Preparations

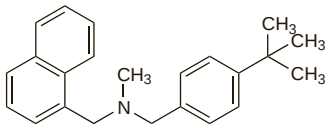
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***India:*** Multifungin H†; Multifungin†.

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

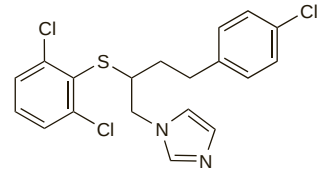
Proprietary Preparations (details are given in Part 3)
Arg.: Buticrem†; Ingebut; ***Austria:*** Zaxem; ***Canad.:*** Scholl Athlete's Foot†; ***Chile:*** Dermacom; ***India:*** Butop†; Fintop; ***Israel:*** Mentax; ***Jpn:*** Mentax; ***Philipp.:*** Funcid; ***USA:*** Lotrimin Ultra; Mentax.

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.

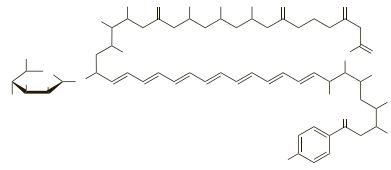
Proprietary Preparations (details are given in Part 3)
Austral.: Gynazole; ***Belg.:*** Gynomyk; ***Braz.:*** Gynazole; ***Canad.:*** Gynazole; ***Fr.:*** Gynomyk; ***Hung.:*** Gynazol; ***Malaysia:*** Gynofort; ***Mex.:*** Gynafem; ***Neth.:*** Gynomyk; ***Pol.:*** Gynazol; ***Rus.:*** Gynofort (Гинофорт);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

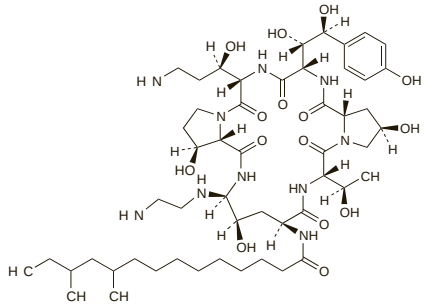
Candicidin is a mixture of antifungal heptaenes produced by *Streptomyces griseus*. It has been used in the treatment of vaginal candidiasis.

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

to be reduced in patients with hepatic impairment (see below).

◊ Reviews.

1. Letscher-Bru V, Herbrecht R. Caspofungin: the first representative of a new antifungal class. *J Antimicrob Chemother* 2003; **51:** 513–21.
2. Deresinski SC, Stevens DA. Caspofungin. *Clin Infect Dis* 2003; **36:** 1445–57.
3. Denning DW. Echinocandin antifungal drugs. *Lancet* 2003; **362:** 1142–51.
4. McCormack PL, Perry CM. Caspofungin: a review of its use in the treatment of fungal infections. *Drugs* 2005; **65:** 2049–68.
5. Morris MI, Villmann M. Echinocandins in the management of invasive fungal infections, part 1. *Am J Health-Syst Pharm* 2006; **63:** 1693–1703.
6. Morris MI, Villmann M. Echinocandins in the management of invasive fungal infections, part 2. *Am J Health-Syst Pharm* 2006; **63:** 1813–20.
7. Falagas ME, *et al*. Caspofungin for the treatment of fungal infections: a systematic review of randomized controlled trials. *Int J Antimicrob Agents* 2007; **29:** 136–43.
8. Hope WW, *et al*. The pharmacology and clinical use of caspofungin. *Expert Opin Drug Metab Toxicol* 2007; **3:** 263–74.
9. Waters L, Nelson M. The use of caspofungin in HIV-infected individuals. *Expert Opin Invest Drugs* 2007; **16:** 899–908.

