QUICK LINKS

Traveler Information

MALARIA

SHORELAND'S RECOMMENDATIONS FOR MALARIA PREVENTION

- Atovaquone/proguanil (Malarone), doxycycline, chloroquine, and mefloquine are equally effective antimalarial drugs when taken as instructed, as long as there is no resistance to the drug at the destination.
    - In areas of chloroquine-resistant *P. falciparum* malaria, mefloquine, atovaquone/proguanil, and doxycycline are equally effective drug options.
    - In areas of mefloquine resistance, either doxycycline or atovaquone/proguanil can be used.
    - Another drug, primaquine, can be used in special cases but is not a first-choice drug for prevention.
- For short-term travelers (less than 2-3 weeks), atovaquone/proguanil may be preferable because travelers can stop taking the drug just 7 days after leaving the malarious area. Longer courses of atovaquone/proguanil appear safe but are more costly than mefloquine or doxycycline.
- For long-term travelers, mefloquine is preferable—if it is tolerated—due to lower cost and once-weekly doses (rather than daily doses).

WHAT'S NEW

The FDA has added a warning to the packaging label for mefloquine, stating that it can cause serious neurological and psychiatric side effects. These reactions can persist for months, years, or permanently, even after discontinuation of mefloquine.

Use of either atovaquone/proguanil (Malarone) or co-artemether (combination artemether-lumefantrine; called Coartem in the U.S. and Riamet in Europe) is preferred for standby emergency treatment, if this strategy is chosen by the traveler. However, co-artemether should not be used in areas where there is resistance to artemisinin, from which 1 of the components of co-artemether is derived.

GENERAL INFORMATION

Malaria is an infection caused by a single-celled blood parasite that lives within red blood cells and is transmitted through the bite of the *Anopheles* mosquito. (Occasionally malaria is transmitted through blood transfusion, congenitally from mother to fetus, or through contaminated needles and syringes.) Malaria remains the most important infectious disease and most frequent infectious cause of death for persons traveling to countries in the tropics and subtropics.

Malaria occurs in more than 100 countries, including those in Africa, Central and South America, the Indian subcontinent, Southeast Asia, the Middle East, and islands of the South Pacific. Most of the world's malaria occurs in sub-Saharan Africa and risk is considerably higher there than anywhere else.

While there is no malaria vaccine available, malaria usually (but not always) can be prevented by the use of antimalarial drugs and personal protection measures against mosquito bites (see *Insect Precautions*) with each exposure to malaria.

SYMPTOMS

Malaria symptoms can develop within days of being exposed or, less commonly, can present weeks or months (or rarely, even years) after leaving a malarious area, when use of preventive drugs has been stopped. Symptoms always include fever and may also include influenza-like symptoms that may come and go, such as chills, sweats, headache, muscle aches, and/or a vague feeling of illness. Vomiting, abdominal pain, diarrhea, cough, anemia, and jaundice (yellowing of the skin and the whites of the eyes) can occur. The symptoms of malaria can mimic almost any other infection that causes fever.

Malaria caused by the malaria strain called *P. falciparum* usually occurs about 10 to 12 days after infection and is *a medical emergency*. If falciparum malaria is not treated immediately and properly, it can proceed to shock, lung and kidney failure, coma, and death. While illness caused by other milder strains (*P. vivax, P. ovale*, and *P. malariae)* is not usually life-threatening, there may be serious health risks to very young or very old persons or to those with underlying illness. Malaria due to *P. vivax* and *P. ovale* may eventually resolve without treatment but can relapse periodically until properly treated. Malaria is always completely curable when the appropriate drug is used.

DISEASE RISK

In most of the world, malaria is a rural disease with minimal or no risk in urban areas. However, as a general rule, malaria risk occurs in both rural *and* urban areas of sub-Saharan Africa and the Indian subcontinent. Malaria is less common above a certain altitude (varies by country, but usually around 5,000 feet), during dry seasons, and among those who stay in air-conditioned and/or screened accommodations.

The risk of getting malaria can vary greatly even within the same country, depending on the intensity of transmission, the season, duration of travel, type of travel, the location within a country (e.g., urban vs. rural), and where an individual spends the evening and nighttime hours. (Malaria is usually transmitted only between dusk and dawn, the time that *Anopheles* mosquitoes generally feed on humans.) Country-specific malaria risk information from health care providers in the form of a Travax country report or a malaria risk map (where available).

