# A.I.M. Malaria Prevention Recommendations (2023)

(Note: These recommendations are intended to be guidelines, but should not substitute for specific medical advice from your personal physician. In particular, these recommendations cover only malaria prophylaxis, not treatment (which, if necessary, should be guided by a health professional and employ medication different from any prophylactic medication used.)

## ABCD'S OF MALARIA: **A**wareness of Risk / **B**ite Prevention / **C**hemoprophylaxis / prompt **D**iagnosis and Treatment

In sub-Saharan Africa, the predominant strain of malaria is Chloroquine-resistant Plasmodium Falciparum. See CDC Yellow Book or the UK Health Security Agency Advisory Committee on Malaria Prevention (ACMP) guidelines for specific country risk regarding malaria.

Malaria is transmitted in endemic countries at altitudes below 2,000 metres (6,500 ft) by the bite of an infected Anopheles mosquito. Transmission can be quite variable depending on location and seasons.

## GENERAL MEASURES FOR PREVENTION:

1) Sleep under insecticide treated bed nets. Anopheles mosquito bite risk is from dusk until dawn.
2) Mosquito screening on houses.
3) Remove or cover standing water in neighborhood to reduce mosquito breeding.
4) Consider insecticide spraying in house.
5) Use personal insect repellant such as DEET 20% to 50% or Picaridan 20%.
6) Wear long sleeves and socks in the evenings.
7) When both sunscreen and DEET are required, DEET should be applied after the sunscreen (updated recommendation, see ACMP page 18).

The ACMP recommends using DEET at concentrations of at least 20%, up to 50%. DEET is safe in pregnancy and for children older than 2 months of age.

8) An alternative option that can be considered is p-menthane 3,8 diol (lemon eucalyptus) (PMD), which gives about the same amount of protection afforded by 15% DEET but is reported to provide a shorter period of protection than extended duration (microencapsulated) DEET.

## MEASURES NOT RECOMMENDED: (from ACMP guidelines page 23-24)

Herbal remedies, homeopathy, electronic buzzers, vitamins B1 or B12, garlic, Marmite, Tea Tree oil, and bath oils have never been proven to prevent mosquito bites or malaria infection.

Whilst oil of citronella-based products do have repellent properties, they provide short-lived protection and are not recommended by the ACMP. Citronella has been withdrawn in Europe.

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## MALARIA PROPHYLAXIS (remember, no prophylaxis is 100% protective):

The choice of malaria prophylaxis is between three medications recommended for choroquine-resistant areas (i.e. Sub-Saharan Africa) by the US Centers for Disease Control and Prevention (CDC) and the ACMP: Doxycycline, Mefloquine (trade name Lariam [see Mefloquine black box warning below]), or Atovaquone-Proguanil (trade name Malarone). The full duration of prophylaxis should be taken; it is unwise to prematurely terminate one's course of prophylactic medications.

**ADULT DOSING:**

DOXYCYCLINE 100mg: 1 tablet daily starting 2 days before entering malaria area and continuing 4 weeks after leaving malaria area.

MEFLOQUINE 250mg: 1 tablet weekly starting 2 to 3 weeks (to assess tolerability) prior to entering malaria area and continuing 4 weeks after leaving malaria area.

ATOVAQUONE 250mg-PROGUANIL 100mg: 1 tablet daily starting 2 days before entering malaria area and continuing 1 week after leaving malaria area.

**PEDIATRIC DOSING**: (dosing mainly based on body weight, start and end time same as adult instructions)

DOXYCYCLINE 100mg: Children aged 8 years and older. 8 years and older (US) or 12 years and older (UK) – 1 tablet daily.

MEFLOQUINE 250mg:

5kg to 15.9kg take ¼ tablet weekly;
16kg to 24.9 take ½ tablet weekly;
25kg to 44.9kg take ¾ tablet weekly;
45kg and above take 1 tablet weekly.

