# Malaria

## Traveler Summary

### Key Points

- Malaria is a parasitic infection of the red blood cells and is acquired through the bite of mosquitoes that generally feed between dusk and dawn. Malaria occurs worldwide, mainly in tropical countries.
- Risk is much higher in Africa, eastern Indonesia, and Papua New Guinea than anywhere else and is increased in travelers who visit or live in rural areas of affected countries.
- Symptoms always include fever and influenza-like symptoms (chills, sweats, muscle aches, headache). Vomiting, abdominal pain, diarrhea, cough, and jaundice (yellow skin and eyes) may also occur.
- Consequences of infection may include shock, lung and kidney failure, coma, and death. Some forms of malaria can persist for many months and relapse periodically.
- Prevention includes medications taken during the trip and for a short period thereafter, wearing clothing that covers as much skin as practicable, and observing personal protective measures against mosquito bites.
- Atovaquone-proguanil (Malarone or generic), doxycycline, mefloquine, and tafenoquine are equally effective antimalarial drugs when taken as instructed.
- For short-stay travel (< 2-3 weeks), atovaquone-proguanil may be preferable because travelers can stop taking the drug just 7 days after leaving the malarious area; it may also be preferable to tafenoquine because of concise dosing instructions and because prior blood testing is not needed.
- Weekly tafenoquine, which cannot be used for longer than 6 months, may be convenient for longer trips, but has detailed dosing requirements and requires a blood test before the first time it is used.
- For long-stay travel of more than 6 months, mefloquine is preferable (if tolerated and no resistance to the drug exists) due to the lower cost and once-weekly doses (rather than daily doses).
- In certain uncommon situations where access to medical care or effective treatment drugs within 24 hours of developing a fever while in a malarious area may not be possible, a physician may prescribe a drug to be carried for self-treatment.

## Introduction

Malaria is caused by a parasite (primarily the ***Plasmodium*** species: ***P. falciparum*** and ***P. vivax*** ) and is primarily transmitted by the bite of ***Anopheles*** mosquitoes, generally between dusk and dawn. Malaria remains the most frequent infectious cause of death for travelers going to affected tropical countries, but infection can usually be prevented by using antimalarial drugs and observing personal protective measures against mosquito bites. (See ***Insect Precautions***.)

## Risk Areas

Malaria occurs in approximately 90 countries, mostly in Africa, but also in Central and South America, South Asia, Southeast Asia, the Middle East, and South Pacific islands. Most of the world's malaria occurs in sub-Saharan Africa where risk is considerably higher than anywhere else.

In most parts of the world, malaria is a rural disease with minimal or no risk in urban areas. However, malaria risk occurs in both rural and urban areas of sub-Saharan Africa and South Asia. Malaria does not occur above 2,500 m (8,200 ft), during dry seasons, and among persons who stay in air-conditioned and/or screened accommodations.

Country-specific malaria risk information is available from health care providers in the form of a Travax country report malaria recommendation map (where available).

## Transmission

Malaria is mainly transmitted through the bite of ***Anopheles*** mosquitoes, which generally feed on humans at night (between dusk and dawn). Occasionally, malaria is transmitted through a blood transfusion, transferal from mother to fetus, or contaminated needles and syringes.

## Risk Factors

The risk of getting malaria can vary greatly within a country depending on the intensity of transmission, the traveler's itinerary, season, duration and type of travel, the location (e.g., urban vs. rural), and where an individual spends the evening and nighttime hours. For example, short-stay travelers visiting urban centers and staying in air-conditioned hotels will be at much lower risk than long-stay, adventurous travelers living in rural areas. However, brief exposure, such as a 1-night stay in a malarious area or a nighttime train trip through a malarious area, requires that protective measures be taken, including insect precautions and possibly a full course of prescription antimalarial drugs. Malaria may also be contracted during brief stopovers at airports in malarious zones if health officials have not taken proper measures to rid the area of mosquitoes. Airports off the main circuit of international travel are particularly suspect.

Adults who grew up in malarious areas should be aware that immunity to malaria disappears within 6 months of the last exposure to malaria and risk is the same as for first-time travelers going to a malarious region.

## Symptoms

Symptoms most commonly develop within 10 to 14 days after being exposed. Less commonly, symptoms can appear weeks, months, or even a few years after leaving a malarious area (when use of preventive drugs has been stopped).

