LEISHMANIA

	Drug	Adult dosage	Pediatric dosage
Visceral[1,2]			
Drug of choice:	Liposomal amphotericin B[4]	3 mg/kg/d IV d 1-5, 14 and 21[3]	3 mg/kg/d IV d 1-5, 14 and 21[3]
OR	Sodium stibogluconate*	20 mg Sb/kg/d IV or IM x 28d	20 mg Sb/kg/d IV or IM x 28d
OR	Miltefosine[5]*	2.5 mg/kg/d PO (max 150 mg/d) x 28d	2.5 mg/kg/d PO (max 150 mg/d) x 28d
Alternative:	Meglumine antimonate*	20 mg Sb/kg/d IV or IM x 28d	20 mg Sb/kg/d IV or IM x 28d
OR	Amphotericin B[6]	1 mg/kg IV daily x 15-20d or every second day for up to 8 wks	1 mg/kg IV daily x 15-20d or every second day for up to 8 wks
OR	Paromomycin[6,7,8]*	15 mg/kg/d IM x 21d	15 mg/kd/d IM x 21d
Cutaneous[1,9]			
Drugs of choice:	Sodium stibogluconate*	20 mg Sb/kg/d IV or IM x 20d	20 mg Sb/kg/d IV or IM x 20d
OR	Meglumine antimonate*	20 mg Sb/kg/d IV or IM x 20d	20 mg Sb/kg/d IV or IM x 20d
OR	Miltefosine[5]*	2.5 mg/kg/d PO (max 150 mg/d) x 28d	2.5 mg/kg/d PO (max 150 mg/d) x 28d
Alternative:[10]	Paromomycin[6,7,8]*	Topically 2x/d x 10-20d	Topically 2x/d x 10-20d
OR	Pentamidine[6]	2-3 mg/kg IV or IM daily or every second day x 4-7 doses[11]	2-3 mg/kg IV or IM daily or every second day x 4-7 doses[11]
Mucosal[1,12]			
Drug of choice:	Sodium stibogluconate*	20 mg Sb/kg/d IV or IM x 28d	20 mg Sb/kg/d IV or IM x 28d
OR	Meglumine antimonate*	20 mg Sb/kg/d IV or IM x 28d	20 mg Sb/kg/d IV or IM x 28d
OR	Amphotericin B[6]	0.5-1 mg/kg IV daily or every second day for up to 8wks	0.5-1 mg/kg IV daily or every second day for up to 8wks
OR	Miltefosine[5]*	2.5 mg/kg/d PO (max 150 mg/d) x 28d	2.5 mg/kg/d PO (max 150 mg/d) x 28d

* Availability problems. See table below.

