To promote healthy resettlement, CDC provides supplemental guidance to panel physicians caring for US-bound refugees. The Overseas Refugee Health Guidance provides panel physicians with supplemental guidance on vaccination, pre-departure treatments for malaria and intestinal parasites and fitness to travel. These activities are coordinated with the International Organization for Migration (IOM).

Learn more about the role of panel physicians in the US refugee resettlement program.

Vaccination Program for U.S.-bound Refugees

The table below describes the overseas immunization schedule recommended for U.S.-bound refugees and V93s. As part of the Vaccination Program for US-bound Refugees and V93s:

Vaccination Program for U.S.-bound Refugees – PDF version for printing [PDF – 4 pages]

- Refugees and Visa 93 applicants are offered immunizations depending on age, vaccine history, and eligibility. Although the goal is to provide up to 2 doses of each vaccine, the vaccines administered depend on availability and logistics at each site. Receiving states should refer to each arriving refugee's or V93's U.S. Department of State's Vaccination Documentation Worksheet (DS-3025) to determine what vaccinations were received overseas.
    - Valid historical vaccination records (such as camp vaccine cards) are counted toward the immunization schedule when applicable. These will be documented in the "vaccine history" columns on the DS-3025 Vaccination Documentation Worksheet.

- Refugees who undergo repeated medical examinations overseas may receive additional vaccine doses.
- Live-virus vaccines will not routinely be administered less than 4 weeks before departure, except during disease outbreaks or in other exceptional situations. CDC will provide additional notification to states in most of these situations, but please review each refugee's DS-3025 worksheet.
    - In the event that a live-virus vaccine is given within 4 weeks of departure, tuberculin skin tests (TST), interferon-gamma release assays (IGRA), or other live-virus vaccines (e.g., varicella; oral polio vaccine (OPV); measles, mumps, and rubella (MMR); measles, mumps, rubella, and varicella (MMRV)) should not be administered for at least 28 days as part of the domestic examination after arrival. More information is available in the Morbidity and Mortality Weekly Report. Other routine post-arrival screening and immunization activities should continue in accordance with standard CDC guidance.
- The Technical Instructions for Polio Vaccination, which apply to U.S.-bound refugees, are available on the CDC IRMH website and the Global Polio Eradication Initiative .
- Before hepatitis B vaccination, refugees and V93s of all ages are tested for hepatitis B virus infection by using hepatitis B surface antigen (HBsAg), where available. All HBsAg results will be documented on the DS forms.
    - HBsAg-positive persons do not receive hepatitis B vaccination overseas. They are counseled about the infection and about transmission prevention. Positive results are documented on the DS forms.
    - HBsAg-negative persons receive up to two hepatitis B vaccine doses overseas, if due and if there are no known contraindications.
    - HBsAg-negative household contacts of HBsAg-positive persons may be given an additional (third) dose of hepatitis B vaccine overseas to complete the series for full protection, if there is time to do so before departure. Because the third dose may be given near the time of departure, states should be aware that HBsAg results may be falsely positive within the first month after hepatitis B vaccination. CDC advises waiting at least 30 days following receipt of hepatitis B vaccine before testing for HBsAg.

Routine vaccination of U.S.-bound refugees before travel to the United States is not legally required. However, routine vaccinations are strongly recommended and offered overseas as part of this Vaccination Program to protect health, prevent travel delays due to disease outbreaks, and, for children, to allow more rapid integration into schools after arrival in the United States.

The vaccination schedule is modified periodically based on changing Advisory Committee on Immunization Practices (ACIP) recommendations, logistics, or availability.

Vaccination Program for U.S.-bound Refugees: Immunization Schedule (updated January 2021)

Prepared by the Immigrant, Refugee, and Migrant Health Branch, Division of Global Migration and Quarantine, CDC

Vaccines Given to Eligible U.S.-bound Refugees (depending on availability and eligibility)	
Age	**Vaccines [1]**
Birth-adult	HepB x 2 doses [2]
6 wks-<15 wks	Rotavirus x 2 doses (maximum age for dose 2 is 8 mos)
6 wks-<5 yrs	Hib (x 2 doses if <15 mos; x 1 dose if 15 mos-5 yrs) [3] PCV (x 2 doses if <2 yrs; x 1 dose if 2-5 yrs) [4]
6 wks -<7 yrs	DTP x 1 dose [5]
6 wks-<11 yrs	Polio x 2 doses (OPV, IPV, or one of each)
7 yrs-adult	Td x 2 doses MenACWY x 1 dose
≥ 1 yr-<20 yrs **≥ 1 yr-born ≥ 1957**	Varicella x 1 dose MMR x 2 doses