Symptoms of malaria always include fever and influenza-like symptoms (chills, sweats, muscle aches, headache) that may come and go. Vomiting, abdominal pain, diarrhea, cough, and jaundice (yellow skin and eyes) can occur. The symptoms of malaria can mimic almost any other infection that causes fever. Malaria infection may be more severe in pregnant women.

## Consequences of Infection

Malaria caused by ***P. falciparum*** can progress to shock, lung and kidney failure, coma, and death, without immediate and proper treatment; suspected malaria is a medical emergency that must be evaluated immediately by a competent medical provider. Malaria caused by ***P. vivax*** rarely results in severe disease, but parasites can persist in the liver for many months and relapse periodically until treated.

## Need for Medical Assistance

Malaria is always completely curable when the appropriate drug is used.

Persons who develop symptoms of malaria (especially fever and/or influenza-like symptoms) should seek medical attention immediately because delay of appropriate treatment can lead to serious or fatal consequences. Inform the health care provider that risk of malaria existed on a recent travel itinerary. Request "thick and thin blood films" or a malaria rapid diagnostic card test for diagnosis. One negative blood film does not rule out malaria; if symptoms persist, 2 additional films should be performed 12 to 24 hours apart. Similarly, a negative rapid malaria test should be followed with up to 3 thick/thin blood films.

Certain species of malaria can lie dormant in the liver and cause malaria symptoms months or even 2 or 3 years after leaving the malaria risk area and discontinuing malaria drugs. The development of fever or influenza-like symptoms is reason to seek medical attention and to advise the health care provider of previous travel to a malarious area.

Travelers should be aware that the medical management of malaria in countries where the disease routinely occurs may differ from their country of origin. In many countries where malaria is common, a limited number of effective medications may be available for treatment. Some of the drugs used may be ineffective for persons, such as travelers, without partial immunity to malaria or may be associated with unacceptable adverse effects.

## Prevention

No vaccine is available for the prevention of malaria in travelers. Prevention in travelers typically involves a combination of personal protective measures, chemoprophylaxis (no regimen is 100% effective), and prompt medical evaluation of fever or influenza-like illness, or standby emergency treatment when medical evaluation is unavailable.

### Personal Protective Measures

Personal protective measures can reduce the risk of malaria, but appropriate chemoprophylaxis should be considered. Mosquitoes that transmit malaria (***Anopheles*** spp.) are generally night biters with activity between dusk and dawn. Travelers should:

- Wear clothing that covers as much skin as practicable.
- Apply a repellent to all exposed, nonsensitive areas of the body during biting activity time. When both repellent and sunscreen are used, apply the sunscreen first, using a product with an SPF of 30 to 50. Limited data suggest some reduction of repellency when sunscreen is applied over the repellent.
- Use a repellent containing DEET (N,N-diethyl-meta-toluamide; 30%–35% concentration) or, alternatively, a repellent containing picaridin (20% concentration or greater for tropical destinations; also known as icaridin). Picaridin, unlike DEET, has a pleasant smell and does not dissolve plastic materials.
- Treat outer clothing, boots, tents, and sleeping bag liners with permethrin (or other pyrethroid) when traveling in an area of very high risk for mosquito-borne or tick-borne diseases.
- Sleep under a permethrin-impregnated bed net when at high risk of malaria if not sleeping in a sealed, air-conditioned room. Regularly check the net for rips and tears and keep it tucked in around the bed at all times. Ensure that all open windows have insect screens.
- Use spatial repellent products in the form of an aerosol spray, vaporizer device, or smoldering coil. These products usually contain a pyrethroid (e.g., metofluthrin or allethrin).

See ***Insect Precautions***.

## Antimalarial Drugs

Atovaquone-proguanil (Malarone or generic), doxycycline, mefloquine (do not use in Southeast Asia), and tafenoquine are equally effective antimalarial drugs when taken as instructed. Choice of drug depends on certain traveler and personal-choice factors. Different drugs must be started at different times with respect to the beginning of travel. This has to do with the time it takes to build up effective blood levels as well as the need to assess for any serious side effects prior to departure.

Malarious countries may not have malaria in all areas. In determining antimalarial regimens, note that the first day in a malarious area may not correspond to the first day in that country; many itineraries may begin in a nonmalarious area. An individual who will be in a nonmalarious area of the country for several days or weeks before entering a malarious area does not need to start taking the drug until the appropriate time before the actual malaria exposure begins. The traveler will need to continue to take antimalarials for as long as malaria risk occurs, in some cases months or even years, and then continue taking the antimalarial drugs for a specified period after leaving the malaria risk area. See below for information on the drugs that may be prescribed. Some long-stay travelers or expatriates may travel into malarious areas only periodically and thus may need to take antimalarials only periodically. A health care provider can determine the best strategy.