1. To maximize effectiveness and minimize toxicity, the choice of drug, dosage, and duration of therapy should be individualized based on the region of disease acquisition, a likely infecting species, and host factors such as immune status (BL Herwaldt, Lancet 1999; 354:1191). Some of the listed drugs and regimens are effective only against certain *Leishmania* species/strains and only in certain areas of the world (J Arevalo et al, Clin Infect Dis 2007; 195:1846). Medical Letter consultants recommend consultation with physicians experienced in management of this disease.
2. Visceral infection is most commonly due to the Old World species *L. donovani* (kala-azar) and *L. infantum* and the New World species *L. chagasi*.
3. The FDA-approved dosage regimen for immunocompromised patients (e.g., HIV infected) is 4 mg/kg/d IV on days 1-5, 10, 17, 24, 31 and 38. The relapse rate is high; maintenance therapy (secondary prevention) may be indicated, but there is no consensus as to dosage or duration.
4. Liposomal amphotericin B *(AmBisome)* is the only lipid formulation of amphotericin B FDA-approved for treatment of visceral leishmania, largely based on clinical trials in patients infected with *L. infantum* (A Meyerhoff, Clin Infect Dis 1999; 28:42). Two other amphotericin B lipid formulations, amphotericin B lipid complex *(Abelcet)* and amphotericin B cholesteryl sulfate *(Amphotec)* have been used, but are considered investigational for this condition and may not be as effective (C Bern et al, Clin Infect Dis 2006; 43:917).
5. Effective for both antimony-sensitive and -resistant *L. donovani* (Indian); miltefosine *(Impavido)* is manufactured in 10- or 50-mg capsules by Zentaris (Frankfurt, Germany at info@zentaris.com) and is available through consultation with the CDC. The drug is contraindicated in pregnancy; a negative pregnancy test before drug initiation and effective contraception during and for 2 months after treatment is recommended (H Murray et al, Lancet 2005; 366:1561). In a placebo-controlled trial in patients ≥12 years old, oral miltefosine 2.5 mg/kg/d x 28d was also effective for treatment of cutaneous leishmaniasis due to *L.(V.) panamensis* in Colombia, but not *L.(V.) braziliensis* or *L. mexicana* in Guatemala (J Soto et al, Clin Infect Dis 2004; 38:1266). "Motion sickness," nausea, headache and increased creatinine are the most frequent adverse effects (J Soto and P Soto, Expert Rev Anti Infect Ther 2006; 4:177).
6. Not FDA-approved for this indication.
7. Paromomycin should be taken with a meal.
8. Paromomycin IM has been effective against leishmania in India; it has not yet been tested in South America or the Mediterranean and there is insufficient data to support its use in pregnancy (S Sundar et al, N Engl J Med 2007; 356:2371). Topical paromomycin should be used only in geographic regions where cutaneous leishmaniasis species have low potential for mucosal spread. A formulation of 15% paromomycin/12% methylbenzethonium chloride *(Leshcutan)* in soft white paraffin for topical use has been reported to be partially effective against cutaneous leishmaniasis due to *L. major* in Israel and *L. mexicana* and *L. (V.) braziliensis* in Guatemala, where mucosal spread is very rare (BA Arana et al, Am J Trop Med Hyg 2001; 65:466). The methylbenzethonium is irritating to the skin; lesions may worsen before they improve.
9. Cutaneous infection is most commonly due to the Old World species *L. major* and *L. tropica* and the New World species *L. mexicana*, *L. (Viannia) braziliensis*, and others.
10. Although azole drugs (fluconazole, ketoconazole, itraconazole) have been used to treat cutaneous disease, they are not reliably effective and have no efficacy against mucosal disease (AJ Magill, Infect Dis Clin North Am 2005; 19:241). For treatment of *L. major* cutaneous lesions, a study in Saudi Arabia found that oral fluconazole, 200 mg once/d x 6wks appeared to speed healing (AA Alrajhi et al, N Engl J Med 2002; 346:891). Thermotherapy may be an option for cutaneous *L. tropica* infection (R Reithinger et al, Clin Infect Dis 2005; 40:1148). A device that generates focused and controlled heating of the skin has been approved by the FDA for this indication (*ThermoMed* – ThermoSurgery Technologies Inc., Phoenix, AZ, 602-264-7300; www.thermosurgery.com).
11. At this dosage pentamidine has been effective in Colombia predominantly against *L. (V.) panamensis* (J Soto-Mancipe et al, Clin Infect Dis 1993; 16:417; J Soto et al, Am J Trop Med Hyg 1994; 50:107). Activity against other species is not well established.
12. Mucosal infection is most commonly due to the New World species *L. (V.) braziliensis*, *L. (V.) panamensis*, or *L. (V.) guyanensis*.

Information provided by The Medical Letter. For a copy of the entire ***Drugs for Parasitic Infections*** *article, go to: www.medicalletter.org/parasitic_cdc*