For example, short-term travelers living in 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 night-time train trip through a malarious area, requires that protective measures be taken, including insect precautions and a full course of prescription anti-malarial drugs. It is also possible to contract malaria 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 international circuit 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. Malaria preventive medications are indicated for these individuals just as for first-time travelers to the region.

PREVENTIVE THERAPY

The use of preventive medications ("chemoprophylaxis") and personal protection measures against mosquito bites are important safeguards for travelers to malarious areas. (See *Insect Precautions.*) Travelers to a malarious area should get expert medical advice regarding malaria prevention; travel medicine advisors are the most qualified to provide this advice. They can explain which destinations require preventive measures and will choose an appropriate, itinerary-specific anti-malarial drug.

In some areas of the world, where it is still effective against the malaria parasite, chloroquine is the drug of choice for malaria prevention. In many other areas, however, the parasite has become resistant to chloroquine, and other drugs must be prescribed. In these cases, there are 3 drugs that are considered to be equally effective in preventing *P. falciparum* malaria: atovaquone/proguanil (Malarone), mefloquine, and doxycycline. Choice of drug depends on patient, itinerary, and economic factors, and each drug has advantages and disadvantages in this regard. Primaquine is a second-line option only when all other choices have been eliminated, and then only for short-term travel to areas where *P. vivax* constitutes all or nearly all of the malaria cases.

Travelers should inform their doctors of any serious underlying health problems (such as kidney, heart, or liver disease, or allergies) so that these problems can be taken into consideration in choosing the drug for malaria prevention. Individuals who have a serious, unusual, or unexpected reaction after taking an antimalarial drug should seek medical attention promptly and indicate to their health care providers that they have taken such medication. An overdose of antimalarial drugs (particularly chloroquine) can be fatal. Medicine should be stored in childproof containers, out of children's reach.

Remember that there is always the risk of potential side effects, no matter which medication is used to prevent malaria. However, any possible minor side effects of antimalarial medications must always be weighed against the risk of severe and potentially fatal infection with *P. falciparum*. Disabling side effects are uncommon with most antimalarial drugs.

In addition, remember that although the use of preventive drugs and insect precautions will decrease the chance of getting malaria by up to 97%, such measures do not guarantee protection.

Travelers will encounter fellow travelers en route who have been prescribed a wide variety of regimens, some highly effective but many others much less so. This may include drugs not available in the U.S. Travelers should be instructed to stick to their own regimen at all times. If intolerable side effects arise, they should make every effort to contact the original prescribing health provider

by e-mail, fax, or telephone for advice. Should medications need to be changed mid-course due to side effects, special considerations apply with respect to duration of therapy; a knowledgeable physician should review the traveler's case with him or her.

TIMING OF ANTIMALARIAL DRUGS

Travelers need to start taking the anti-malaria drugs before entering a malarious area and continued while in the risk area and for a time after leaving the area. 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.

Not all malarious countries have malaria in all areas of that country. When to start the drug does not always correspond to when a traveler reaches the first destination; rather, it depends on when the traveler will first arrive in an actual malarious area of that country or a subsequent country on the itinerary. For example, an individual who will be traveling to a major city where there is no risk of malaria 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 starts. The travel will need to continue to take antimalarials for as long as malaria risk occurs, in some cases months or even years, and continue taking the antimalarial drugs for a period of time after leaving the malaria risk area. See below for information on the drug that may be prescribed. Some long-term travelers or expatriates, who may be overseas for months or years, may be traveling into malarious areas only periodically and may need to take antimalarials only periodically. A health care provider can determine the best strategy.

ANTIMALARIAL DRUGS

Atovaquone/Proguanil (Malarone)

Malarone (a combination of atovaquone and proguanil) is available in a single tablet. The recommended adult dose is a 250 mg/100 mg tablet, taken orally once a day. Start taking Malarone 1 day before arriving in a malarious area, take it daily while in the risk area, and continue taking it daily for 1 week after leaving the malarious area. 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. Malarone should be taken with a meal or milk, at the same meal time each day.

This drug works equally as well as mefloquine, doxycycline, or primaquine. It appears to be very safe and effective, but somewhat expensive for a long-stay traveler.

When Malarone is used for malaria *prevention*, no definite side effects are evident. However, nausea, vomiting, abdominal pain, and diarrhea may occur when higher doses of the drug are used for treatment. Convulsions and rash have rarely been reported.

Malarone should not be used by pregnant women, persons with severe renal failure, or persons with an allergy to either drug that make up Malarone (atovaquone and proguanil).

In South Africa, Malarone is called Malanil.