Administration in children. Caspofungin is not licensed for use in paediatric patients, but has been prescribed.[1] A retrospective study[2] of 25 immunocompromised children with a median age of 9.8 years, given at least one dose of caspofungin, found that it appeared to be safe and well tolerated. Patients weighing less than 50 kg had a dose of 0.8 to 1.6 mg/kg daily, while those over 50 kg were given 50 to 75 mg daily. Another retrospective review[3] of 64 immunocompromised children with a median age of 11.5 years, reported a success rate of 67.7% with caspofungin at a median daily maintenance dose of 1.07 mg/kg, either as monotherapy or with another antifungal. A case series[4] of 10 neonates (9 preterm) with invasive candidiasis not responsive to amphotericin B and/or fluconazole reported that *Candida* spp. were cleared from the blood in all patients in a mean of 4.3 days after starting caspofungin therapy. Nine neonates were given an initial dose of 1 mg/kg daily for the first 2 days followed by 2 mg/kg daily for 15 to 21 days; the other was given a lower dose.

1. Lehrnbecher T, Groll AH. Experiences with the use of caspofungin in paediatric patients. *Mycoses* 2008; **51** (suppl 1): 58–64.
2. Franklin JA, *et al*. Retrospective study of the safety of caspofungin in immunocompromised pediatric patients. *Pediatr Infect Dis J* 2003; **22:** 747–9.
3. Groll AH, *et al*. Treatment with caspofungin in immunocompromised paediatric patients: a multicentre survey. *J Antimicrob Chemother* 2006; **57:** 527–35.
4. Odio CM, *et al*. Caspofungin therapy of neonates with invasive candidiasis. *Pediatr Infect Dis J* 2004; **23:** 1093–7.

Administration in hepatic impairment. Patients with mild hepatic impairment do not require dosage adjustment. In patients with moderate hepatic impairment, a daily dose of caspofungin 35 mg should be used after the initial dose of 70 mg; appropriate doses for patients with severe hepatic impairment have not been established.

Preparations

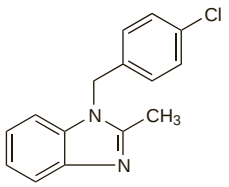
Proprietary Preparations (details are given in Part 3)
Arg.: Cancidas; ***Austral.:*** Cancidas; ***Belg.:*** Cancidas; ***Braz.:*** Cancidas; ***Canad.:*** Cancidas; ***Chile:*** Cancidas; ***Cz.:*** Cancidas; ***Denm.:*** Cancidas; ***Fin.:*** Cancidas; ***Fr.:*** Cancidas; ***Ger.:*** Cancidas; ***Gr.:*** Cancidas; ***Hong Kong:*** Cancidas; ***Hung.:*** Cancidas; ***Irl.:*** Cancidas; ***Israel:*** Cancidas; ***Ital.:*** Cancidas; ***Malaysia:*** Cancidas; ***Neth.:*** Cancidas; ***Norw.:*** Cancidas; ***NZ:*** Cancidas; ***Philipp.:*** Cancidas; ***Pol.:*** Cancidas; ***Port.:*** Cancidas; ***Rus.:*** Cancidas (Кансидас); ***Singapore:*** Cancidas; ***Spain:*** Cancidas; ***Swed.:*** Cancidas; ***Switz.:*** Cancidas; ***Thai.:*** Cancidas; ***Turk.:*** Cancidas; ***UK:*** Cancidas; ***USA:*** Cancidas; ***Venez.:*** Cancidas.

Chlormidazole Hydrochloride *(BANM, rINNM)*

Chlormidazole, Chlorhydrate de; Chlormidazoli Hydrochloridum; Clomidazole Hydrochloride; Hidrocloruro de clormidazol. 1-(4-Chlorobenzyl)-2-methylbenzimidazole hydrochloride.

Хлормидазола Гидрохлорид

$C_{15}H_{13}ClN_2,HCl$ = 293.2.
CAS — 3689-76-7 (chlormidazole); 5411 8-67-1 (chlormidazole hydrochloride).
ATC — D01AC04.
ATC Vet — QD01AC04.



