

Preparations**Proprietary Preparations** (details are given in Part 3)**Multi-ingredient:** *India:* Multifungin H†; Multifungin†.**Butenafine Hydrochloride** (BANM, USAN, rINNM)Butenafinihydrokloridi; 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

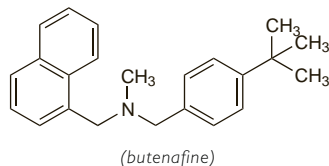
C₂₃H₂₇N.HCl = 353.9.

CAS — 101828-21-1 (butenafine); 101827-46-7

(butenafine hydrochloride).

ATC — D01AE23.

ATC Vet — QD01AE23.

**Profile**

Butenafine is a benzylamine antifungal with actions similar to those of the allylamine antifungal terbinafine (p.546). The hydrochloride is used typically 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; **Canada:** Scholl Athlete's Foot†; **Chile:** Dermacom; **India:** Butop†; Fintop; **Israel:** Mentax; **Jpn:** Mentax; **Philipp.:** Fucid; **USA:** Lotrimin Ultra; Mentax.**Butoconazole Nitrate** (BANM, USAN, rINNM)

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

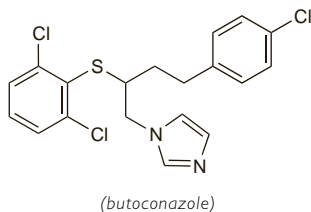
Бутоконазола Нитрат

C₁₉H₁₇Cl₃N₂S.HNO₃ = 474.8.

CAS — 64872-76-0 (butoconazole); 64872-77-1 (butoconazole nitrate).

ATC — G01AF15.

ATC Vet — QG01AF15.

**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; **Canada:** Gynazole; **Fr.:** Gynomyk; **Hung.:** Gynazol; **Malaysia:** Gynofort; **Mex.:** Gynafem; **Neth.:** Gynomyk; **Pol.:** Gynazol; **Rus.:** Gynofort (Гинофорт); **Singapore:** Gynofort; **USA:** Gynazole; Mycelex-3.**Candididin** (BAN, USAN, rINN)

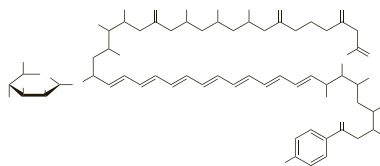
Candidina; Candidine; Candidinum; Kandicidin; Kandisiidini; NSC-94219.

КАНДИЦИДИН

CAS — 1403-17-4.

ATC — G01AA04.

ATC Vet — QG01AA04.

**Profile**Candididin 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; Kaspofungiinasettaatti; Kaspofunginacetat; L-743873; MK-0991. (4R,5S)-5-[(2-Aminoethyl)amino]-N²-(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.

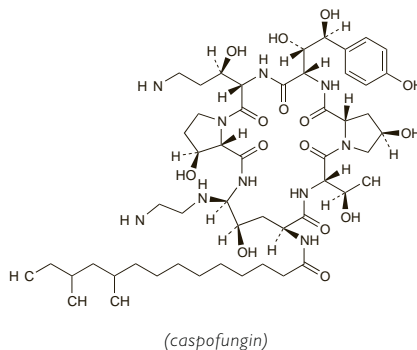
Каспифунгина Ацетат

C₅₂H₈₈N₁₀O₁₅.2C₂H₄O₂ = 1213.4.

CAS — 179463-17-3.

ATC — J02AX04.

ATC Vet — QJ02AX04.

**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 hista-

mine-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 ActionCaspofungin 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