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.
5. López-Vélez R, *et al.* Amphotericin B lipid complex versus no treatment in the secondary prophylaxis of visceral leishmaniasis in HIV-infected patients. *J Antimicrob Chemother* 2004; **53:** 540–3.
6. Molina I, *et al.* Efficacy of liposomal amphotericin B for secondary prophylaxis of visceral leishmaniasis in HIV-infected patients. *J Antimicrob Chemother* 2007; **60:** 837–42.
7. Giri OP. Amphotericin B therapy in kala-azar. *J Indian Med Assoc* 1993; **91:** 91–3.
8. Mishra M, *et al.* Amphotericin versus pentamidine in antimony-unresponsive kala-azar. *Lancet* 1992; **340:** 1256–7.
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.
16. Sundar S, *et al.* Treatment of antimony-unresponsive Indian visceral leishmaniasis with ultra-short courses of amphotericin-B-lipid complex. *Ann Trop Med Parasitol* 1998; **92:** 755–64.
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.
19. Sampaio RNR, Marsden PD. Mucosal leishmaniasis unresponsive to glucantime therapy successfully treated with AmBisome. *Trans R Soc Trop Med Hyg* 1997; **91:** 77.
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.

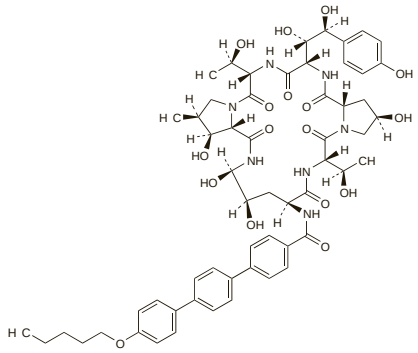
Multi-ingredient: ***Austria:*** Mysteclin; ***Braz.:*** Anfoterin†; Gino-Teracin; Novasutin; Talsutin; Tericin AT; Tricocilin B; Vagiklin; ***Chile:*** Talseclin†; ***Fr.:*** Amphocycline; ***Ger.:*** Mysteclin; ***Hong Kong:*** Talsutin; ***Indon.:*** Talsutin; ***Ital.:*** Anfocort; ***Malaysia:*** 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

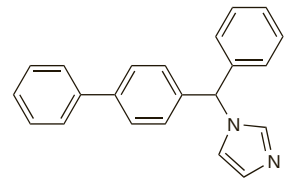
Proprietary Preparations (details are given in Part 3)
Cz.: Ecalta; ***Port.:*** Ecalta; ***UK:*** Ecalta; ***USA:*** Eraxis.

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.

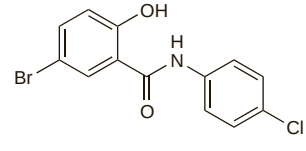
Multi-ingredient: ***Arg.:*** Empecid Pie; Micatex†; Piecidex NF; Prurisedan Antimicotico†; ***Austria:*** Canesten Bifonazol comp; Fungiderm comp†; ***Chile:*** Mycosporan Onycoset†; ***Cz.:*** Mycospor Sada na Nehty; ***Fr.:*** Amycor Onychoset; ***Ger.:*** Canesten Extra Nagelset; Mycospor Nagelset†; ***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.

Preparations

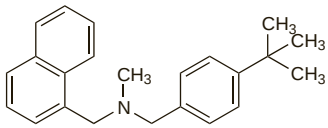
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***India:*** Multifungin H†; Multifungin†.

Butenafine Hydrochloride *(BANM, USAN, rINNM)*

Butenafiinihydrokloridi; Buténafine, Chlorhydrate de; Butenafinhydroklorid; Butenafini Hydrochloridum; Hidrocloruro de butenafina; KP-363. *N*-(*p*-*tert*-Butylbenzyl)-*N*-methyl-1-naphthalenemethylamine hydrochloride; 4-*tert*-Butylbenzyl(methyl)(1-naphthalenemethyl)amine hydrochloride.

Бутенафина Гидрохлорид

$C_{23}H_{27}N,HCl$ = 353.9.
CAS — 101828-21-1 (butenafine); 101827-46-7 (butenafine hydrochloride).
ATC — D01AE23.
ATC Vet — QD01AE23.



(butenafine)

Profile

Butenafine is a benzylamine antifungal with actions similar to those of the allylamine antifungal terbinafine (p.546). The hydrochloride is used topically as a 1% cream for the treatment of superficial dermatophyte infections (see Skin Infections, p.521).

◊ Reviews.

