Malaria Prophylaxis for Travellers

Guideline for Healthcare Workers

Anti-Malaria Campaign
Ministry of Health – Sri Lanka

Keep Sri Lanka Malaria Free

A-Aware of the risk of malaria in the country to be visited

B- Avoid mosquito **B**ites

C-Chemoprophylaxis when indicated

D-Diagnosis in fever patients

E-Early and Effective treatment

F-Fatal if diagnosis and treatment delayed

ANTI-MALARIA CAMPAIGN

Malaria Prophylaxis for Travellers
Guideline for Healthcare Workers

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MESSAGE FROM THE DIRECTOR GENERAL OF HEALTH SERVICES

All Provincial Directors of Health Services
All Regional Directors of Health Services
All Hospital Directors/ Medical Superintends
All District Medical Officers/MOIC
All Medical Offices of Health

Guideline for health care workers on malaria chemoprophylaxis for travellers

Sri Lanka successfully controlled malaria transmission, eliminated the disease and certified by the World Health Organization as a "malaria-free" country in September 2016. In the absence of local transmission of malaria in Sri Lanka, the risk of re-introduction of the disease is high due to, increasing number of malaria infected persons entering Sri Lanka from countries endemic for malaria and the prevalence of the vector mosquito in most parts of the country.

Sri Lankans who travel to malaria endemic countries are at a high risk of acquiring the disease as they currently lack immunity against malaria. Among the annually reported imported malaria patients, about three fourth comprise of Sri Lankan travellers.

It is with great pleasure and pride I write this letter for the Anti Malaria Campaign (AMC) for preparing the guideline for healthcare workers on malaria chemoprophylaxis for travellers which is definitely a timely need with the globalization and frequent travels to and from overseas where malaria is endemic.

The Sustainable Developmental Goal 3, the Good health is a fundamental human right and crucial to achieve by 2030 and maintaining the zero mortality of malaria in Sri Lanka through applying preventive measures such as avoiding mosquito bites through physical barriers and taking chemoprophylaxis before travelling to malaria endemic countries which is very important.

The AMC play a vital role in the treatment of malaria and Prevention of Re-Introduction (POR) of malaria to the country through their strong technical role at the National level and subnational level through the Regional Malaria Offices. This guideline is the perfect recommendations of highly renowned public health professionals and Technical Support Group (TSG) for POR of malaria of the Anti Malaria Campaign to share their expertise knowledge with regard to chemoprophylaxis.

You are kindly requested to disseminate the contents among the healthcare workers and other health care professionals of your institutions. Please ensure that the anti-malarial chemoprophylaxis are obtained by the travellers to malaria endemic countries in your region and advice on other precautions on avoiding mosquito bites. For further clarifications please contact the Anti Malaria Campaign.

Dr Anil Jasinghe
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Ministry of Health, Nutrition and Indigenous Medicine

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INTRODUCTION

Sri Lanka successfully controlled malaria transmission, eliminated the disease and was certified by the World Health Organization as a "malaria-free" country in September 2016. In the absence of local transmission of malaria in Sri Lanka, the risk of re-introduction of the disease is high due to following reasons.

a) Increasing number of malaria infected persons entering Sri Lanka from countries endemic for malaria. Among the annually reported imported malaria patients, approximately three fourth comprise of Sri Lankan travellers who acquire the disease while travelling to malaria endemic countries.

b) Prevalence of the vector mosquitoes in most parts of the country.

Sri Lankans who travel to the malaria endemic countries are at a higher risk of acquiring the disease as they currently lack immunity against malaria. The risk of infection during travel can be reduced by the use of appropriate preventive measures for mosquito bites and **chemoprophylaxis** (**preventive medication**).

This guideline on Malaria Prophylaxis for Travellers is prepared primarily for

1. Medical officers in the Anti Malaria Campaign Head Quarters (AMC HQ)
2. Regional Malaria Officers (RMO)

This could also serve as a source of information for the medical professionals in private and public health sectors. All medical professionals and health care providers are advised to refer potential travellers to AMC HQ or to RMO offices to obtain updated information, advices, medications and for follow- up.

RISK GROUPS FOR MALARIA IN SRI LANKA

Most of the imported malaria infections reported in Sri Lanka during the past 6 years (since 2012) have been acquired either in India or in sub-Saharan Africa. Many countries in South Asia and South East Asia neighboring Sri Lanka are highly malarious. Travellers to these countries are at risk of contracting the disease. Some groups of travellers, such as young children, pregnant women and individuals with a weakened immune system, are at increased risk of developing severe illness if they become infected with malaria.

