MUCOCUTANEOUS LEISHMANIASIS. Amphotericin B is used in mucocutaneous leishmaniasis unresponsive to antimonials. Successful treatment with liposomal amphotericin B has been reported in immunocompetent[19] and immunocompromised[20] patients.

1. Gradoni L, *et al.* Treatment of Mediterranean visceral leishmaniasis. *Bull WHO* 1995; **73:** 191–7.
2. Syriopoulou V, *et al.* Two doses of a lipid formulation of amphotericin B for the treatment of Mediterranean visceral leishmaniasis. *Clin Infect Dis* 2003; **36:** 560–6.
3. Davidson RN, *et al.* Liposomal amphotericin B (AmBisome) in Mediterranean visceral leishmaniasis: a multi-centre trial. *Q J Med* 1994; **87:** 75–81.
4. Russo R, *et al.* Visceral leishmaniasis in HIV infected patients: treatment with high dose liposomal amphotericin B (AmBisome). *J Infect* 1996; **32:** 133–7.
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7. Giri OP. Amphotericin B therapy in kala-azar. *J Indian Med Assoc* 1993; **91:** 91–3.
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9. Mishra M, *et al.* Amphotericin versus sodium stibogluconate in first-line treatment of Indian kala-azar. *Lancet* 1994; **344:** 1599–1600.
10. Thakur CP, *et al.* Amphotericin B deoxycholate treatment of visceral leishmaniasis with newer modes of administration and precautions: a study of 938 cases. *Trans R Soc Trop Med Hyg* 1999; **93:** 319–23.
11. Sundar S, *et al.* Amphotericin B treatment for Indian visceral leishmaniasis: response to 15 daily versus alternate-day infusions. *Clin Infect Dis* 2007; **45:** 556–61.
12. Thakur CP, *et al.* Comparison of three treatment regimens with liposomal amphotericin B (AmBisome) for visceral leishmaniasis in India: a randomized dose-finding study. *Trans R Soc Trop Med Hyg* 1996; **90:** 319–22.
13. Sundar S, *et al.* Treatment of Indian visceral leishmaniasis with single or daily infusions of low dose liposomal amphotericin B: randomised trial. *BMJ* 2001; **323:** 419–22.
14. Sundar S, *et al.* Single-dose liposomal amphotericin B in the treatment of visceral leishmaniasis in India: a multicenter study. *Clin Infect Dis* 2003; **37:** 800–4.
15. Sundar S, *et al.* Short-course, low-dose amphotericin B lipid complex therapy for visceral leishmaniasis unresponsive to antimony. *Ann Intern Med* 1997; **127:** 133–7.
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17. Dietze R, *et al.* Treatment of kala-azar in Brazil with Amphocil (amphotericin B cholesterol dispersion) for 5 days. *Trans R Soc Trop Med Hyg* 1995; **89:** 309–11.
18. Berman JD, *et al.* Efficacy and safety of liposomal amphotericin B (AmBisome) for visceral leishmaniasis in endemic developing countries. *Bull WHO* 1998; **76:** 25–32.
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20. Amato VS, *et al.* Mucocutaneous leishmaniasis associated with HIV infection treated successfully with liposomal amphotericin B (AmBisome). *J Antimicrob Chemother* 2000; **46:** 341–2.

Primary amoebic meningoencephalitis. Amphotericin B is active *in vitro* against *Naegleria fowleri* and has been recommended for the treatment of primary amoebic meningoencephalitis (see Naegleria Infections, p.822) caused by this amoeba. There have been some case reports[1-7] of survival after the use of intravenous and intrathecal amphotericin B. In all cases amphotericin B was combined with other antimicrobials, notably oral rifampicin.

1. Anderson K, Jamieson A. Primary amoebic meningoencephalitis. *Lancet* 1972; **i:** 902–3.
2. Seidel JS, *et al.* Successful treatment of primary amebic meningoencephalitis. *N Engl J Med* 1982; **306:** 346–8.
3. Brown RL. Successful treatment of primary amebic meningoencephalitis. *Arch Intern Med* 1991; **151:** 1201–2.
4. Poungvarin N, Jariya P. The fifth nonlethal case of primary amoebic meningoencephalitis. *J Med Assoc Thai* 1991; **74:** 112–15.
5. Loschiavo F, *et al.* Acute primary meningoencephalitis from entamoeba Naegleria fowleri: report of a clinical case with a favourable outcome. *Acta Neurol (Napoli)* 1993; **15:** 333–40.
6. Wang A, *et al.* Successful treatment of amoebic meningoencephalitis in a Chinese living in Hong Kong. *Clin Neurol Neurosurg* 1993; **95:** 249–52.
7. Jain R, *et al.* Naegleria meningitis: a rare survival. *Neurol India* 2002; **50:** 470–2.

