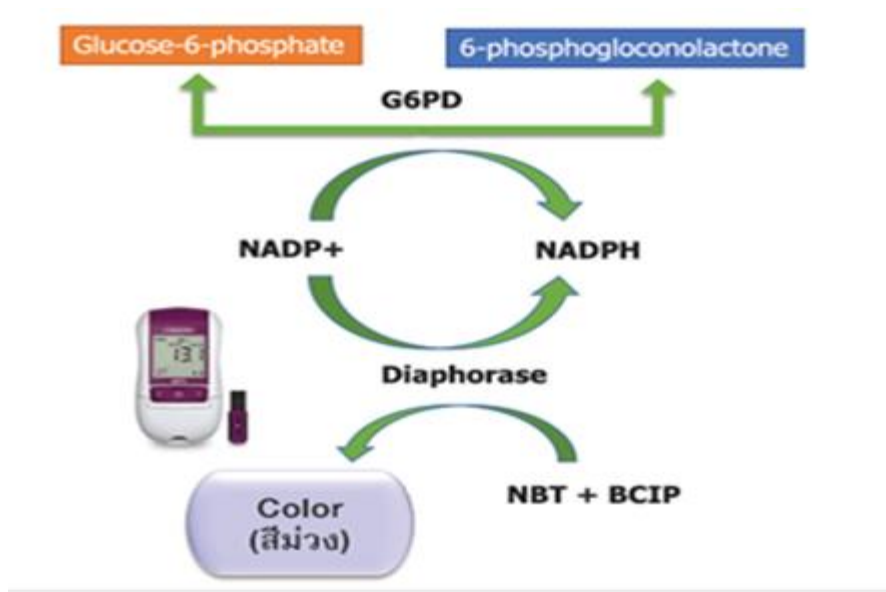


Figure 5: Reaction of test by SD Biosensor STANDARD G6PD test

Report form for post-treatment follow-up

Health facility

Date of exam.....

Name of health facility..... Address: No. Village No. Sub-district.....

District..... Province

Patient's information

Name of patient Age year Sex: ☐ Male ☐ Female Body weight kg

Patient's address No. Village No. Sub-district District Province Tel.....

ID card:..... ☐ Patient serial No.: O HN:

Result of examination

Parasite species: ☐ Pf ☐ Pm ☐ Pv ☐ Po ☐ Pk ☐ Mixed Detected by ☐ ACD ☐ PCD

Result of G6PD test ☐ Normal ☐ deficient

Drug

☐ DHA-PIP ☐ children dosage 20/160 mg tablet ☐ adult dosage 40/320 mg tablet

☐ Artesunate-Pyronaridine tablet ☐ primaquine Mg tablet

☐ Chloroquine tablet ☐ Artesunate IV ampule

☐ ATS + MQ (FD-ACT) tablet ☐ Mefloquine tablet

☐ Tetracycline capsule ☐ Quinine IV ampule

☐ Atovaquone-proguanil tablet ☐ Quinine tablet

☐ Artemether-Lumefantrine tablet ☐ Other drug (specify) tablet/ampule

Appointment date	D0.././..	D3.././..	D7.././..	D14.././..	D28.././..	D42.././..	D60.././..	D90.././..	remark
Actual date the patient came	.././..	.././..	.././..	.././..	.././..	.././..	.././..	.././..	
Body temperature (°C)									
Parasite No. trophozoite/WBC									

Side effects

Date../././.... ☐ nausea ☐ vomit ☐ headache ☐ body pain ☐ diarrhear ☐ skin rash ☐ others (specify)

Date../././.... ☐ nausea ☐ vomit ☐ headache ☐ body pain ☐ diarrhear ☐ skin rash ☐ others (specify)

Date../././.... ☐ nausea ☐ vomit ☐ headache ☐ body pain ☐ diarrhear ☐ skin rash ☐ others (specify)

Action:

1. Advice on how to take drug: ☐ D0 ☐ D1 ☐ D2 ☐ D3 ☐ D4 ☐ D5 ☐ D6 ☐ D7 ☐ D8 ☐ D9 ☐ D10 ☐ D11 ☐ D12 ☐ D13
2. Vomit within 30 minutes after taking drugs on the 1st day: ☐ yes ☐ no: If yes, did the patient take repeated dosage ☐ yes ☐ no.
3. Prepare 2 slides of thick and thin blood films on the same slide:
☐ D0 ☐ D3 ☐ D7 ☐ D14 ☐ D28 ☐ D42 ☐ D60 ☐ D90
4. Collect 3 drops of blood on filter paper: ☐ D0 ☐ D3 ☐ D7 ☐ D14 ☐ D28 ☐ D42 ☐ D60 ☐ D90