ATOVAQUONE 250mg-PROGUANIL 100mg ADULT tablet:

11kg to 20kg take ¼ adult tablet daily;
21kg to 30kg take ½ adult tablet daily;
31kg to 40 kg take ¾ adult tablet daily;
Greater than 40kg take 1 adult tablet daily.

ATOVAQUONE 62.5mg-PROGUANIL 25mg PEDIATRIC tablet:

5kg-8kg take ½ pediatric tablet daily;
8.1kg to 10kg take ¾ pediatric tablet daily;
10.1kg to 20kg take 1 pediatric tablet daily;
20.1kg to 30kg take 2 pediatric tablets daily;
30.1kg to 40kg take 3 pediatric tablets daily;
Greater than 40kg take 4 pediatric tablets daily.

(Note for Atovaquone-Proguanil Pediatric dosing: The CDC prophylaxis dosing for under 11kg is an off-label use.)

**PREGNANCY:**

Rigorous attention to general preventative measures should be observed. Mefloquine is the only medication recommended for malaria chemoprophylaxis during pregnancy.

**SIDE EFFECTS:**

DOXYCYCLINE: Headache and upset stomach. Doxycycline hydrochloride preparations are acidic and may produce esophageal burning, especially if taken without food / liquids, or on an empty stomach and/or just before lying down. Rarely, doxycycline may cause photosensitivity (increased sunburn sensitivity) which is mostly mild and transient. Doxycycline is a broad spectrum antibiotic and may predispose to vaginal candidiasis (vaginal yeast infections).

MEFLOQUINE: Sleep disturbances, vivid dreams, rarely psychosis. In 2013 the FDA issued a black box warning for Mefloquine and added the following product label:

"**WARNING: Mefloquine may cause neuropsychiatric adverse reactions that can persist after mefloquine has been discontinued. Mefloquine should not be prescribed for prophylaxis in patients with major psychiatric disorders. During prophylactic use, if psychiatric or neurologic symptoms occur, the drug should be discontinued and an alternative medication should be substituted (see WARNINGS)".**

This warning was added because of case reports of persistent neurologic symptoms (dizziness, vertigo, loss of balance, tinnitus [ringing in ears]) or psychiatric symptoms (anxiety, confusion, paranoia, and depression). Dizziness, loss of balance, tinnitus, or vertigo persisted for months to years after mefloquine was discontinued, and permanent vestibular

damage was diagnosed in some cases. These symptoms interfered with patients' daily activities and ability to work. Some of the psychiatric symptoms also persisted for months to years after mefloquine was discontinued. For more information, see http://www.fda.gov/drugs/drugsafety/ucm362227.htm.

Nevertheless, "mefloquine remains an important prophylactic agent which is tolerated by most travellers who take it" (ACMP, page 31).

ATOVAQUONE-PROGUANIL: Headache and upset stomach.

**CONTRAINDICATIONS:**

DOXYCYCLINE: Doxycycline should not be used by children under 12 years of age (UK) or 8 years of age (US). Should not be used during pregnancy or by women who are breastfeeding, and anyone with an allergy to tetracyclines.

MEFLOQUINE: Mefloquine should not be used by those with a current or previous history of depression, neuropsychiatric disorders or epilepsy; or with hypersensitivity to quinine. Should not be used in infants weighing less than 5kg. Mefloquine is not recommended for scuba divers or pilots or those with a history of cardiac conduction disorders.

ATOVAQUONE-PROGUANIL: Allergy to either component. There is inadequate data looking at use during pregnancy, currently the manufacturer advises against use during pregnancy. Atovaquone-proguanil should generally be avoided in breastfeeding, but ACMP advises that atovaquone-proguanil can be used when breastfeeding if there is no suitable alternative antimalarial. Should not be used in children weighing less than 5kg.

**DRUG TO DRUG INTERACTIONS:**

DOXYCYCLINE: The metabolism of doxycycline is accelerated by carbamazepine and phenytoin. At present, there are no data to support a change in the dose of doxycycline used for malaria prophylaxis in individuals taking one or more of these agents. Tetracyclines possibly enhance the anticoagulant effect of coumarins (e.g. warfarin), and may increase plasma concentration of cyclosporin. It may temporarily reduce the contraceptive effect of estrogens.