MANUFACTURERS OF DRUGS USED TO TREAT PARASITIC INFECTIONS

albendazole – *Albenza* (GlaxoSmithKline)
Albenza (GlaxoSmithKline) – albendazole
Alinia (Romark) – nitazoxanide
AmBisome (Gilead) – amphotericin B, liposomal
amphotericin B – *Fungizone* (Apothecon), others
amphotericin B, liposomal – *AmBisome* (Gilead)
Ancobon (Valeant) – flucytosine
§ *Antiminth* (Pfizer) – pyrantel pamoate
• *Aralen* (Sanofi) – chloroquine HCl and chloroquine phosphate
§ artemether – *Artenam* (Arenco, Belgium)
§ artemether/lumefantrine – *Coartem, Riamet* (Novartis)
§ *Artenam* (Arenco, Belgium) – artemether
§ artesunate – (Guilin No. 1 Factory, People's Republic of China)
atovaquone – *Mepron* (GlaxoSmithKline)
atovaquone/proguanil – *Malarone* (GlaxoSmithKline)

(continued)

azithromycin – *Zithromax* (Pfizer), others
• *Bactrim* (Roche) – TMP/Sulfa
§ benznidazole – *Rochagan* (Brazil)
• *Biaxin* (Abbott) – clarithromycin
§ *Biltricide* (Bayer) – praziquantel
† bithionol – *Bitin* (Tanabe, Japan)
† *Bitin* (Tanabe, Japan) – bithionol
§ *Brolene* (Aventis, Canada) – propamidine isethionate
chloroquine HCl and chloroquine phosphate – *Aralen* (Sanofi), others
clarithromycin – *Biaxin* (Abbott), others
• *Cleocin* (Pfizer) – clindamycin
clindamycin – *Cleocin* (Pfizer), others
Coartem (Novartis) – artemether/lumefantrine
crotamiton – *Eurax* (Westwood-Squibb)
dapsone – (Jacobus)
§ *Daraprim* (GlaxoSmithKline) – pyrimethamine USP
† diethylcarbamazine citrate (DEC) – *Hetrazan*
• *Diflucan* (Pfizer) – fluconazole
§ diloxanide furoate – *Furamide* (Boots, United Kingdom)
doxycycline – *Vibramycin* (Pfizer), others
eflornithine (Difluoromethylornithine, DFMO) – *Ornidyl* (Aventis)
§ *Egaten* (Novartis) – triclabendazole
Elimite (Allergan) – permethrin
Ergamisol (Janssen) – levamisole
Eurax (Westwood-Squibb) – crotamiton
• *Flagyl* (Pfizer) – metronidazole
§ *Flisint* (Sanofi-Aventis, France) – fumagillin
fluconazole – *Diflucan* (Pfizer), others
flucytosine – *Ancobon* (Valeant)
§ fumagillin – *Flisint* (Sanofi-Aventis, France)
• *Fungizone* (Apothecon) – amphotericin
§ *Furamide* (Boots, United Kingdom) – diloxanide furoate
§ furazolidone – *Furozone* (Roberts)
§ *Furozone* (Roberts) – furazolidone
† *Germanin* (Bayer, Germany) – suramin sodium
§ *Glucantime* (Aventis, France) – meglumine antimonate
† *Hetrazan* – diethylcarbamazine citrate (DEC)
Humatin (Monarch) – paromomycin
§ *Impavido* (Zentaris, Germany) – miltefosine
iodoquinol – *Yodoxin* (Glenwood), others
itraconazole – *Sporanox* (Janssen-Ortho), others
ivermectin – *Stromectol* (Merck)
ketoconazole – *Nizoral* (Janssen), others
† *Lampit* (Bayer, Germany) – nifurtimox
Lariam (Roche) – mefloquine
§ *Leshcutan* (Teva, Israel) – topical paromomycin
levamisole – *Ergamisol* (Janssen)
lumefantrine/artemether – *Coartem*, *Riamet* (Novartis)
Malarone (GlaxoSmithKline) – atovaquone/proguanil
malathion – *Ovide* (Medicis)
mebendazole – *Vermox* (McNeil), others
mefloquine – *Lariam* (Roche)
§ meglumine antimonate – *Glucantime* (Aventis, France)
† melarsoprol – *Mel-B*
† *Mel-B* – melarsoprol
Mepron (GlaxoSmithKline) – atovaquone
metronidazole – *Flagyl* (Pfizer), others