### Atovaquone-Proguanil (Malarone and Generics)

The adult dose of atovaquone-proguanil is a 250 mg/100 mg tablet, taken orally once daily. Start taking atovaquone-proguanil 1 to 2 days before arrival in a malaria risk area, take it daily while in the risk area, and continue taking it daily for 1 week after leaving the malarious area. Atovaquone-proguanil should be taken with a meal or milk at the same time each day.

A missed dose can be taken later the same day, but individuals should not double the next day's dose if a dose is missed completely. After a missed dose occurring at a time when exposure to malaria is possible, atovaquone-proguanil must be continued for a minimum of 4 more weeks after resuming the medication and for a minimum of 1 week after the last day of exposure. After a missed dose during the week after exposure, atovaquone-proguanil must be continued for a minimum of 4 weeks after the last day of exposure.

When atovaquone-proguanil is used for malaria prevention, side effects are uncommon. However, nausea, vomiting, stomach pain, and diarrhea may occur.

Atovaquone-proguanil should not be used by pregnant women, persons with severe kidney failure, or persons with an allergy to the drug.

### Doxycycline

The adult dose of doxycycline is a 100 mg tablet, taken orally once daily. Start taking doxycycline 1 to 2 days before arrival in a malaria risk area, take it daily while in the risk area, and continue taking it daily for 4 weeks after leaving the malarious area. Doxycycline, which can cause irritation of the esophagus, should be taken while sitting or standing in an upright position, and it should be taken with food or a liberal amount of fluid. Do not lie down for 30 minutes after taking this drug. Do not take Pepto Bismol or antacids while taking doxycycline because they can interfere with absorption of the drug.

Late doses can be made up on the same day, resuming the normal schedule the following day. Do not double the dose the next day if a dose is completely missed one day.

Skin sensitivity to sunlight is a common side effect and can lead to severe sunburn. Risk of this complication can be lowered by using a sunscreen that blocks both UVA and UVB rays, wearing protective clothing (including a hat), and avoiding prolonged exposure to sunlight. Women who take doxycycline may develop vaginal yeast infections and should carry an antifungal drug for self-treatment.

Doxycycline should not be used by persons with an allergy to the drug.

## Mefloquine (Lariam and Generics)

The adult dose of mefloquine is a 250 mg tablet taken orally once weekly. Start taking mefloquine 2 to 3 weeks before arrival in a malaria risk area, take it weekly while in the risk area, and continue taking it weekly for 4 weeks after leaving the malarious area.

A missed dose should be taken as soon as possible that same week (but not the day before the next regularly scheduled dose), resuming the schedule on the next normally scheduled day. Do not double the dose the next week if a dose is completely missed one week.

Mefloquine usually is well tolerated but may cause side effects affecting the gastrointestinal tract, nerves, and emotional and mental processes. Minor side effects include headache, stomach upset, dizziness, and bad dreams, which tend to be mild or temporary. Individuals who plan to drive, pilot a plane, or operate machinery should be aware that mild dizziness is a possible side effect.

Severe adverse reactions may include serious neurological and psychiatric side effects, which can persist for months, years, or permanently, even after discontinuation of mefloquine. Stop taking the drug if the following symptoms occur while taking the drug for malaria prevention: acute anxiety, depression, restlessness, or confusion. In this case, an alternative medication should be obtained from a health care provider.

Mefloquine should not be used by persons with an allergy to the drug; a history of convulsions or epilepsy; conduction abnormalities of the heart; or current or recent history of depression, anxiety disorder, or any major psychiatric disorder.

## Tafenoquine (Arakoda)

Tafenoquine is unique in requiring a blood test prior to first-time use to ensure that a genetic enzyme deficiency of red blood cells does not exist. Persons who are deficient risk life-threatening anemia if they take tafenoquine. The genetic deficiency is inherited; a single normal blood test is applicable for life. The adult dose of tafenoquine is two 100 mg tablets (200 mg total) taken orally once weekly. Start taking tafenoquine once daily for 3 consecutive days before entering a malarious area (loading dose), take it once weekly while in the malarious area (maintenance dose), and take 1 dose 7 days after the previous dose after leaving the malarious area (terminal dose). Tafenoquine should not be crushed or chewed but swallowed whole with food. Travelers may consider taking the loading doses on the Friday, Saturday, and Sunday before entering the malarious area and then take the maintenance doses every Sunday once in the malarious area.