1. McNeely W, Spencer CM. Butenafine. *Drugs* 1998; **55:** 405–12.

Preparations

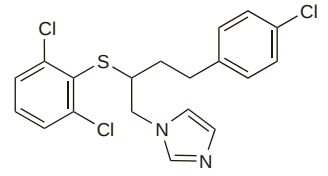
Proprietary Preparations (details are given in Part 3)
Arg.: Buticrem†; Ingebut; ***Austria:*** Zaxem; ***Canad.:*** Scholl Athlete's Foot†; ***Chile:*** Dermacom; ***India:*** Butop†; Fintop; ***Israel:*** Mentax; ***Jpn:*** Mentax; ***Philipp.:*** Funcid; ***USA:*** Lotrimin Ultra; Mentax.

Butoconazole Nitrate *(BANM, USAN, rINNM)*

Butoconazole, Nitrate de; Butoconazoli Nitras; Nitrato de butoconazol; RS-35887; RS-35887-00-10-3. 1-[4-(4-Chlorophenyl)-2-(2,6-dichlorophenylthio)butyl]imidazole mononitrate.

Бутоконазола Нитрат

$C_{19}H_{17}Cl_3N_2S,HNO_3$ = 474.8.
CAS — 64872-76-0 (butoconazole); 64872-77-1 (butoconazole nitrate).
ATC — G01AF15.
ATC Vet — QG01AF15.



(butoconazole)

Pharmacopoeias. In *US*.
USP 31 (Butoconazole Nitrate). A white to off-white crystalline powder. Practically insoluble in water; slightly soluble in acetone, in acetonitrile, in dichloromethane, and in tetrahydrofuran; very slightly soluble in ethyl acetate; sparingly soluble in methyl alcohol. Protect from light.

Adverse Effects and Precautions

Local reactions including burning and irritation and pelvic or abdominal pain or cramping may occur when butoconazole is applied vaginally.

Intravaginal preparations of butoconazole may damage latex contraceptives and additional contraceptive measures are therefore necessary during local application.

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

Effects on the blood. Severe reversible thrombocytopenia was associated with treatment with intravaginal butoconazole.[1] The patient had previously had a drop in white cell count after treatment with intravaginal clotrimazole, suggestive of an idiosyncratic reaction to imidazoles.

1. Maloley PA, *et al.* Severe reversible thrombocytopenia resulting from butoconazole cream. *DICP Ann Pharmacother* 1990; **24:** 143–4.

Antimicrobial Action

Butoconazole is an imidazole antifungal with antimicrobial activity similar to that of ketoconazole (p.539) including activity against *Candida* spp.

Pharmacokinetics

About 5% of a dose of butoconazole is absorbed after vaginal use. The plasma half-life is 21 to 24 hours.

Uses and Administration

Butoconazole is an imidazole antifungal used locally as the nitrate in the treatment of vulvovaginal candidiasis (p.518). It is given intravaginally as a 100-mg pessary or as 5 g of a 2% cream for 3 consecutive nights; a single application of the cream has also been used.

Preparations

USP 31: Butoconazole Nitrate Vaginal Cream.

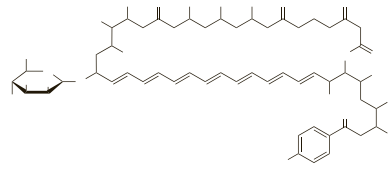
Proprietary Preparations (details are given in Part 3)
Austral.: Gynazole; ***Belg.:*** Gynomyk; ***Braz.:*** Gynazole; ***Canad.:*** Gynazole; ***Fr.:*** Gynomyk; ***Hung.:*** Gynazol; ***Malaysia:*** Gynofort; ***Mex.:*** Gynafem; ***Neth.:*** Gynomyk; ***Pol.:*** Gynazol; ***Rus.:*** Gynofort (Гинофорт); ***Singapore:*** Gynofort; ***USA:*** Gynazole; Mycelex-3.

Candicidin *(BAN, USAN, rINN)*

Candicidina; Candicidine; Candicidinum; Kandicidin; Kandisidiini; NSC-94219.

Кандицидин

CAS — 1403-17-4.
ATC — G01AA04.
ATC Vet — QG01AA04.



(candicidin D)

Profile

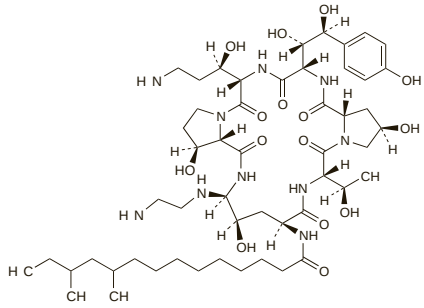
Candicidin is a mixture of antifungal heptaenes produced by *Streptomyces griseus*. It has been used in the treatment of vaginal candidiasis.