Preparations

BP 2008: Amphotericin Lozenges; Amphotericin Oral Suspension; ***USP 31:*** Amphotericin B Cream; Amphotericin B for Injection; Amphotericin B Lotion; Amphotericin B Ointment.

Proprietary Preparations (details are given in Part 3)
Arg.: Abelcet; AmBisome; Amfostat†; Amphotec; Anfogen; ***Austral.:*** Abelcet; AmBisome; Amphocil; Fungilin; Fungizone; ***Austria:*** Abelcet; AmBisome; Ampho-Moronal; Amphocil; ***Belg.:*** Abelcet; AmBisome; Fungizone; ***Braz.:*** Abelcet; AmBisome†; Amphocil; Anforicin B; Fungi B; Fungizon; ***Canad.:*** Abelcet; AmBisome; Amphotec†; Fungizone; ***Chile:*** Fungizon; ***Cz.:*** Abelcet; Amphocil; ***Denm.:*** Abelcet; AmBisome; Fungilin†; Fungizone; ***Fin.:*** Abelcet; AmBisome; Fungizone; ***Fr.:*** Abelcet; AmBisome; Fungizone; ***Ger.:*** Abelcet; AmBisome; Ampho-Moronal; ***Gr.:*** Abelcet; AmBisome; Amphipral; Amphocil; Fungizone; ***Hong Kong:*** Abelcet; AmBisome; Amphocil†; Fungizone; ***Hung.:*** Abelcet; AmBisome; Amphocil; Fungizone; ***India:*** Fungizone; ***Indon.:*** Fungizone; ***Irl.:*** Abelcet; AmBisome; Amphocil; Fungizone; ***Israel:*** AmBisome; Amphocil; Fungilin†; Fungizone†; ***Ital.:*** Abelcet; AmBisome; Fungilin; Fungizone; ***Jpn:*** AmBisome; ***Malaysia:*** Abelcet†; Amphocil; Fungizone; ***Mex.:*** Amfostat; Amphocil; Candipres; ***Neth.:*** Abelcet; AmBisome; Amphocil; Fungizone; ***Norw.:*** Abelcet; AmBisome; Fungizone; ***NZ:*** Abelcet; AmBisome; Fungilin; Fungizone; ***Philipp.:*** Fungizone; ***Pol.:*** AmBisome; Amphocil; ***Port.:*** Abelcet; AmBisome; Amphocil; Fungizone; ***Rus.:*** AmBisome (АмБизом); Amphoglucamin (Амфоглюкамин); ***S.Afr.:*** AmBisome; Fungizone; ***Singapore:*** Abelcet; AmBisome; Amphocil†; Fungizone; ***Spain:*** Abelcet; AmBisome; Amphocil; Funganiline†; Fungizona; ***Swed.:*** Abelcet†; AmBisome; Fungizone; ***Switz.:*** Abelcet†; AmBisome; Ampho-Moronal; Fungizone; ***Thai.:*** AmBisome†; Amphocil; Fungizone; ***Turk.:*** Abelcet; AmBisome; Fungizone; ***UK:*** Abelcet; AmBisome; Amphocil; Fungilin; Fungizone; ***USA:*** Abelcet; AmBisome; Amphotec; Fungizone†; ***Venez.:*** Amphotec; Fungizone.

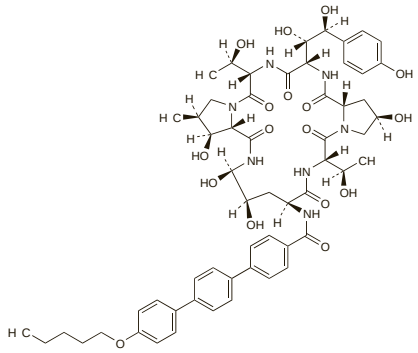
Multi-ingredient: ***Austria:*** Mysteclin; ***Braz.:*** Anfoterin†; Gino-Teracin; Novasutin; Talsutin; Tericin AT; Tricocilin B; Vagiklin; ***Chile:*** Talseclin†; ***Fr.:*** Amphocycline; ***Ger.:*** Mysteclin; ***Hong Kong:*** Talsutin; ***Indon.:*** Talsutin; ***Ital.:*** Anfocort; ***Malaysia:*** Talsutin†; ***Philipp.:*** Vagimycin; ***S.Afr.:*** Vagmycin; ***Spain:*** Gine Heyden†; Sanicel; Trigon Topico; ***Venez.:*** Talsutin†.