Hepatitis B (HepB); Haemophilus influenzae type B (Hib); pneumococcal conjugate vaccine (PCV); diphtheria, tetanus, pertussis (DTP); oral polio vaccine (OPV); inactivated polio vaccine (IPV); tetanus, diphtheria (Td); meningococcal conjugate vaccine with protection against serogroups A, C, W, and Y (MenACWY); measles, mumps, and rubella (MMR)

[1] For some sites (including most Asia sites and some others), those ≥6 months old (including adults) may receive the inactivated influenza vaccine (1–2 doses depending on age and vaccination history)

[2] Refugees and V93s are tested for hepatitis B virus infection (HBsAg) before vaccination, and are vaccinated only if negative (and if a dose is due).

[3] One dose of Hib vaccine will be recommended for unimmunized asplenic persons regardless of age, and for unimmunized HIV-positive patients up to age 18 years.

[4] When available, PCV13 will be given to children 6 weeks to <5 years of age. A second dose will be given to children up to age 2 years. One dose of PCV13 will also be recommended for all immunocompromised persons, regardless of age.

[5] Children residing in refugee camps often receive several doses of whole-cell pertussis (DTwP) as part of the Expanded Program on Immunization (EPI). Therefore, children participating in the Vaccination Program for U.S.-bound Refugees will receive only 1 dose of DTwP/DTaP from International Organization for Migration panel physicians, if due, in order to reduce the risk of severe local reactions associated with over-vaccination with tetanus-containing vaccines.

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Intestinal Parasite Guidance

Parasitic Treatment: Strongyloidiasis, Schistosomiasis, and Soil-Transmitted Helminth Infections

Updates – the following are content updates from the previous version of the overseas guidance, which was posted in 2008

- Latin American and Caribbean refugees are now included, in addition to Asian, Middle Eastern, and African refugees.
- Recommendations for management of Strongyloides in refugees from Loa loa-endemic areas emphasize a screen-and-treat approach, rather than presumptive high-dose albendazole.

- Presumptive treatment with albendazole during any trimester of pregnancy is no longer recommended.

Intestinal Parasite Guidance – PDF version for printing
[PDF – 12 pages]

Summary of Recommendations

This guidance is intended for the International Organization for Migration (IOM) physicians and other panel physicians who administer overseas predeparture presumptive treatment for intestinal parasites, but may also be referenced by U.S. medical providers caring for refugees who will be receiving presumptive treatment after they arrive in the United States.

While these recommendations have been implemented in many overseas sites, logistical and procurement issues still limit their full implementation in some. All Middle Eastern, Asian, North African, Latin American, and Caribbean refugees should receive presumptive therapy with:

- All Middle Eastern, Asian, North African, Latin American, and Caribbean refugees should receive presumptive therapy with:
  - Albendazole, single dose of 400 mg (200 mg for children 12-23 months)
    AND
  - Ivermectin, two doses 200 mcg/Kg orally once a day for 2 days before departure to the United States.
- All African refugees who did not originate from or reside in countries where *Loa loa* infection is endemic (Box 1) should receive presumptive therapy with:
  - Albendazole, single dose of 400 mg (200 mg for children 12-23 months)
    AND

    - Ivermectin, two doses 200 mcg/Kg orally once a day for 2 days
      AND
    - Praziquantel, 40 mg/kg, which may be divided in two doses before refugees depart for the United States.
- All sub-Saharan African refugees who originated from or resided in countries where *Loa loa* infection is endemic (Box 1) should receive presumptive therapy with:
    - Albendazole, single dose of 400 mg (200 mg for children 12-23 months)
      AND
    - Praziquantel, 40 mg/kg, which may be divided in two doses before departure to the United States.
    - Refugees from *Loa loa*-endemic countries (Box 1) in Africa should not receive presumptive ivermectin for strongyloidiasis prior to departure. Management of *Strongyloides* should be deferred until arrival in the United States, unless *Loa loa* is excluded by reviewing a daytime (10 AM to 2 PM) Giemsa-stained blood smear. Deferral of treatment for *Strongyloides* until after the refugee arrives in the United States is acceptable. Guidance is available for management of *Strongyloides* following arrival in the United States in the Domestic Intestinal Parasite Screening Guidance.
- Special instructions:
    1. Pre-departure presumptive and directed malaria treatment regimens must be administered as directly observed therapy.
    2. Test results and pre-departure treatment should be documented on the pre-departure medical screening form. If treatment was not administered, this should be clearly indicated along with the reason that treatment was not administered.