Caspofungin Acetate *(BANM, USAN, rINNM)*

Acetato de caspofungina; Caspofungine, Acétate de; Caspofungini Acetas; Kaspofungiiniasetaatti; Kaspofunginacetat; L-743873; MK-0991. (4*R*,5*S*)-5-[(2-Aminoethyl)amino]-N^2-(10,12-dimethyltetradecanoyl)-4-hydroxy-L-ornithyl-L-threonyl-*trans*-4-hydroxy-L-prolyl-(*S*)-4-hydroxy-4-(*p*-hydroxyphenyl)-L-threonyl-*threo*-3-hydroxy-L-ornithyl-*trans*-3-hydroxy-L-proline cyclic (6→1)-peptide diacetate.

Каспофунгина Ацетат

$C_{52}H_{88}N_{10}O_{15},2C_2H_4O_2$ = 1213.4.
CAS — 179463-17-3.
ATC — J02AX04.
ATC Vet — QJ02AX04.



(caspofungin)

Adverse Effects and Precautions

Adverse experiences reported with caspofungin have included anaemia, diarrhoea, nausea and vomiting, flushing, headache, fever, tachycardia, and venous complications around the infusion site. Possible histamine-mediated symptoms have been rash, facial swelling, pruritus, sensation of warmth, or bronchospasm. Anaphylaxis has occurred.

Isolated cases of hepatotoxicity have occurred and patients who develop abnormal liver function tests should be monitored for deterioration in hepatic function. Caspofungin may need to be given in reduced doses to patients with hepatic impairment (see below).

Breast feeding. Caspofungin is excreted in the breast milk of lactating *animals*, but the risk to breast-fed infants is suggested to be low. Recommendations in licensed product information vary: in the UK it recommends against use in women who are breast feeding, while in the USA caution is advised.

Pregnancy. Caspofungin has been shown to cross the placenta in *animal* studies and was shown to be embryotoxic in *rats* and *rabbits*; it was noted that there were no adequate and well-controlled studies in human pregnancy. Caspofungin is generally only recommended in pregnancy if the benefits to the mother are considered to outweigh the risks to the fetus.

Interactions

Although caspofungin is not metabolised by the hepatic cytochrome P450 system, drugs that induce hepatic enzymes may increase its clearance. Such effects have been noted with carbamazepine, dexamethasone, efavirenz, nevirapine, phenytoin, and rifampicin, and an increase in the dose of caspofungin should be considered in patients who are also taking these drugs and who are not clinically responding (see Uses and Administration, below).

When caspofungin has been given with ciclosporin, an increase in the area under the concentration-time curve for caspofungin, as well as increases in hepatic enzymes, were observed and use of the two drugs together is not recommended.

Caspofungin has resulted in decreased blood concentrations of tacrolimus and therapeutic drug monitoring and appropriate dosage adjustments to tacrolimus are recommended.

Antimicrobial Action

Caspofungin inhibits the synthesis of β-1,3-D-glucan, an essential component of the cell wall of many fungi. Caspofungin exhibits *in-vitro* activity against many *Aspergillus* spp. and is fungicidal against *Candida* spp. including non-albicans strains.

Pharmacokinetics

Plasma concentrations of caspofungin decline in a polyphasic manner after intravenous infusion. The initial short α-phase occurs immediately post-infusion and is followed by a β-phase with a half-life of 9 to 11 hours; an additional longer γ-phase also occurs with a half-life of 40 to 50 hours. Plasma clearance is dependent on distribution rather than on biotransformation or excretion. Caspofungin is highly bound to plasma protein. There is slow metabolism of caspofungin by hydrolysis and *N*-acetylation and excretion in faeces and urine.

Uses and Administration

Caspofungin is an echinocandin antifungal used in the treatment of invasive aspergillosis (p.517) in patients who are refractory to, or intolerant of, other therapy. It is also used in the treatment of invasive candidiasis and as empirical therapy for presumed fungal infections in febrile, neutropenic patients.

Caspofungin is used as the acetate but doses are expressed in terms of the base; caspofungin acetate 77.7 mg is equivalent to about 70 mg of caspofungin. It is given by slow intravenous infusion over about 1 hour. A loading dose of 70 mg is given on the first day and is followed by 50 mg daily; in adult patients weighing more than 80 kg, and in patients taking hepatic-enzyme inducing drugs who fail to respond, a daily dose of 70 mg is recommended. Doses may need