Specify the reasons of incomplete follow-up visits

Name of responsible officer Date

Instructions for reporting of post treatment follow-up of malaria cases

Health facilities

1. To use for all malaria patients
2. Health facilities: to fill up name and address of place of diagnosis

Patient's information

1. Name-surname: to fill up name and surname of patients
2. Age: to fill up age in year
3. Sex: to tick ✓ in front of the box-male or female
4. Body weight: to fill up patient's body weight in Kg
5. Present address: to fill up house No., village No., subdistrict, district and province of the patient's residence. In case of non-Thai case, may use employer's address.

Result of examination

1. Parasite species: to tick ✓ in front of parasite species detected.
2. Result of G6PD test: to tick ✓ in front of the examination result.

Drug

1. Type of drugs prescribed: to tick ✓ in front of the drug box and fill up total No. of tablets given.

Appointment date

1. Appointment date/month/year: to fill up date, month and year of the post treatment follow-up as per scheduled.
Fill up actual date, month and year that the patient came for follow-up.
2. Temperature in degree Celcius: to measure oral temperature of the patient. If measure axillar temperature, must add up 0.5 degree Celcius.
3. Number of ring forms/white blood cells:
For health facilities that use microscope, fill up number of ring forms. In case that the last oil field added up to more than 200 WBC, to use the actual total WBC that were counted, such as 250 ring forms against 203 WBC, to fill up 250/203. If do not find parasites, fill up 0.
4. Side effects: to tick ✓ in front of the side effect box.
5. Name of responsible officer: to fill up name and surname of the responsible officer
6. Please write clearly.

Action

1. Advice on how to take drug: to tick ✓ in the action box
2. If vomit within 30 minutes: to tick ✓ in the box - yes or no.
3. To prepare 2 blood slides: to tick ✓ in the box on date of action.
4. Collect blood: to tick ✓ in the box on date of action.

Document on importance of taking medication in front of staff, complete drug intake and post-treatment follow-up

When your blood is examined and malaria parasites are found, you will receive antimalarial drugs. The drugs are the best for treating you. They can kill parasites rapidly as you can notice that you are getting better after taking drugs. You will take the drugs in front of the staff, village headman, volunteer, relative or anyone whom you know. After that you will be followed-up to monitor the treatment outcome by health facility staff using microscopes on Day 3, 7, 28, and 42 if falciparum malaria is found, and on Day 14, 28, 60 and 90 if vivax or ovale malaria is found.

Why drugs must be taken in front of staff and to complete the entire dosage.

1. To ensure that you take all tablets.
2. To allow the observer to observe your symptoms after taking drugs. If there is drug allergy, the observer will inform staff or staff will refer you to be treated at hospital immediately.
3. If you take incomplete dosage, you will not be cured. This will result in unsuccessful treatment if the same drug is given again, because the parasites resist to the drug.

Why we have to follow-up to monitor treatment outcome.

1. To ensure that malaria parasites disappear from your body, and you are cured from malaria.
2. If malaria parasites are found in your body, the staff will treat you according to the protocol immediately.
3. If you have malaria parasites in your body, even if you do not have symptoms, you can further transmit malaria to others when mosquito bites.

For staff:

☐ Staff to explain importance of taking drug in front of observer and taking complete dosage to the patient.

☐ Staff to tell the patient that after follow-up on taking drugs in front of the staff, there will be follow-up to monitor treatment outcome by the staff of health facility where microscope is available according to appointment dates.

.....
(.....)

Staff's signature

.....
Day/Month/Year

For patient:

☐ You understand the importance of taking drugs in front of observer and taking complete dosage.

☐ You are aware that after follow-up on taking drugs in front of the staff, there will be follow-up to monitor treatment outcome by the staff of health facility where microscope is available on Day 3, 7 and 28.

.....

(.....)

Patient's signature or fingerprint.

.....

Day/Month/Year



Antimalarial drug dosage

Table 1 DHA-PIP dosage for treatment of uncomplicated falciparum malaria

Body weight (kg)	Dihydroartemisinin-Piperaquine (mg per day)	Dihydroartemisinin-Piperaquine (No. of tablet per day)
5 to < 8 kg	20/160	1/2
8 to < 11 kg	30/240	3/4
11 to < 17 kg	40/320	1
17 to < 25 kg	60/480	1 ½
25 to < 36 kg	80/640	2
36 to < 60 kg	120/960	3
60 to < 80 kg	160/1,280	4
over 80 kg	200/1,600	5

Remark:

- Dihydroartemisinin-Piperaquine 1 tablet consists of Dihydroartemisinin 40 mg and Piperaquine 320 mg.
- Should not take the drug with fatty food because it will increase absorption of Piperaquine and thus, may cause cardiac arrhythmia.
- Patients with body weight lower than 11 kg or age less than 1 year should be treated only by a doctor.