Generic versions of Malarone are available.

Chloroquine (Aralen and Generics)

Chloroquine is a safe and effective medication that may be used to prevent malaria in areas where chloroquine resistance has not occurred. The adult dose of chloroquine (brand name Aralen) is 500 mg taken orally once a week. Start taking chloroquine 1 week before arrival in a malarious area, take it continuously (weekly) while in the risk area, and continue to take 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 take a double dose if a dose is completely missed one week. Most people find Sunday the most convenient and easy day to remember for weekly medication.

Individuals should not take chloroquine if they are allergic to the drug or have eye problems called retinopathy. Those taking chloroquine for long periods of time may need regular eye check-ups, periodic blood work, or periodic check-ups for muscle weakness. Chloroquine can worsen psoriasis or porphyria (a disorder that causes abnormalities in the production of a component of hemoglobin) and should be used with caution by those who have preexisting hearing damage, liver disease, alcoholism, or a blood deficiency called G6PD.

Serious side effects of chloroquine are uncommon. Minor side effects may occur, such as upset stomach, headache, dizziness, blurred vision, and itching (the latter most often in African Americans). Persons with epilepsy may be at risk for seizures. Rarely, hematological or cardiac changes can occur; serious side effects such as seizures, psychosis, and encephalopathy have also occurred with chloroquine use. The few people who experience stomach upset may tolerate chloroquine better by taking it with meals or in divided, twice-weekly doses. Chloroquine has been shown to be safe for infants and pregnant women. Chloroquine tablets should be kept in child-proof containers, well out of reach of children; as few as 2 tablets can be fatal to a young child.

In some countries, chloroquine may be prescribed in combination with proguanil (a drug that is not available by itself in the U.S.) to those who are going to chloroquine-resistant areas and cannot take mefloquine, doxycycline, atovaquone/proguanil, or primaquine. Proguanil may be purchased in Canada, Europe, and in many countries in Africa. However, the chloroquine plus proguanil combination is much less effective than the drugs mentioned above.

Mefloquine Hydrochloride (Lariam and Generics)

For travel to risk areas where there is chloroquine-resistant malaria, mefloquine is 1 of the drugs of choice. The adult dose of mefloquine is 1 tablet containing 250 mg taken orally once a week. Start taking mefloquine 2-3 weeks before arrival in a malarious area, take it continuously (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 gastrointestinal, neurological, and psychological side effects.

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.)

About 5% of users develop disabling anxiety, dizziness, depression, insomnia, or irritability that is bad enough to make them stop taking the drug. However, it is important to remember that about 95% of mefloquine users tolerate the drug without discontinuing it, and for long stay travelers to chloroquine-resistant areas, this weekly medication is the most convenient regimen.

Severe adverse events, such as psychosis, seizures, and encephalopathy may occur in about 1 out of 6,000 to 10,000 users. Neuropsychiatric and vestibular adverse reactions can persist for months, years, or permanently, even after discontinuation of mefloquine. Very rarely, mefloquine can cause inflammation of the lung tissue.

Individuals who have an allergy to the drug; history of convulsions; current or recent history of depression; anxiety disorder, psychosis, schizophrenia, or other major psychiatric disorder; cardiac conduction abnormalities; or are taking halofantrine or ketoconazole should not take 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, it will need to obtain an alternative medication from a health care provider.

Note: Lariam (Roche brand of mefloquine) is no longer available in the U.S.; generic mefloquine remains available.

Doxycycline

Travelers to areas of resistance to chloroquine or mefloquine can use doxycycline. The adult dose of doxycycline is a 100 mg tablet, taken orally once daily. Start taking doxycycline 1 day before entering a malaria risk area, continue taking it (daily) while in the risk area, and continue the drug (daily) for 4 weeks after leaving the malarious area. 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. Doxycycline 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 this drug, as they can interfere with absorption of doxycycline.

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

Individuals who are pregnant, younger than 8 years of age in the U.S. or younger than 12 years of age in the U.K., or have an allergy to doxycycline or tetracycline should not take doxycycline.

Persons taking long-term minocycline or related medications should not use these drugs for malaria chemoprophylaxis; these persons

should switch to doxycycline 1-2 days before travel. Minocycline should be restarted only after the full course of doxycycline has been completed.