§ miconazole – *Monistat i.v.*
§ miltefosine – *Impavido* (Zentaris, Germany)
§ *Monistat i.v.* – miconazole
NebuPent (Fujisawa) – pentamidine isethionate
§ niclosamide – *Yomesan* (Bayer, Germany)
† nifurtimox – *Lampit* (Bayer, Germany)
nitazoxanide – *Alinia* (Romark)
Nix (GlaxoSmithKline) – permethrin
• *Nizoral* (Janssen) – ketoconazole
§ ornidazole – *Tiberal* (Roche, France)
Ornidyl (Aventis) – eflornithine (Difluoromethylornithine, DFMO)
Ovide (Medicis) – malathion
§ oxamniquine – *Vansil* (Pfizer)
§ *Paludrine* (AstraZeneca, United Kingdom) – proguanil
paromomycin – *Humatin* (Monarch); *Leshcutan* (Teva, Israel; topical formulation not available in US)
Pentam 300 (Fujisawa) – pentamidine isethionate
pentamidine isethionate – *Pentam 300* (Fujisawa), *NebuPent* (Fujisawa)
† *Pentostam* (GlaxoSmithKline, United Kingdom) – sodium stibogluconate
permethrin – *Nix* (GlaxoSmithKline), *Elimite* (Allergan)
§ praziquantel – *Biltricide* (Bayer)
primaquine phosphate USP
§ proguanil – *Paludrine* (AstraZeneca, United Kingdom)
proguanil/atovaquone – *Malarone* (GlaxoSmithKline)
§ propamidine isethionate – *Brolene* (Aventis, Canada)
§ pyrantel pamoate – *Antiminth* (Pfizer)
pyrethrins and piperonyl butoxide – *RID* (Pfizer), others
§ pyrimethamine USP – *Daraprim* (GlaxoSmithKline)
Qualaquin – quinine sulfate (Mutual Pharmaceutical Co/AR Scientific)
quinacrine
* quinidine gluconate (Eli Lilly)
§ quinine dihydrochloride
quinine sulfate – *Qualaquin* (Mutual Pharmaceutical Co/AR Scientific)
Riamet (Novartis) – artemether/lumefantrine
• *RID* (Pfizer) – pyrethrins and piperonyl butoxide
• *Rifadin* (Aventis) – rifampin
rifampin – *Rifadin* (Aventis), others
§ *Rochagan* (Brazil) – benznidazole
* *Rovamycine* (Aventis) – spiramycin
† sodium stibogluconate – *Pentostam* (GlaxoSmithKline, United Kingdom)
* spiramycin – *Rovamycine* (Aventis)
• *Sporanox* (Janssen-Ortho) – itraconazole
Stromectol (Merck) – ivermectin
sulfadiazine – (Eon)
† suramin sodium – *Germanin* (Bayer, Germany)
§ *Tiberal* (Roche, France) – ornidazole
Tindamax (Mission) – tinidazole
tinidazole – *Tindamax* (Mission)
TMP/Sulfa – *Bactrim* (Roche), others
§ triclabendazole – *Egaten* (Novartis)
§ *Vansil* (Pfizer) – oxamniquine
• *Vermox* (McNeil) – mebendazole
• *Vibramycin* (Pfizer) – doxycycline
• *Yodoxin* (Glenwood) – iodoquinol
§ *Yomesan* (Bayer, Germany) – niclosamide
• *Zithromax* (Pfizer) – azithromycin

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* Available in the US only from the manufacturer.

§ Not available commercially. It may be obtained through compounding pharmacies such as Panorama Compounding Pharmacy, 6744 Balboa Blvd, Van Nuys, CA 91406 (800-247-9767) or Medical Center Pharmacy, New Haven, CT (203-688-6816). Other compounding pharmacies may be found through the National Association of Compounding Pharmacies (800-687-7850) or the Professional Compounding Centers of America (800-331-2498, www.pccarx.com).

† Available from the CDC Drug Service, Centers for Disease Control and Prevention, Atlanta, Georgia 30333; 404-639-3670 (evenings, weekends, or holidays: 770-488-7100).

• Also available generically.