MEFLOQUINE: Mefloquine antagonizes the anticonvulsant effect of anti-epileptics and interacts with a number of cardiac drugs.

ATOVAQUONE-PROGUANIL: May enhance the anticoagulant effect of warfarin. Absorption reduced by oral magnesium salts, and concurrent use of tetracyclines, metoclopramide, and rifampins. Anti-folate effect is increased when given with pyrimethamine.

**LENGTH OF USE:**

The ACMP recommendations for long term expats (the studies were likely all done among adults) estimate that, in the absence of significant side effects, it's safe to take Doxycycline for up to two years and beyond, Mefloquine three years and beyond, and Atovaquone-Proguanil one year. For all three options, "longer term use (is) possible if justified by the risk of exposure to malaria." (Table 10)

Important note: All these lengths are longer than the British National Formulary and the American FDA approvals for length of use. The ACMP acknowledges that: "Long term use of malaria chemoprophylaxis outside licensing restrictions is based on the cumulative evidence of lack of harm rather than positive evidence of safety. This situation is unlikely to change." (p. 78)

**DRUG AVAILABILITY:**

Doxycycline is inexpensive and readily available in pharmacies in most major towns. Note that European and some Indian pharmaceutical companies have a better quality control track record than African companies. Mefloquine is more expensive but usually available in larger towns/ cities. Atavaquone-Proguanil is the most expensive of the three and most difficult to find.

**REFERENCES:**

UK Health Security Agency, "Guidelines for malaria prevention in travellers from the UK 2021": https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1102955/guidelines-for-malaria-prevention-in-travellers-from-the-UK-2021.pdf. For ongoing updates, see also www.gov.uk/government/publications/malaria-prevention-guidelines-for-travellers-from-the-uk

The US Centers for Disease Control 2020 Yellow Book: https://wwwnc.cdc.gov/travel/page/yellowbook-home-2020

**PROPHYLAXIS ADVICE:**

Malaria Reference Laboratory (MRL): www.malaria-reference.co.uk

National Travel Health Network and Centre (NaTHNaC): www.nathnac.org
Advice line for healthcare professionals (UK): 020 7383 7474

Liverpool School of Tropical Medicine (LSTM): www.lstmed.ac.uk

**WEBSITES:**

CDC Travel Health: wwwnc.cdc.gov/travel

British National Formulary (BNF): www.bnf.org

British Infection Association (BIA): www.britishinfection.org

Department of Health (UK): www.dh.gov.uk

Electronic Medicines Compendium (for Summaries of Product Characteristics): www.medicines.org.uk/emc

Hospital for Tropical Diseases (UK): https://www.uclh.nhs.uk/our-services/our-hospitals/Hospital-of-Tropical-Diseases

Liverpool School of Tropical Medicine (LSTM): www.lstmed.ac.uk

London School of Hygiene and Tropical Medicine (LSHTM): www.lshtm.ac.uk

Malaria Reference Laboratory (MRL): www.malaria-reference.co.uk

Medicines and Healthcare Products Regulatory Agency (MHRA): www.mhra.gov.uk

National Travel Health Network and Centre (NaTHNaC): www.nathnac.org

Royal Society of Tropical Medicine and Hygiene (RSTM&H): www.rstmh.org

UK Health Security Agency: https://www.gov.uk/government/organisations/uk-health-security-agency

World Health Organization (WHO) International Travel and Health: https://www.who.int/publications/i/item/9789241580472; (Chapter 7 – Malaria was updated for 2020: https://cdn.who.int/media/docs/default-source/travel-and-health/9789241580472-eng-chapter-7.pdf?sfvrsn=8be7067_13). Cf. also Malaria Fact Sheet https://www.who.int/news-room/fact-sheets/detail/malaria.

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