CDC Recommendations for Overseas Presumptive Parasite Treatment

Region	Artemether-lumefantrine (malaria)	Praziquantel (Schistosoma)	Albendazole (soil-transmitted helminths)	Ivermectin* (Strongyloides)
Africa, non-Loaloa areas	Recommended	Recommended	Recommended	Recommended
Africa, Loa loa areas	Recommended	Recommended	Recommended	Not Recommended

Asia	Not Recommended	Not Recommended	Recommended	Recommended
Middle East	Not Recommended	Not Recommended	Recommended	Recommended
Latin America	Not Recommended	Not Recommended	Recommended	Recommended

* If available in country

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Background

In 1997, a Centers for Disease Control and Prevention (CDC) pilot project evaluated single-dose albendazole presumptive treatment in U.S.-bound Barawan Somali refugees. [1] This project demonstrated decreases in soil-transmitted parasites in refugees who received presumptive treatment. In May 1999, CDC extended this recommendation to all refugees resettling from sub-Saharan Africa (SSA) and Asia. In 2008, the recommendation was extended to refugees from the Middle East. Currently, most refugees from the countries listed in the Treatment Schedules for Presumptive Parasitic Infections for U.S.-Bound Refugees and without a contraindication are receiving a single dose of albendazole prior to departure.

Data indicates that pre-departure albendazole treatment has dramatically decreased the overall prevalence of soil-transmitted helminth infections in refugees. A large evaluation including more than 26,000 African and Asian refugees demonstrated single dose albendazole resulted in an absolute reduction of the prevalence of any soil-transmitted helminth from 20.8% to 4.7%, as measured by stool ova and parasite examination. [2] These findings support previous data in African refugees resettling to the United States, showing a similar decrease in soil-transmitted helminths following implementation of pre-departure albendazole treatment. Evaluations of the cost has shown clear cost-savings and estimated reduction in morbidity and mortality through conducting presumptive-treatment compared to post-arrival screen and treat, or no treatment program. [8] Despite this documented decrease in the overall prevalence of soil-transmitted helminth infections, a single dose of albendazole has very limited effect on infection with *Strongyloides* and no effect against *Schistosoma* spp. [2,3,4,5] A recent prospective evaluation of more than 2000 refugees resettling to the U.S. from camps on the Thailand-Burma border showed a dramatic decrease in soil-transmitted helminths and a decrease in potentially associated conditions in children (e.g. anemia, malnutrition) following treatment. [9] This evaluation also clearly demonstrated a reduction in the Strongyloides burden with the single dose albendazole in combination with ivermectin treatment prior to

departure for the United States.

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Recommendations for overseas presumptive treatment of intestinal parasites

Refugees originating from the Middle East, Asia, North Africa, Latin America, and the Caribbean

Prior to departure for the United States, all refugees originating from the Middle East, Asia, North Africa, Latin American, & Caribbean should receive presumptive therapy with ivermectin for *Strongyloides* infection and with albendazole for infections caused by soil-transmitted helminths (Table 1). Dosing for ivermectin may be based on weight and available tablet size (Table 2).

Refugees originating from sub-Saharan Africa

Soil-transmitted helminths

All refugees originating from sub-Saharan Africa should receive presumptive therapy with albendazole for infections caused by soil-transmitted helminths (Table 1).

Strongyloides

Refugees from sub-Saharan Africa should also receive presumptive therapy for *Strongyloides* infection with ivermectin (Table 1), but this will depend on whether they have originated from or resided in countries where *Loa loa* is endemic (Box 1). The drug of choice for *Strongyloides* infection is ivermectin. However, cases of encephalopathy have occurred in patients treated with ivermectin during large-scale public health campaigns in areas of Africa where *Loa loa* is endemic. Although rare, this reaction is related to *Loa loa* microfilarial load. Therefore, ivermectin should be given only to persons originating from Africa who have resided in or come from countries or areas not considered endemic for *Loa loa* (Box 1). Sub-Saharan African refugees who have resided in or are coming from areas endemic for *Loa loa* should *not* receive presumptive ivermectin, and management of *Strongyloides* should be deferred until they arrive in the United States (unless *Loa loa* is excluded by reviewing a daytime [10 AM to 2 PM] Giemsa-stained blood smear). High-dose albendazole (400 mg twice a day for 7 days) is an acceptable alternative and is

considered safe in *Loa loa* infected people, if *Loa loa* infection cannot be excluded.

