AMEBIC MENINGOENCEPHALITIS, primary and granulomatous

	Drug	Adult dosage	Pediatric dosage
Naegleria			
Drug of choice:	Amphotericin B[1,2]	1.5 mg/kg/d IV in 2 doses x 3d, then 1 mg/kg/d x 6d plus 1.5 mg/d intrathecally x 2d, then 1 mg/d every other day x 8d	1.5 mg/kg/d IV in 2 doses x 3d, then 1 mg/kg/d x 6d plus 1.5 mg/d intrathecally x 2d, then 1 mg/d every other day x 8d
Acanthamoeba			
Drug of choice:	Several patients with granulomatous amebic encephalitis (GAE) have been successfully treated with combinations of **pentamidine, sulfadiazine, flucytosine,** and either **fluconazole** or **itraconazole**.[3] GAE in an AIDS patient was treated successfully with **sulfadiazine, pyrimethamine** and **fluconazole** combined with surgical resection of the CNS lesion.[4] Chronic *Acanthamoeba* meningitis was successfully treated in 2 children with a combination of oral **trimethoprim/sulfamethoxazole, rifampin** and **ketoconazole**.[5] Disseminated cutaneous infection in an immunocompromised patient was treated successfully with IV **pentamidine, topical chlorhexidine** and 2% **ketoconazole** cream, followed by oral **itraconazole**[6] and with **voriconazole** and **amphotericin B lipid complex**.[7] Other reports of successful therapy have been described.[8] Susceptibility testing of *Acanthamoeba* isolates has shown differences in drug sensitivity between species and even among strains of a single species; antimicrobial susceptibility testing is advisable.[9]		
Balamuthia mandrillaris			
Drug of choice:	*B. mandrillaris* is a free-living ameba that causes subacute to fatal granulomatous amebic encephalitis (GAE) and cutaneous disease. Two cases of *Balamuthia* encephalitis have been successfully treated with **flucytosine, pentamidine, fluconazole** and **sulfadiazine** plus either **azithromycin** or **clarithromycin** (**phenothiazines** were also used) combined with surgical resection of the CNS lesion.[10] Another case was successfully treated following open biopsy with **pentamidine, fluconazole, sulfadiazine** and **clarithromycin**.[11]		
Sappinia diploidea			
Drug of choice:	A free-living ameba once thought not to be pathogenic to humans. *S. diploidea* has been successfully treated with **azithromycin, pentamidine, itraconazole** and **flucytosine** combined with surgical resection of the CNS lesion.[12]		

* Availability problems. See table below.

1. Not FDA-approved for this indication.
2. A *Naegleria fowleri* infection was treated successfully in a 9-year old girl with combination of amphotericin B and miconazole both intravenous and intrathecal, plus oral rifampin (JS Seidel et al NEJM 1982;306:346). Amphotericin B and miconazole appear to have synergistic effect, but Medical Letter consultants believe the rifampin probably had no additional effect (GS Visvesvara et al, FEMS Immunol Med Microbiol 2007; 50:1). Parenteral miconazole is no longer available in the US. Azithromycin has been used successfully in combination therapy to treat *Balmuthia* infection, but was changed to clarithromycin because of toxicity concerns and for better penetration into the cerebrospinal fluid. *In vitro,* azithromycin is more active than clarithromycin against *Naegleria*, so may be a better choice combined with amphotericin B for treatment of *Naegleria* (TR Deetz et al, Clin Infect Dis 2003; 37:1304; FL Schuster and GS Visvesvara, Drug Resistance Updates 2004; 7:41). Combinations of amphotericin B, ornidazole and rifampin (R Jain et al, Neurol India 2002; 50:470) and amphotericin B, fluconazole and rifampin have also been used (J Vargas-Zepeda et al, Arch Med Research 2005; 36:83). Case reports of other successful therapy have been published (FL Schuster and GS Visvesvara, Int J Parasitiol 2004; 34:1001).
3. GS Visvesvara et al, FEMS Immunol Med Microbiol 2007; 50:1, epub Apr 11.
4. M Seijo Martinez et al, J Clin Microbiol 2000; 38:3892.
5. T Singhal et al, Pediatr Infect Dis J 2001; 20:623.
6. CA Slater et al, N Engl J Med 1994; 331:85.
7. R Walia et al, Transplant Infect Dis 2007; 9:51
8. FL Schuster and GS Visvesvara, Drug Resistance Updates 2004; 7:41
9. FL Schuster and GS Visvesvara, Int J Parasitiol 2004; 34:1001.
10. TR Deetz et al, Clin Infect Dis 2003; 37:1304
11. S Jung et al, Arch Pathol Lab Med 2004; 128:466.
12. BB Gelman et al, J Neuropathol Exp Neurol 2003; 62:990.

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)
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)

(continued)

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: 404-639-2888).

• Also available generically.