Table 2 Artesunate-Pyronaridine dosage for treatment of uncomplicated falciparum malaria

Body weight (kg)	Artesunate-Pyronaridine (mg per day)	Artesunate-Pyronaridine (No. of tablet per day)
< 20 kg	Do not prescribe the drug	
20 to < 24 kg	60/180	1
24 to < 45 kg	120/360	2
45 to < 65 kg	180/540	3
over 65 kg	240/720	4

Remark:

- Artesunate-Pyronaridine 1 tablet consists of Artesunate 60 mg and Pyronaridine 180 mg.
- For patients of body weight lower than 20 kg, another regimen should be considered instead.

Table 3 Primaquine dosage for treatment of uncomplicated falciparum malaria.

Body weight (kg)	Primaquine (15mg) (tablet)	Primaquine (7.5mg) (tablet)
<11 kg (less than 1 yr)	Do not prescribe the drug	Do not prescribe the drug
11 to < 15 kg	Do not prescribe the drug	Do not prescribe the drug
15 to < 25 kg	-	1 ½
25 to < 50 kg	1	-
≥ 50 kg	2	-

Remark:

- There are two tablet sizes of Primaquine: 7.5 and 15 mg per tablet.

Table 4 Dosage of Chloroquine and Primaquine for treatment of uncomplicated vivax or ovale malaria.

Body weight (kg)	Day 0			Day 1			Day 2			Day 3-13		Total drugs		
	C (tab)	P(15) (tab)	P(7.5) (tab)	C (tab)	P(15) (tab)	P(7.5) (tab)	C (tab)	P(15) (tab)	P(7.5) (tab)	P(15) (tab)	P(7.5) (tab)	C (tab)	P(15) (tab)	P(7.5) (tab)
<11 kg (less than 1 yr)	2	Do not prescribe.		1	Do not prescribe.		1	Do not prescribe.		Do not prescribe.		4	Do not prescribe.	
11 to < 15 kg	2	Do not prescribe.		1	Do not prescribe.		1	Do not prescribe.		Do not prescribe.		4	Do not prescribe.	
15 to < 25 kg	3	-	1	1	-	1	1	-	1	-	1	5	-	14
25 to < 50 kg	4	-	1 ½	1	-	1 ½	1	-	1 ½	-	1 ½	6	-	21
≥50 kg	4	1	-	4	1	-	2	1	-	1	-	10	14	-

Remark:

- C = Chloroquine 150 mg base/tablet
- P = Primaquine 7.5 and 15 mg per tablet
- In G6PD deficient patients, to prescribe Primaquine (0.75 mg/kg) once weekly for 8 weeks.

Table 5 Dosage of Chloroquine for treatment of uncomplicated malariae and knowlesi malaria.

Body weight (kg)	Day 0 (tablet)	Day 1 (tablet)	Day 2 (tablet)	Total drugs (tablet)
<11 kg	2	1	1	4
11 to < 15 kg	2	1	1	4
15 to < 25 kg	3	1	1	5
25 to < 50 kg	4	1	1	6
≥50 kg	4	4	2	10

Remark: Chloroquine 150 mg base per tablet

Table 6 Dosage of Artemether-Lumefantrine

Body weight (kg)	Artemether-Lumefantrine (mg per day)	Artemether-Lumefantrine (No. of tablet per day)
< 15 kg	20/120	1
15 to < 25 kg	40/240	2
25 to < 35 kg	60/360	3
over 35 kg	80/480	4

Remark: Artemether-Lumefantrine 1 tab consists of Artemether 20 mg and Lumefantrine 120 mg.

Table 7 Dosage of Atovaquone-Proguanil

Body weight (kg)	Dihydroartemisinin-Piperaquine (mg per day)	Dihydroartemisinin-Piperaquine (No. of tablet per day)
5 - 8 kg	125/50	1/2
9 - 10 kg	187.5/75	3/4
11 - 20 kg	250/100	1
21 - 30 kg.	500/200	2
31 - 40 kg	750/300	3
over 40 kg	1,000/400	4

Remark: Atovaquone-Proguanil 1 tab consists of Atovaquone 250 mg and Proguanil 100 mg.

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