WHEN TO SUSPECT MALARIA?

Malaria is a potentially life-threatening disease caused by *Plasmodium* species parasites that are transmitted through the bite of the female *Anopheles* mosquito. Symptoms of malaria infection are nonspecific and may manifest as flu like illness with fever, chills, headache, malaise and muscle aches. Left untreated, the disease can lead to severe manifestations with organ failure and, in some cases, death. malaria symptoms appear following an incubation period of seven days or longer after an infective mosquito bite.

The classic presentation of malaria may not be observed in all and the disease may present with atypical manifestations. Thus, travellers who become ill with a fever or a flu-like illness either while traveling in a malaria-risk area or after returning home (for up to 1 year) should seek immediate medical attention and should inform the physician regarding their travel to a malaria endemic country in order to be screened for malaria. Screening for malaria is done free of charge at the AMC HQ, Regional Malaria Office's and all major hospitals in the country.

Irrespective of chemoprophylaxis, if a traveller developed fever up to one (01) year following return from a malaria endemic country, testing for malaria is advisable. If the initial test is negative for suspicious patients with a travel history and fever, repeated testing for 3 consecutive days is recommended before excluding malaria (Please refer General Circular No.02-112/2014 dated 18th August 2014 issued by the DGHS "Guidelines on malaria chemotherapy and management of patients with malaria" for further details).

All travellers to malaria endemic countries should be assessed by a clinician before deciding on preventive measures and all travellers should be advised on mosquito bite prevention methods. Chemoprophylaxis is indicated for countries where the transmission of malaria is present (Annex I).

PREVENTING MOSQUITO BITES

Anopheles vector, a night biting mosquito, generally bites between dusk and dawn. Prevention of mosquito bites is therefore, the first line of defense against malaria. Avoiding unnecessary travel (especially pregnant women and children) to places where malaria is endemic, staying indoors during the peak mosquito biting times and lodging in a safe place with mosquito mesh for windows are recommended for all travellers.

RECOMMENDATIONS FOR PREVENTING MOSQUITO BITES

- Sleeping under bed nets preferably Long-Lasting Insecticidal Nets (LLIN)
- Using insect repellents containing DEET (N, N-diethyl-3-methylbenzamide)
- Using protective clothing (ex: long sleeve shirts, long trousers)
- Using sprays, mats, or vaporizers recommended /approved by health authorities

RISK ASSESSMENT OF THE TRAVELLER

- Risk assessment for contracting malaria should be done carefully before prescribing any malaria chemoprophylaxis.
- The full details of travel should be obtained including time of departure, journey plan and duration of stay in each malarious region /country in the itinerary.
- If the person travels only to areas where there is no malaria transmission, then chemoprophylaxis is not necessary even if, the country is identified as a malaria endemic country.

CHEMOPROPHYLAXIS (PREVENTIVE MEDICATION)

- Depending on the malaria risk in the area/s to be visited (Annex I), travellers may also need to take chemoprophylaxis prior to, during and upon return from their travel.
- Consultation on chemoprophylaxis must be offered two to three weeks before the travel.
- Detailed medical history should be obtained including current and previous illnesses including malaria, drug history and presence of drug allergies, G6PD deficiency, etc.
- The most appropriate chemoprophylaxis for the destination(s) should be prescribed, in the correct dosages for the recommended period.
- Advise to travellers that no antimalarial prophylactic regime gives complete protection. However, adherence to the recommended drug regime, significantly reduces the risk of fatal disease of malaria.
- Depending on the type of most prevalent *plasmodium* species at the destination, travellers should be advised on possible late-onset malaria caused by *P.ovale* and *P.vivax*.
- All chemoprophylactic drugs should be taken with unfailing regularity for the entire duration prescribed.
- If a traveller develops a severe adverse effect after taking a chemoprophylactic drug, he/she should be advised to stop medication and seek medical advice immediately (this applies particularly to neurological or psychological disturbances which may be experienced with mefloquine prophylaxis.).
- Mild nausea, occasional vomiting or loose stools should not warrant discontinuation of prophylaxis, but medical advice should be sought if symptoms persist
- An individual who experiences fever a week or more after entering to a malarious area should consult qualified doctor immediately to obtain a correct diagnosis.

