Guidelines for Overseas Presumptive Treatment of Strongyloidiasis, Schistosomiasis, and Soil-Transmitted Helminth Infections for Refugees Resettling to the United States

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention
National Center for Emerging and Zoonotic Infectious Diseases
Division of Global Migration and Quarantine

February 6, 2019

Accessible version: https://www.cdc.gov/immigrantrefugeehealth/guidelines/overseas/intestinal-parasites-overseas.html

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***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 and de-emphasize a presumptive high-dose albendazole approach.**
- **Presumptive use of albendazole during any trimester of pregnancy is no longer recommended.**
- **Links to a new table for the Treatment Schedules for Presumptive Parasitic Infections for U.S.-Bound Refugees, administered by IOM.**

Contents

Summary of Recommendations

These guidelines are recommendations for the International Organization for Migration (IOM) physicians and other panel physicians who administer overseas predeparture presumptive treatment for intestinal parasites. While most recommendations have been implemented, not all refugee populations listed in this document are receiving all recommended pre-departure medications, due to funding restrictions and logistical challenges. For current implementation status in specific populations, see the Treatment Schedules for Presumptive Parasitic Infections for U.S.-Bound Refugees, administered by IOM. The recommendations in these guidelines 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.

- All Middle Eastern, Asian, North African, Latin American, and Caribbean refugees, with exceptions noted in this document, 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), with exceptions noted in this document, 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), with exceptions noted in this document, 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 Guidelines.

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 Burmese refugees resettling to the U.S. showed a dramatic decrease in soil-transmitted helminths and an associated conditions in children (e.g. anemia) with 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.

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, with exceptions noted in this document, 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.

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 guidelines 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 cystercercosis should **not** receive presumptive treatment with either albendazole or praziquantel.

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

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.

References

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Table 1. Recommended medication regimen and standard dosing for presumptive treatment of parasitic infections

Refugee Population	**Regimens by Pathogen**		
	Soil-transmitted helminths: Albendazole[1]	Strongyloidiasis: Ivermectin[1]	Schistosomiasis[2]: Praziquantel[3]
Adults			
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 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).

[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.

Pregnant women			
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			
Asia, Middle East, North Africa, Latin America & Caribbean	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 Should not be used presumptively if ≤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 months of age.	Ivermectin, 200 mcg/kg/day orally once a day for 2 days. Should not be used presumptively if ≤15 kg or from *Loa loa*-endemic country.	Children under ≤ 4 years of age should not receive presumptive treatment with praziquantel. Only for children from sub-Saharan Africa

Table 2. Praziquantel and ivermectin dosing based on weight and tablet size for predeparture presumptive treatment of US- bound refugees

Drug and dosing	Weight (kg)
Praziquantel[1,2]	
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]	
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

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.

Box 1. Endemicity of *Loa loa* in African countries

African countries <u>NOT</u> 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 Mauritius Morocco Mozambique Namibia Niger Rwanda Senegal Sierra Leone Somalia South Africa Sudan Swaziland Tanzania Togo Uganda Zambia Zimbabwe	Angola Cameroon Central African Republic Chad Republic of Congo Democratic Republic of the Congo Equatorial Guinea Gabon Nigeria South Sudan

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