Schistosomiasis

Refugees from sub-Saharan Africa should also receive presumptive pre-departure therapy with praziquantel for schistosomiasis (Table 1). Pre-departure dosing may be based on weight and available tablet size (Table 2). If the refugee has never received presumptive therapy as part of a mass anti-helminth treatment campaign, and if it is logistically feasible, administering praziquantel first, followed by albendazole and ivermectin, may reduce the risk of adverse events caused by the release of antigens by dying parasites in persons with high parasite loads. However, if the refugee has received previous therapy, their parasite load can be assumed to be lower, and there would be no contraindication to administering praziquantel together with albendazole and ivermectin.

Special instructions for administration of presumptive pre-departure therapy

- Pre-departure regimens for presumptive treatment of intestinal parasites should be administered as directly observed therapy. While prescription and first-dose observation should be done by medical personnel, subsequent doses can be observed by nonmedical staff.
- Pregnancy testing should be performed before ivermectin or albendazole is administered.
- Ivermectin and albendazole may be administered concurrently according to World Health Organization (WHO) recommendations. In areas where refugees have received previous rounds of mass anti-helminth treatment, ivermectin, albendazole, and praziquantel co-administration is well tolerated. [6]
- Praziquantel may be better tolerated if divided into two doses.
- There is no known contraindication to co-administration of these intestinal treatment regimens with malaria treatment medications. When time allows, spacing may improve tolerability. A sample 3-day combined treatment regimen for both parasites and malaria is presented in Table 3.

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Precautions and contraindications to presumptive treatment

Children

- ***Albendazole***
  Children <1 year of age should not receive *presumptive* treatment with albendazole. Further information on use of albendazole in pediatric patients can be found at the CDC, Division of Parasitic Diseases website.
- ***Ivermectin***
  Children weighing <15 kg or measuring <90 cm should not receive *presumptive* treatment with ivermectin. Further information on use of ivermectin in pediatric patients can be found at the CDC, Division of Parasitic Diseases website.
- ***Praziquantel***
  The safety of praziquantel has not been established in children <4 years of age or <94 cm in height, so these children should not receive *presumptive* treatment. Further information on use of praziquantel in pediatric patients can be found at the CDC, Division of Parasitic Diseases website.

Pregnant women

- ***Albendazole***
  Albendazole is currently a category C drug in the United States, and it should not be administered as *presumptive* treatment for U.S.-bound refugees during any trimester of pregnancy. When a reliable history of the woman's last menstrual period cannot be obtained, a pregnancy test should be performed. Pregnant women should have presumptive treatment deferred until after they arrive in the United States. Further information on use of albendazole during pregnancy can be found at the CDC, Division of Parasitic Diseases website.
- ***Ivermectin***
  Ivermectin is a pregnancy category C drug. This medication should not be administered as a presumptive medication to a pregnant woman. When a reliable history of the woman's last menstrual period cannot be obtained, a pregnancy test should be performed before *presumptive* treatment is administered. Further information on use of ivermectin during pregnancy can be found at the CDC, Division of Parasitic Diseases website.
- ***Praziquantel***
  Praziquantel is considered a pregnancy category B drug, and WHO recommends the *presumptive* treatment of pregnant women during any trimester of pregnancy in women from schistosomiasis-endemic areas. Further information on use of praziquantel during pregnancy can be found at the CDC, Division of Parasitic Diseases website.

Women who are breastfeeding

- ***Albendazole***
  Albendazole presumptive therapy may be administered to women who are breastfeeding. Further information on use of albendazole during lactation can be found at the CDC, Division of Parasitic Diseases website.
- ***Ivermectin***
  Presumptive treatment with ivermectin should not be administered to women who are breastfeeding during the first week after birth. Further information on use of ivermectin during lactation can be found at the CDC, Division of Parasitic Diseases website.
- ***Praziquantel***
  Praziquantel is excreted in low concentrations in human milk. According to WHO guidance for mass prevention campaigns, the use of praziquantel during lactation is safe. [7] For individual patients in clinical settings, praziquantel should be used in breast-feeding women only when the risk to the infant is outweighed by the risk of disease progression in the mother in the absence of treatment. Further information on use of praziquantel during lactation can be found at the CDC, Division of Parasitic Diseases website.