RECOMMENDED ANTIMALARIAL DRUGS FOR PROPHYLAXIS IN TRAVELLERS

Generic name	Dosage regimen	Duration of prophylaxis	Pregnancy, breast feeding and children	Contraindications and cautions.	Comments
Chloroquine **Recommended for *P. vivax* risk countries only**	Weekly dose • **Adult**: 300 mg chloroquine base (2 tablets) weekly as a single dose • **Children:** 5 mg base/kg weekly as a single dose	• Start 1 week before departure • Take weekly on the same day of the week • Continue for 4 weeks after return.	• **Pregnancy and breastfeeding:** Safe • **Children**: Safe for short term use	**Contraindications:** • Hypersensitivity to chloroquine **Caution:** • Renal, Visual or Hepatic impairment • Psoriasis, neurological (e.g. epilepsy), retinal or gastrointestinal disorders, as chloroquine may exacerbate these conditions. • G6PD deficiency	• Concurrent use of chloroquine may reduce the antibody response to intradermally administered human diploid-cell rabies vaccine. • Not a good choice for last minute travellers • Not recommended for long-term use in children
Hydroxychloroquine **Recommended for *P. vivax* risk countries only**	Weekly dose • **Adult:** 310 mg base (400 mg salt) orally, once/week • **Children:** 5 mg/kg base (6.5 mg/kg salt) orally, once/week				

Generic name	Dosage regimen	Duration of prophylaxis	Pregnancy, breast feeding and children	Contraindications and cautions.	Comments
Mefloquine **Recommended for *P.falciparum* risk and Chloroquine resistant *P. vivax* risk countries**	Weekly dose • **Adult**: 1 tablet of 250 mg weekly • **Children** - 5 mg/kg weekly	• Start at least 1 week (preferably 2–3 weeks) before departure • Take weekly on the same day of the week • Continue for 4 weeks after return	• **Pregnancy and Breastfeeding:** Safe • **Children**: Not recommended for those with body weight under 5 kg / 3months of age	**Contraindications:** • Hypersensitivity to mefloquine; • Active psychiatric illness (including depression, schizophrenia, generalized anxiety disorders, psychosis any major psychiatric illness) • Epilepsy or history of convulsions • History of severe neuropsychiatric disease • Concomitant halofantrine treatment • Treatment with mefloquine in previous 4 weeks • Patients have had cerebral malaria **Caution:** • Hepatic impairment & patients with cardiac diseases • Ampicillin, tetracycline and metoclopramide may increase mefloquine blood levels. • Increased risk of cardiac events with calcium channel blockers , digoxin, amiadarone, B blockers , etc	• The tablets should be swallowed whole preferably after a meal with plenty of liquid. • Mefloquine is usually safe as a chemoprophylaxis for all trimesters of pregnancy but some studies advice to avoid during 1st trimester. • Do not give mefloquine within 12h of quinine treatment. • Mefloquine and other cardioactive drugs may be given concomitantly only under close medical supervision. • Not a good choice for last minute travellers • Do not give concomitantly with oral typhoid vaccine.

Generic name	Dosage regimen	Duration of prophylaxis	Pregnancy, breast feeding and children	Contraindications and cautions.	Comments
Atovaquone–Proguanil combination tablet **Recommended for *P.falciparum* risk and Chloroquine resistant *P. vivax* risk countries**	Single dose daily • **Adult**: **>40kg**: 1 adult tablet (250 mg atovaquone plus 100 mg proguanil) daily • **Children**: **11–20 kg**: 62.5 mg atovaquone plus 25 mg proguanil (One paediatric tablet) daily **21–30 kg**: Two paediatric tablets daily **31–40 kg**: Three paediatric tablets daily	• Start 1 day before departure • Take daily on the same time of the day • Continue for 7 days after return	• **Pregnancy and breastfeeding**: Limited data not recommended • **Children**: Limited data, not recommended	**Contraindications:** • Hypersensitivity to atovaquone and/or proguanil • severe renal insufficiency (creatinine clearance < 30 ml/min) **Caution:** • Decrease hepatic, renal or cardiac functions (such as elderly)	• Take with food or milky drink to increase absorption. • Plasma concentrations of atovaquone are reduced when it is co-administered with rifampicin, rifabutin, metoclopramide or tetracycline. • May interfere with live typhoid vaccine. • Currently not a registered drug in Sri Lanka