Primaquine

Primaquine is a second-line choice for primary malaria prevention when all other options have been eliminated, and then only for short-term travel to areas where all or nearly all the malaria cases are caused by *P. vivax*. The adult dose of primaquine, when used for prevention, is 30 mg taken orally once a day. Primaquine must be started 1 day before arrival in a malarious area, taken daily while in the risk area, and continued (daily) for 1 week after leaving the malarious area. Primaquine should be taken with food in order to reduce stomach upset. Late doses can be made up on the same day. Do not double the dose the next day if a dose is missed completely.)

Primaquine may be prescribed for use after leaving certain malarious areas, to prevent certain kinds of malaria (*P. vivax* or *P. ovale*) from occurring ("relapsing") weeks or months (or rarely even years) after routine preventive medications have been stopped—this is generally for persons who have had prolonged exposure (more than 6 months) in certain malarious areas.

Individuals who are pregnant or have low levels of glucose-6-phosphate dehydrogenase (G6PD) should not take this drug (it can cause severe anemia in persons who are deficient in this blood enzyme). This enzyme deficiency is most common in African Americans, Mediterraneans, South Asians, and East Asians. Primaquine should be used only after a blood test for G6PD deficiency has been performed and found to be normal. Individuals who have a genetic deficiency of methemoglobin reductase may experience a condition called methemoglobinemia when taking primaquine.

PREGNANCY

In general, pregnant women should not travel to a malarious area unless the travel is absolutely unavoidable, because malaria poses a very serious threat to both mother and fetus. In fact, malaria can cause more severe problems in pregnant women than in those who are not pregnant; malaria increases the risk of maternal death and fetal prematurity, miscarriage, and stillbirth. Pregnant women who cannot avoid travel to a malaria risk area should recognize that it is very important to consult a health care provider or travel medicine advisor, take preventive medication, and take measures to protect against mosquito bites. (See *Insect Precautions.*)

Chloroquine is the drug of choice for pregnant women in malaria risk areas where it is still effective. Chloroquine has not been shown to be harmful to the fetus during pregnancy.

In areas of chloroquine resistance, mefloquine is the drug of choice and can be used during all trimesters, although there are less data available on mefloquine use during the first trimester.

Doxycycline, atovaquone/proguanil, and primaquine should not be used during pregnancy.

BREASTFEEDING

Very small amounts of antimalarial drugs can be passed on to breastfed infants, but the amount received by the infant in the breast milk is not thought to be harmful. However, it is also not enough to protect infants against malaria; therefore, infants need to be given appropriate drugs in dosages according to their weight.

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, atovaquone/proguanil, or primaquine.

Doxycycline should not be given to infants and children younger than 8 years of age in the U.S. or younger than 12 years in the U.K. If a physician prescribes chloroquine or 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 (for example, ice cream, jam, honey, or chocolate sauce) or drink. Malarone is available (in the U.S. and Canada) in a pediatric tablet that is one-fourth the strength of the adult tablet. Using pediatric-strength tablets, the dose is based on weight.

Dosage will need to be adjusted according to the increasing weight of a growing child, if he or she is a long-term traveler or expatriate. A travel medicine provider can advise parents or guardians before departing for long-term travel on adjusting the child's dosage.

WHEN TO SEEK MEDICAL ATTENTION

Individuals who think they might have symptoms of malaria (especially fever and/or "flu"-like symptoms) should seek medical attention immediately. Delay of appropriate therapy can have serious—even fatal—consequences. Inform a health care provider that risk of malaria exists and where travel occurred. 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 strains of malaria can lie dormant in the liver and cause malaria symptoms long after leaving the malaria risk area (months or even years later) and stopping taking malaria drugs. The development of fever or influenza-like symptoms—even months after returning—is cause to seek medical attention and advise the health care provider of previous travel to a malarious area.

SELF-TREATMENT OF PRESUMPTIVE MALARIA

In most cases travelers will not need to carry self-treatment drugs when using an appropriate, 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.*

Coartem (co-artemether; artemether/lumefantrine) and Malarone are available in the U.S. and either drug can be used for self-treatment, as long as the same drug was not used for prevention. However, Coartem should not be used in areas where there is resistance to artemisinin, from which 1 of the components of Coartem is derived. Consult a travel medicine provider.

- Adult self-treatment using Coartem consists of 6 doses taken over 3 days. 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 pregnant women, persons with a heart condition called QTc prolongation, or those with an allergy to either component of the drug (artemether/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 Malarone consists of 4 tablets taken once daily for 3 days.
  - Malarone should be taken with food.
  - Malarone should not be used by pregnant women, persons with renal failure, or those who are allergic to either component of the drug.

The 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 Malarone 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 there is no other alternative.