Refugees with cysticercosis infection

Persons who have neurocysticercosis infection may have seizures following treatment with albendazole or praziquantel, since these medications kill *Taenia solium* cysticerci, causing inflammation and provoking seizure activity in the brain. The true prevalence of neurocysticercosis in refugee populations is not well documented. Confirmed case reports of adverse events after treatment with albendazole or praziquantel remain rare in refugees. Refugees with known neurocysticercosis, an unexplained seizure disorder, or subcutaneous nodules consistent with cysticercosis should **not** receive presumptive treatment with either albendazole or praziquantel.

Physicians should consult the package inserts for additional information about ivermectin, albendazole, and praziquantel.

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Documentation

Test results and pre-departure treatment should be documented on the Predeparture Medical Screening (PDMS) form. IOM providers should also enter the information in the Migrant Management & Operational Systems Application (MiMOSA) prior to the refugees' arrival, so it can be transmitted to CDC's Electronic Disease Notification (EDN) system. The paper form, after entry into the electronic format, should be placed

in the medical folder inside the IOM travel bag. These documents are physically carried by the refugees to the United States. If treatment was not administered, this should be clearly documented, along with the reason that treatment was not administered. For children and pregnant and breastfeeding women who do not receive presumptive therapy, the need for subsequent treatment should be clearly documented.

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Table 1

Recommended medication regimen and standard dosing for presumptive treatment of parasitic infections.

Adults			
Refugee Population	**Regimens by Pathogen**		
	Soil-transmitted helminths: Albendazole [1]	**Strongyloidiasis: Ivermectin [1]**	**Schistosomiasis [2]: Praziquantel [3]**
Asia, Middle East, North Africa, Latin American, & Caribbean	400 mg orally for 1 day	Ivermectin, 200 mcg/kg/day orally once a day for 2 days	Not recommended
Sub-Saharan Africa, non-Loa loa-endemic area	400 mg orally for 1 day	Ivermectin, 200 mcg/kg/day orally once a day for 2 days	Praziquantel, 40 mg/kg (may be divided and given in two doses for better tolerance).
Sub-Saharan Africa, Loa loa–endemic area	400 mg orally for 1 day	If Loa loa cannot be excluded, treatment may be deferred until after arrival in the United States -OR- Albendazole 400 mg twice a day for 7 days	Praziquantel, 40 mg/kg (may be divided and given in two doses for better tolerance).

Pregnant Women	

Refugee Population	Treatment Regimens by Pathogen		
	Soil-transmitted helminths: Albendazole [1]	Strongyloidiasis: Ivermectin [1]	Schistosomiasis [2]: Praziquantel [3]
Asia, Middle East, North Africa, Latin America & Caribbean	Not recommended	Not recommended	Not applicable
Sub-Saharan Africa	Not recommended	Not recommended	Praziquantel, 40 mg/kg (may be divided and given in two doses for better tolerance).

Children			
Refugee Population	**Treatment Regimens by Pathogen**		
	Soil-transmitted helminths: Albendazole [1]	**Strongyloidiasis: Ivermectin [1]**	**Schistosomiasis [2]: Praziquantel [3]**
Asia, Middle East, North Africa, Latin America & Carribean	12-23 months of age: 200 mg orally for 1 day. Presumptive therapy is not recommended for any infant less than 12 months of age.	Ivermectin, 200 mcg/kg/day orally once a day for 2 days Presumptive therapy is not recommended for any child weighing ≤15 kg	Not applicable
Sub-Saharan Africa	12-23 months of age: 200 mg orally for 1 day. Presumptive therapy is not recommended for any infant less than 12	Ivermectin, 200 mcg/kg/day orally once a day for 2 days Presumptive therapy is not recommended for any child weighing ≤15 kg or for any child from a Loa loa-endemic country.	Children under ≤ 4 years of age should not receive presumptive treatment with praziquantel. Only for children from sub-

months of age.	Saharan Africa

1. Although WHO states ivermectin and albendazole may be given concurrently, it is recommended that ivermectin be taken on an empty stomach and albendazole with fatty foods.
2. All sub-Saharan African countries except Lesotho are considered endemic for schistosomiasis.
3. Praziquantel, if not co-administered, should be administered at least one day prior to either ivermectin or albendazole. Praziquantel should be taken with liquids during a meal.