Generic name	Dosage regimen	Duration of prophylaxis	Pregnancy, breast feeding and children	Contraindications and cautions.	Comments
Doxycycline **Recommended for *P.falciparum* risk and Chloroquine resistant *P. vivax* risk countries**	Single dose daily • **Adult**: 1 tablet of 100 mg daily • **Children** :1.5 mg salt/kg daily	• Start 1 day before departure • Take daily on the same time of the day • Continue for 4 weeks after return	• **Pregnancy and breastfeeding**: Contraindicated • **Children**: Contraindicated under 8 years of Age	**Contraindications:** • Hypersensitivity to tetracyclines • Liver dysfunction **Caution:** • Caution with SLE patients	• The capsules should be swallowed with plenty of fluid in either the resting or standing position and well before going to bed for the night to reduce the likelihood of oesophageal irritation and ulceration. • If gastric irritation occurs, it is recommended that Doxycycline Capsules be given with food or milk. • Doxycycline makes the skin more susceptible to sunburn. People with sensitive skin should use a highly protective (UVA) sunscreen and avoid prolonged direct sunlight, or switch to another drug. • May increase the risk of vaginal Candida infections. • May reduce the efficacy of oral anticoagulants and oral contraceptives

- See package insert of drugs for full information on contraindications and precautions.
- For children the drug should be calculated according to the body weight and should not exceed the adult recommended dose.
- Inform all Adverse drug Reactions to the Anti Malaria Campaign.

WHEN A DOSE IS MISSED

For a weekly drug, prophylactic drug levels in blood can remain adequate if they are only 01–02 days late. If this is the case, the traveller can take a dose as soon as possible, then resume weekly doses on the originally scheduled day. If consuming the drug is more than 2 days late, blood levels may not be adequate. The traveller should take a dose as soon as possible. The weekly doses should resume at this new day of the week (the next dose is one week later, then weekly thereafter).

For a daily drug, if the traveller is 01–02 days late, protective blood levels are less likely to be maintained. They should take a dose as soon as possible and resume the daily schedule at the new time of day.

LONG TERM CHEMOPROPHYLAXIS

Long term chemoprophylaxis can be considered for the people with long term exposure to risk of malaria infection (ex: Sri Lankan forces in UN peace keeping missions). Even though, only few studies have been done on chemoprophylaxis use for more than 6 months, after excluding long term adverse effects of the drugs, prophylaxis can be recommended to cover a period of one year in a malaria endemic country. Monitoring of liver and renal functions is recommended for long term chemoprophylactic users.

LONG TERM CHEMOPROPHYLAXIS

- The risk of serious side-effects associated with long-term prophylactic use of chloroquine is low. All individuals who have taken chloroquine for greater than one year or hydroxychloroquine for greater than five years should referred to annual screening for retinopathy.
- There is no increased risk of serious side-effects with long-term use of mefloquine if the drug is tolerated in the short term. Pharmacokinetic data indicate that mefloquine does not accumulate during long-term intake.
- Available data on long-term chemoprophylaxis with doxycycline (i.e. more than 12 months) are limited but reassuring.
- Atovaquone–proguanil is licensed to use up to one year duration in some European countries.

Some groups of travellers, especially young children, pregnant women and immunosuppressed individuals, are at particular risk of serious consequences if they become infected with malaria.

PREGNANT WOMEN

Malaria in a pregnant woman increases the risk of maternal death, miscarriage, stillbirth and low birth weight with associated risk of neonatal death. Pregnant women should be advised to avoid travelling to areas where malaria transmission occurs. When travel cannot be avoided, it is important to follow the recommendations given below.

Mosquito bite prevention during pregnancy

Pregnant women are particularly susceptible to mosquito bites and should therefore be vigilant in using protective measures, including insect repellents and insecticide-treated mosquito nets. They should take care not to exceed the recommended usage of insect repellents.

CHEMOPROPHYLAXIS FOR PREGNANT WOMEN

- Chloroquine is reported to be safe during pregnancy. If a pregnant woman is at risk, chloroquine should be used at the recommended dosage for prophylaxis wherever chloroquine-sensitive malaria is prevalent.
- WHO indicates Mefloquine as chemoprophylaxis during pregnancy for chloroquine resistant malaria.
- Doxycycline is contraindicated during pregnancy.

- **Women who may become pregnant during or after travel:** Malaria prophylaxis may be taken, but pregnancy should preferably be avoided during the period of drug intake and for 1 week after doxycycline and 3 months after the last dose of mefloquine prophylaxis. Appropriate contraceptive methods need to be prescribed accordingly.

YOUNG CHILDREN

P. falciparum malaria in a young child is a medical emergency. It may be rapidly fatal. Medical help should be sought immediately if a child develops a febrile illness within 1 year (or rarely later) of travelling to a malaria-endemic country/territory. In infants, malaria should be suspected even in non-febrile illness.