Anidulafungin *(USAN, rINN)*

Anidulafungina; Anidulafungine; Anidulafunginum; LY-303366; V-Echinocandin. (4*R*,5*R*)-4,5-Dihydroxy-*N*^{2}-{[4″-(pentyloxy)-*p*-terphenyl-4-yl]carbonyl}-L-ornithyl-L-threonyl-*trans*-4-hydroxy-L-prolyl-(*S*)-4-hydroxy-4-(*p*-hydroxyphenyl)-L-threonyl-L-threonyl-(3*S*,4*S*)-3-hydroxy-4-methyl-L-proline cyclic (6→1)-peptide; 1-((4*R*,5*R*)-4,5-Dihydroxy-*N*^{2}-{[4″-(pentyloxy)(1,1′:4′,1″-terphenyl)-4-yl]carbonyl}-L-ornithine)-echinocandin B.

Анидулафунгин

$C_{58}H_{73}N_7O_{17}$ = 1140.2.
CAS — 166663-25-8.
ATC — J02AX06.
ATC Vet — QJ02AX06.



Adverse Effects and Precautions

As for Caspofungin, see p.528.

Dose adjustments are not required in patients with hepatic or renal impairment.

Interactions

Few drug interactions are expected with anidulafungin, as it is not metabolised by the hepatic cytochrome P450 system and almost no renal clearance occurs.

Antimicrobial Action

As for Caspofungin, see p.528.

Pharmacokinetics

Steady state plasma concentrations of anidulafungin are achieved after the first loading dose; systemic clearance is about 1 litre/hour and the terminal elimination half-life is 40 to 50 hours. Anidulafungin is 84% bound to plasma proteins and the volume of distribution is 30 to 50 litres. It is not metabolised, but undergoes slow chemical degradation to inactive peptide degradants. Less than 10% of the intact drug is eliminated in the faeces and less than 1% is excreted in the urine.

◊ References.

1. Dowell JA, *et al.* Population pharmacokinetic analysis of anidulafungin, an echinocandin antifungal. *J Clin Pharmacol* 2004; **44:** 590–8.
2. Benjamin DK, *et al.* Safety and pharmacokinetics of intravenous anidulafungin in children with neutropenia at high risk for invasive fungal infections. *Antimicrob Agents Chemother* 2006; **50:** 632–8.

Uses and Administration

Anidulafungin is an echinocandin antifungal active against *Aspergillus* and *Candida* spp. It is used in the treatment of candidaemia, oesophageal candidiasis, and other forms of invasive candidiasis.

Anidulafungin is given by intravenous infusion, the rate of which should not exceed 1.1 mg/minute. For candidaemia and other invasive candidiasis a loading dose of 200 mg is given on the first day followed by 100 mg daily thereafter. For oesophageal candidiasis the loading dose is 100 mg followed by 50 mg daily.

◊ Reviews.

1. Murdoch D, Plosker GL. Anidulafungin. *Drugs* 2004; **64:** 2249–58.
2. Vazquez JA, Sobel JD. Anidulafungin: a novel echinocandin. *Clin Infect Dis* 2006; **43:** 215–22.

Preparations

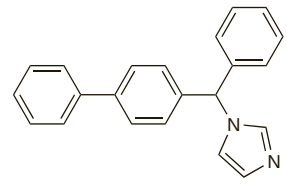
Proprietary Preparations (details are given in Part 3)
Cz.: Ecalta; ***Port.:*** Ecalta; ***UK:*** Ecalta; ***USA:*** Eraxis.

Bifonazole *(BAN, USAN, rINN)*

Bay-h-4502; Bifonatsoli; Bifonazol; Bifonazolas; Bifonazolum. 1-(α-Biphenyl-4-ylbenzyl)imidazole.