A missed loading dose should be taken as soon as possible to ensure that a total of 3 consecutive daily loading doses have been taken; the maintenance dose should be started 1 week after the last loading dose.

Two missed loading doses should be taken as soon as possible on 2 consecutive days so that a total of 3 daily loading doses have been taken; begin maintenance dose 1 week after the last loading dose.

One or 2 missed maintenance doses should be taken on any day up to the time of the next scheduled dose.

If 3 or more maintenance doses are missed, 2 doses should be taken once daily for 2 days up to the time of the next weekly dose.

If the terminal dose is missed, 1 dose should be taken as soon as remembered.

Tafenoquine may cause side effects such as include nausea, vomiting, abdominal pain, corneal deposits, or psychosis.

Tafenoquine should not be used in persons under 18 years of age, pregnant women, persons with unknown glucose 6-phosphate dehydrogenase (G6PD) status or with known moderate-to-severe G6PD deficiency (because of the potential for life-threatening destruction of red blood cells), or in persons with a history of psychotic disorders or current psychotic symptoms.

# Infants and Children

All children (including young infants) who travel to malaria risk areas should be protected against insects and should take drugs to prevent malaria. The dosage will depend on the child's age and/or weight.

Young children should avoid travel to areas of chloroquine-resistant falciparum malaria unless they can take an effective drug such as mefloquine, doxycycline, or atovaquone-proguanil.

- Doxycycline should not be given to infants and children younger than 8 years in the US or younger than 12 years in the UK
- If a physician prescribes mefloquine for a child, the pharmacist can crush the tablets (which have a bitter flavor) and place the powder in gelatin capsules with calculated pediatric doses. Children may tolerate antimalarial medications more readily if the crushed powder is mixed in food (e.g., honey or chocolate sauce) or drink.
- Atovaquone-proguanil is available (in the US and Canada) in a pediatric formulation that can be crushed and mixed with condensed milk for children who have difficulty swallowing tablets.
- Medications should be stored in child-proof containers out of children's reach.
- The dosage will need to be adjusted according to the increasing weight of a growing child if he or she is a long-stay traveler or expatriate. A travel medicine provider can advise parents or guardians on adjusting the child's dosage before departing for long-stay travel.

## Self-Treatment of Presumptive Malaria

In most cases, travelers will not need to carry self-treatment drugs when using the recommended medication to prevent malaria. However, in rare situations in which a less effective medication must be used and access to medical care within 24 hours of developing a fever while in a malarious area may not be possible, it may be prudent to carry a drug for self-treatment. ***The treatment drug should not be the same as the prevention drug.***

Stop taking the antimalarial drug for prevention while taking the antimalarial drug for treatment.

- Resume the preventive medication immediately upon completion of self-treatment if atovaquone-proguanil will be used for ongoing prevention.
- Resume the preventive medication 1 week after ***initiating*** self-treatment if another antimalarial (except atovaquone-proguanil) will be used for ongoing prevention.

Atovaquone-proguanil or coartemether (artemether-lumefantrine combination; called Coartem in the US and Riamet in Europe) can be used for emergency self-treatment as long as the same drug was not used for prevention.

Adult self-treatment using Coartem consists of 6 doses (a total of 24 tablets) taken over 3 days. On the first day, 4 tablets are taken, followed by 4 more tablets 8 hours later. On the second and third days, 4 tablets are taken every 12 hours.

- Coartem needs to be taken with food. Do not take with grapefruit juice.
- Coartem should not be used by persons with a heart condition called QTc prolongation or those with an allergy to either component of the drug (artemether or lumefantrine).
- The most frequently reported side effects in adults include loss of appetite, muscle aches, and joint pain. The most common side effects in children are fever, cough, vomiting, loss of appetite, and headache.

The adult self-treatment dose for atovaquone-proguanil consists of 4 tablets taken once daily for 3 days.

- Atovaquone-proguanil should be taken with food.
- Atovaquone-proguanil should not be used by pregnant women or persons who are allergic to either component of the drug.

The self-treatment drug should be taken promptly (according to a health care provider's instructions) if fever and illness occur during travel and medical care is not available within 24 hours. Remember that self-treatment is only a temporary measure and medical attention should be sought as soon as possible.

An alternative to Coartem or atovaquone-proguanil for self-treatment is quinine plus doxycycline, but this drug has a much more complex schedule of doses and is frequently associated with adverse effects.

Mefloquine should not be used for self-treatment unless no other alternative exists.