Parents should be advised not to take infants or young children to areas where there is risk of *P.falciparum* malaria. If travel cannot be avoided, children must be effectively protected against mosquito bites and should be given appropriate chemoprophylactic drugs.

Mosquito bite prevention for young children

Infants should be kept under insecticide-treated mosquito nets as much as possible between dusk and dawn. The manufacturer's instructions on the use of insect repellents should be followed diligently, and the recommended doses must not be exceeded.

CHEMOPROPHYLAXIS FOR YOUNG CHILDREN

- Chloroquine and mefloquine are safe in young children. Chloroquine is safe for infants and mefloquine may be given to infants of more than 5 kg body weight.
- Doxycycline is contraindicated in children below 8 years of age.
- Breastfed, as well as bottle-fed, infants should be given chemoprophylaxis
- Dosage schedules for children should be based on body weight and should not exceed adult dose.
- Tablets should be crushed and ground as necessary. The bitter taste of the tablets can be disguised with sugar or other foods.
- Long-term travellers should adjust the chemoprophylaxis dosage according to the increasing weight of the growing child.
- All antimalarial drugs should be kept out of the reach of children and stored in childproof containers.

CONTACT DETAILS OF RMO OFFICES

Ampara	063-2223464	Kandy	081-2210687	Matale	066-2222295
Anuradhapura	025-2221844	Kalmunai	067-2220206	Monaragala	055-2276698
Badulla	055-2229560	Kegalle	035-2223480	Mullaitivu	021-2060007
Batticoloa	065-2222931	Killinochchi	021-2285517	Polonnaruwa	027-2226018
Colombo	011-2519284	Kurunegala A	037-2222193	Puttalam	032-2265319
Embilipitiya	047-2230301	Kurunegala B	037-2222193	Trincomalee	026-2222584
Hambantota	047-2258135	Maho	037-2275254	Vauniya	024-2222954
Jaffna	021-2227924	Mannar	023-3239547		

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3. World Health Organization. 2015. *Guidelines for the Treatment of Malaria*, Third Edition, WHO. [Accessed 31 October 2019] Available from https://www.who.int/malaria/publications/atoz/9789241549127/en/

Annex I Countries and territories with malarious areas which call for chemoprophylaxis (*Adopted from International travel and health, WHO, 2019.)*

Countries for which mefloquine, doxycycline or atovaquone-proguanil is recommended (risk of *P.falciparum* malaria or presence of chloroquine resistant *P.vivax*).

Afghanistan	DPR of Korea (Southern province)	Kenya	Sao Tome and Principe
Angola	Democratic Republic of Congo	Lao People's Democratic Republic	Saudi Arabia (Yemen Boarder)
Azerbaijan	Djibouti	Liberia	Senegal
Bangladesh	Dominician Republic	Madagascar	Sierra Leone
Belize	Ecuador	Malawi	Solomon Islands
Benin	Egypt	Malaysia	Somalia
Bhutan	El Salvador	Mali	South Africa
Bolivia	Equatorial Guinea	Mauritania	South Sudan
Botswana	Eritrea	Mayotte	Sudan
Brazil	Eswatini	Mexico	Suriname
Brunei Darussalam	Ethiopia	Mozambique	Tajikistan
Burkina Faso	French Guiana	Myanmar	Thailand
Burundi	Gabon	Namibia	Timor-Leste
Cabo Verde	Gambia	Nicaragua	Togo
Cambodia	Ghana	Niger	Uganda
Cameroon	Guatemala	Nigeria	United Republic of Tanzania
Central African Republic	Guinea	Pakistan	Vanuatu
Chad	Guinea-Bissau	Panama	Venezuela
Colombia	Guyana	Papua New Guinea	Viet Nam
Comoros	Honduras	Peru	Yemen
Congo	Indonesia	Philippines	Zambia
Côte d'Ivoire	Iran(Islamic Republic of)	Rwanda	Zimbabwe

Countries for which chloroquine is recommended (risk of P.vivax malaria)

India Nepal Haiti

*India and Nepal are considered as low risk for *P.falciparum* and in Haiti there is no resistance reported for chloroquine.

In some malaria endemic countries some territories have a negligible risk of malaria transmission and people travelling only to these areas may not require malaria prophylaxis. Please refer latest International travel and health, WHO via https://www.who.int/ith/ith-country-list-new.pdf

Any traveller is planning to visit a malaria endemic country should be referred to the Anti Malaria Campaign or Regional Malaria Offices to seek a medical consultation on preventive methods at least a week before commencement of travel (Hotline- 0117 626 626)

Anti-Malaria Campaign

Ministry of Health

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