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Table 2

Praziquantel and ivermectin dosing based on weight and tablet size for predeparture presumptive treatment of US-bound refugees

Praziquantel [1,2]	
Drug and dosing	**Weight (kg)**
Not recommended	<15
1 tablet (600 mg)	15-18
1 ½ tablets (900 mg)	19-25
2 tablets (1200 mg)	26-30
2 ½ tablets (1500 mg)	31-40
3 tablets (1800mg)	41-50
4 tablets (2400 mg)	51-69
5 tablets (3000 mg)	≥70
Ivermectin [3]	

Drug and dosing	Weight (kg)
Not recommended	<15
1 tablet (3 mg)	15-24
2 tablets (6 mg)	25-35
3 tablets (9 mg)	36-50
4 tablets (12 mg)	51-65
5 tablets (15 mg)	66-79
200 mcg/kg	≥80

1. Better tolerated if divided into two doses
2. Using 600-mg praziquantel tablets
3. Using 3-mg ivermectin tablets

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Table 3

Sample 3-Day Combined Regimen for overseas presumptive treatment of parasites and malaria

Presumptive Tx Day	Morning	Evening*
Day 1	Pregnancy Test Praziquantel #1 Artemether-lumefantrine #1	Praziquantel #2* Artemether-lumefantrine 2*
Day 2	Ivermectin #1 Artemether-lumefantrine #3	Artemether-lumefantrine #4

Day 3	Albendazole Ivermectin #2 Artemether-lumefantrine #5	Artemether-lumefantrine #6

*On the first day, praziquantel and artemether-lumefantrine should be administered 8 hours following initial dose; on days 2 and 3 should be administered twice a day, morning and evening.

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Box 1

Endemicity of Loa loa in African countries

African countries NOT considered endemic for *Loa loa* (may use presumptive ivermectin for *Strongyloides*)	African countries considered endemic for *Loa loa* (presumptive ivermectin should *not* be used for *Strongyloides*)
Algeria Botswana Burkina Faso Burundi Côte d'Ivoire Egypt Ethiopia Eritrea Gambia Ghana Guinea Guinea-Bissau Kenya Liberia Libya Madagascar Malawi Mali Mauritania	Angola Cameroon Central African Republic Chad Republic of Congo Democratic Republic of the Congo Equatorial Guinea Gabon Nigeria South Sudan

Mauritius Morocco Mozambique Namibia Niger Rwanda Senegal Sierra Leone Somalia South Africa Sudan Swaziland Tanzania Togo Uganda Zambia Zimbabwe	

Zouré HGM, Wanji S, Noma M, Amazigo UV, et al. (2011) The Geographic Distribution of *Loa loa* in Africa: Results of Large-Scale Implementation of the Rapid Assessment Procedure for Loiasis (RAPLOA). PLoS Negl Trop Dis 5(6): e1210. doi:10.1371/journal.pntd.0001210.

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Malaria Guidance

Malaria Guidance PDF version for printing [PDF – 8 pages]

In addition to the standard, legally required medical examination of refugees migrating to the United States, CDC recommends the following presumptive treatment for *Plasmodium falciparum* malaria. These recommendations apply to all refugees who are living in

countries that are endemic for *P. falciparum* in sub-Saharan Africa. Currently, CDC does not recommend presumptive therapy for asymptomatic/subclinical malaria for U.S.-bound refugees relocating from lower endemic areas outside sub-Saharan Africa (e.g. Southeast Asia) unless specifically identified in subsequent, separate, documents (see Domestic Malaria Guidance).

These guidance is intended for presumptive pre-departure treatment of asymptomatic/subclinical malaria and for directed treatment for special populations with malaria. Any patient with clinical symptoms of malaria should be referred to a healthcare facility for evaluation and treatment.

Background

Studies have demonstrated high rates of malaria in refugees arriving in the United States and Canada from sub-Saharan Africa [1, 2]. Despite progress in malaria control in the past decade, sub-Saharan Africa still has highly endemic areas. In some parts of Africa, prevalence rates of *P. falciparum* malaria exceed 75%. Beginning in 1999, U.S. bound refugee populations originating in sub-Saharan Africa began to receive predeparture treatment with sulfadoxine-pyrimethamine (SP, Fansidar™) to prevent *P. falciparum* malaria disease following arrival in the U.S. Worldwide, the malaria parasite, *P. falciparum*, has developed resistance to many drugs used for treatment. In many areas of Africa, *P. falciparum* resistance to SP (and chloroquine) has increased to levels where these drugs are no longer effective. Based on efficacy studies showing SP treatment failures [3] and on guidance from the World Health Organization, beginning in 2007, pre-departure SP was discontinued and replaced by artemisinin combination treatment (ACT), generally the fixed combination artemether-lumefantrine (AL).