Бифоназол

$C_{22}H_{18}N_2$ = 310.4.
CAS — 60628-96-8.
ATC — D01AC10.
ATC Vet — QD01AC10.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *Jpn.*
Ph. Eur. 6.2 (Bifonazole). A white or almost white crystalline powder. It exhibits polymorphism. Practically insoluble in water; sparingly soluble in dehydrated alcohol.

Profile

Bifonazole is an imidazole antifungal with a broad spectrum of activity; sensitive fungi include dermatophytes, *Malassezia furfur*, and *Candida* spp. It also has some antibacterial activity.

Bifonazole is mainly used by topical application in the treatment of fungal skin and nail infections (p.521). It is applied once daily as a 1% cream, powder, solution, or gel. Treatment is usually continued for 2 to 4 weeks. More prolonged treatment is necessary for nail infections and bifonazole may be applied initially with a 40% urea paste to soften the nail.

Local reactions including burning and itching have been reported.

For a discussion of the caution needed when using azole antifungals during pregnancy, see under Pregnancy in Precautions of Fluconazole, p.532.

◊ Reviews.

1. Lackner TE, Clissold SP. Bifonazole: a review of its antimicrobial activity and therapeutic use in superficial mycoses. *Drugs* 1989; **38:** 204–25.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Bifonal†; Bimicot; Micosol; Mycospor†; Sinamida Plus; ***Austral.:*** Canesten Once Daily; Mycospor; ***Austria:*** Canesten Bifonazol; Fungiderm†; ***Belg.:*** Canestene Derm Bifonazole; Mycospor†; ***Braz.:*** Mycospor; ***Chile:*** Biocitronil†; Micotopic†; Multifung; Mycosporan; ***Cz.:*** Mycospor; ***Fr.:*** Amycor; ***Ger.:*** Bifomyk; Bifon; Canesten Extra; Mycospor; ***Gr.:*** Aeroderma†; Bifized; Bifon; Compaser†; Fungiderm; Gloryskin; Helpovion†; Kavaderm; Myco-flusemidon; Mycospor; Rye; ***Hong Kong:*** Mycospor; ***Hung.:*** Mycospor; ***Indon.:*** Mycospor; ***Israel:*** Agispor; ***Ital.:*** Azolmen; Bifazol; ***Mex.:*** Mycospor; ***Neth.:*** Mycospor; ***Pol.:*** Mycospor; ***Port.:*** Mycospor; Topical; ***Rus.:*** Bifosin (Бифосин); Mycospor (Микоспор); ***S.Afr.:*** Mycospor; ***Spain:*** Bifokey; Levelina; Moldina†; Mycospor; ***Swed.:*** Mycosporan; ***Turk.:*** Mycospor; ***UK:*** Canesten AF Once Daily†; ***Venez.:*** Mycospor.

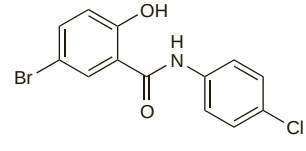
Multi-ingredient: ***Arg.:*** Empecid Pie; Micatex†; Piecidex NF; Prurisedan Antimicotico†; ***Austria:*** Canesten Bifonazol comp; Fungiderm comp†; ***Chile:*** Mycosporan Onycoset†; ***Cz.:*** Mycospor Sada na Nehty; ***Fr.:*** Amycor Onychoset; ***Ger.:*** Canesten Extra Nagelset; Mycospor Nagelset†; ***Israel:*** Agispor Onychoset; Comagis; Keratospor; ***Mex.:*** Mycospor Onicoset; ***Pol.:*** Mycospor Onychoset; ***Port.:*** Mycosport†; ***Rus.:*** Mycospor (Микоспор); ***S.Afr.:*** Mycospor Onycho-set; ***Spain:*** Mycospor Onicoset; ***Turk.:*** Mycospor; ***Venez.:*** Mycospor Onicoset.

Bromochlorosalicylanilide

Bromchlorsalicylanilidum; Bromisalisyyliklоorianilidi; Bromoclorosalicilanilida; Bromsalicylkloranilid. 5-Bromo-4′-chlorosalicylanilide; 5-Bromo-*N*-(4-chlorophenyl)-2-hydroxybenzamide.

Бромохлоросалицилданилин

$C_{13}H_9BrClNO_2$ = 326.6.
CAS — 3679-64-9.
ATC — D01AE01.
ATC Vet — QD01AE01.



Profile

Bromochlorosalicylanilide is a bromsalan antifungal that has been applied topically. Photosensitivity may occur. See also Bromsalans, p.1632.