Refugee populations relocating to the United States from countries outside sub-Saharan Africa would rarely originate in hyper- or holoendemic malaria, making asymptomatic/subclinical *P. falciparum* unlikely. Refugees from areas with lower endemic rates who are infected with *P falciparum* malaria will have clinical symptoms of infection. Therefore, refugee populations relocating to the United States from endemic areas other than sub-Saharan Africa should be tested for malaria if symptomatic. No presumptive treatment is recommended for these populations unless directed in separate guidance.

Special instructions:

1. Pre-departure presumptive and directed malaria treatment regimens must be administered as directly observed therapy.

2. Test results and pre-departure treatment should be documented on the pre-departure medical screening form. If treatment was not administered, this should be clearly indicated along with the reason that treatment was not administered.
3. The malaria treatment should be completed no sooner than 5 days before departure.

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Recommendations

This document provides guidance for presumptive treatment for asymptomatic *P. falciparum* malaria in refugees relocating to the United States (Annex I). Artemisinin derivatives are obtained from the sweet wormwood plant (Chinese: 青蒿 or qīnghāo). The optimal regimen is the artemisinin-based combination therapy, artemether-lumefantrine Tables 1 and 2, Annex 1. However, when it is not accessible, other artemisinin-based combinations may be used until artemether-lumefantrine can be obtained. Currently artesunate-amodiaquine (ASAQ) is currently the preferred second line therapy, Annex 1. Dosing formulations for ASAQ are less standardized. When AL is unavailable and ASAQ will be used as a second option, Centers for Disease Control and Prevention (CDC) should be contacted for specific dosing instructions based on the formulation available in country. Specific populations including infants, pregnant women in the first trimester and those with other contraindications, delineated below, require directed treatment after diagnostic testing and should not receive presumptive treatment for asymptomatic malaria.

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Specific Populations and Precautions / Contraindications to Presumptive Anti-malarial Treatment

Infants who weigh less than 5 kilograms (kg), pregnant women, lactating women breastfeeding infants who weigh under 5 kg were previously considered to have a contraindication for use of AL. In 2015, the World Health Organization (WHO) revised the guidance for the treatment of clinical malaria to include AL treatment for pregnant women during the second and third trimester, children weighing < 5 kg and for lactating women.[5] At this time, presumptive treatment with AL for asymptomatic malaria may be administered to pregnant women during their second and third trimester and to lactating women regardless of the weight of the infant. Children < 5 kg and women in their first trimester of pregnancy should not receive presumptive treatment but should receive testing and treatment if they are found to have malaria. In addition, all persons with a known allergy to AL or any component of the medication should not receive presumptive treatment with AL.

Refugees who do not receive presumptive treatment, including women during their first trimester of pregnancy and children < 5 kg, should have diagnostic testing, and if the tests show they have malaria, receive directed treatment. Diagnostic testing should be performed with blood smears or rapid diagnostic tests (RDT) with a kit agreed upon in consultation with CDC's Division of Global Migration and Quarantine (DGMQ). Both blood smear and RDT have limited sensitivity and do not rule out malaria.[4] Therefore, any refugee who develops clinical symptoms of malaria should receive further evaluation regardless of the screening test results. Treatment for clinical or laboratory confirmed malaria should be given according to national guidance. If no national guidance exist, consult with CDC regarding a treatment plan.

For information regarding domestic management of malaria (screening and presumptive treatment) for refugees after arrival in the United States, please see Domestic Refugee Guidance.

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Table 1

Summary malaria treatment and testing recommendations for asymptomatic refugees in sub-Saharan Africa relocating to the United States

Population	Presumptive treatment without testing	Test by blood smear or rapid diagnostic test [1]	Test result [2]	Treat	Medication
All adults and children (except pregnant women during their first trimester, children who weigh less than 5 kg, and persons with known contraindication to recommended regimen. Lactating women can receive treatment regardless of infant weight.)	Yes	No	N/A	N/A	Option 1: artemether-lumefantrine; Option 2 (only if Option 1 is not available): artesunate-amodiaquine (consult

					CDC)
Pregnant women during the first trimester	No	Yes	Positive	Yes	National guidelines
			Negative	No	None
Infants weighing less than 5 kg	No	Yes	Positive	Yes	National guidelines
			Negative	No	None
Persons with other contraindications to recommended regimen (e.g. known allergy)	No	Yes	Positive	Yes	Discuss with CDC
			Negative	No	None

[1] Test with blood smear or rapid diagnostic test using a test kit agreed upon in consultation with DGMQ
[2] Malaria thick and thin smear or RDT

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Table 2

Dosing of artemether-lumefantrine for asymptomatic *P. falciparum* malaria

Weight (kg)	**Artemether-lumefantrine** Number of tablets per dose Given at 0 hours, 8 hours, 24 hours, 36 hours, 48 hours, and 60 hours
< 5	Not recommended
5–14	1 tablet
15–24	2 tablets

25–34	3 tablets
> 35	4 tablets

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Annex I

Specific information about acceptable pre-departure presumptive anti-malarial therapy regimens for sub-Saharan refugees relocating to the United States

Option 1

- Formulation of artemether-lumefantrine: tablets containing 20 mg of artemether plus 120 mg of lumefantrine.
- Dose: artemether-lumefantrine (AL). Treat with the 6-dose schedule as described below in Table 2.
- Other instructions: Administer with food.
- Metabolism of drug: Maximum blood levels occur 6–12 hours after The half-life is 88 hours in healthy persons and twice as long in persons with malaria. The drug is excreted via the liver and feces.
- Adverse effects: dizziness, fatigue, anorexia, nausea, vomiting, abdominal pain, palpitations, myalgia, sleep disorders, arthralgia, headache, rash.
- Exceptions for the use of artemether-lumefantrine:
    - Children weighing less than 5 kg
    - Pregnant women in the first trimester
    - Persons with known hypersensitivity to either component
- Alternatives approaches for persons who cannot receive artemether-lumefantrine:
    - Children weighing less than 5 kg: Test with blood smear or rapid diagnostic test using a test kit agreed upon in consultation with DGMQ. Children who test positive for malaria should be treated according to national guidelines or consult CDC, if no national guidelines exist.
    - Pregnant women: Test with blood smear or rapid diagnostic test using a test kit agreed upon in consultation with DGMQ. Pregnant or lactating women who test positive for malaria should be treated according to national guidelines or consult CDC, if no national guidelines exist.
    - Persons with known hypersensitivity to either artemether or lumefantrine may receive alternative treatment. If allergic to both artemether component, discuss with CDC.

- Persons with symptomatic malaria should be treated according to national guidelines or consult CDC if no national guidelines exist.

Option 2

- Dosage and Formulation of Artesunate-amodiaquine (ASAQ) combination therapy. Various formulations are available and CDC should be contacted prior to using for guidance based on available formulations in the country of departure.
- Metabolism
  - Artesunate as in Option #1
  - AQ is metabolized primarily in the liver, with plasma half-life of ~5 hours.
- Adverse effects. Nausea, vomiting, abdominal pain, diarrhea, itching, bradycardia (less common). Prolonged QT (avoid with other medications that prolong QT). Can induce toxic hepatitis and fatal agranulocytosis (with prolonged use). Overdosage can cause syncope, spasticity, convulsions and involuntary movements.
- Exceptions of use for artesunate (AS) and amodiaquine (AQ)
  - Children weighing less than 5 kg (AS)
  - First term of pregnancy (AS)
  - Known hypersensitivity to either AS or AQ
  - Known abnormal white blood count, kidney disease or severe hepatic disorder/disease (AQ)
  - Caution should be exercised in patients on treatment drugs for HIV/AIDS (AQ), cases should be discussed with CDC prior to presumptive treatment.
  - Known prolonged QTc or another medication known to lengthen QTc

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1. Maroushek SR, Aguilar EF, Stauffer W, Abd-Alla Malaria among refugee children at arrival in the United States. Ped Infect Dis J 2005;24(5):450-2, 2005.
2. Ndao M, Bandyayera E, Kokosin E, et Comparison of blood smear, antigen detection, and nested-PCR methods for screening from regions where malaria is endemic after a malaria outbreak in Quebec, Canada. *J Clin Microbiol* 2004;42(6):2694-700.
3. Phares CR, Kapella BK, Doney AC, et al. Presumptive treatment to reduce imported malaria among refugees from East Africa resettling in the United States. Amer J Trop Med Hyg 2011;85(4):612-615.

4. Stauffer WM, Newberry A, Cartwright C, Rosenblatt J, et Evaluation of malaria screening in newly arriving refugees to the United States by microscopy and rapid antigen capture assay. *Ped Infect Dis J*. 2006 Oct;25(10):948-50.
5. The World Health Organization. Guidelines for the treatment of malaria. Third Edition. Available online (accessed March 22, 2019)

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Laws and Regulations

Migrant Serum Bank

Related Links

Technical Instructions for Panel Physicians and Civil Surgeons

United States-Mexico Public Health

Global Health

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