(chlormidazole)

Profile
Chlormidazole hydrochloride is an imidazole antifungal used topically as the hydrochloride in the treatment of fungal infections of the skin.

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

Preparations

Proprietary Preparations (details are given in Part 3)
Pol.: Unifungicid.

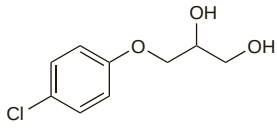
Multi-ingredient: ***Austria:*** Myco-Synalar; ***Pol.:*** Polfungicid; ***Switz.:*** Myco-Synalar†.

Chlorphenesin *(BAN, pINN)*

Chlorphénésine; Chlorphenesinum; Clorfenesina; Kloorifenesiini; Klorfenesin. 3-(4-Chlorophenoxy)propane-1,2-diol.

Хлорфенезин

$C_9H_{11}ClO_3$ = 202.6.
CAS — 104-29-0.
ATC — D01AE07.
ATC Vet — QD01AE07.



Profile
Chlorphenesin has antifungal and antibacterial properties. It has been applied locally in mild uncomplicated dermatophyte and other cutaneous infections and in vaginal infections.

Chlorphenesin carbamate (p.1894) is used as a skeletal muscle relaxant.

Preparations

Proprietary Preparations (details are given in Part 3)
Canad.: Mycil†; ***Ger.:*** Soorphenesin†; ***India:*** Dermicil†.

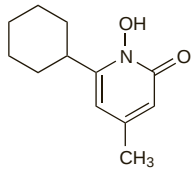
Multi-ingredient: ***Austral.:*** ZSC; ***Austria:*** Aleot; ***Braz.:*** Oto Betnovate.

Ciclopirox *(BAN, USAN, rINN)*

Ciclopiroxum; Ciklopiroksas; Ciklopirox; Hoe-296b; Siklopiroksi. 6-Cyclohexyl-1-hydroxy-4-methyl-2-pyridone.

Циклопирокс

$C_{12}H_{17}NO_2$ = 207.3.
CAS — 29342-05-0.
ATC — D01AE14; G01AX12.
ATC Vet — QD01AE14; QG01AX12.



Pharmacopoeias. In *Eur.* (see p.vii) and *US.*
Ph. Eur. 6.2 (Ciclopirox). A white or yellowish-white, crystalline powder. Slightly soluble in water; freely soluble in alcohol and in dichloromethane. Protect from light.
USP 31 (Ciclopirox). A white to slightly yellowish white, crystalline powder. Slightly soluble in water; freely soluble in dehydrated alcohol and in dichloromethane; soluble in ether. Store at a temperature of 15° to 30°. Protect from light.

Ciclopirox Olamine *(BANM, USAN, rINNM)*

Ciclopirox olamina; Ciclopirox olaminum; Ciclopiroxi Olaminum; Ciclopiroxolamine; Ciclopiroxum Olaminum; Ciklopiroksas olaminas; Ciklopirox olamin; Ciklopiroxolamin; Ciklopiroxolamin; Hoe-296; Siklopiroksiolamiini; Sikloproks Olamin. The 2-aminoethanol salt of 6-Cyclohexyl-1-hydroxy-4-methyl-2-pyridone.

Циклопирокс Оламин

$C_{12}H_{17}NO_2,C_2H_7NO$ = 268.4.
CAS — 41621-49-2.
ATC — D01AE14; G01AX12.
ATC Vet — QD01AE14; QG01AX12.

Pharmacopoeias. In *Chin., Eur.* (see p.vii), and *US.*
Ph. Eur. 6.2 (Ciclopirox Olamine). A white or pale yellow crystalline powder. It exhibits polymorphism. Slightly soluble in water; very soluble in alcohol and in dichloromethane; slightly soluble in ethyl acetate; practically insoluble in cyclohexane. A 1% solution in water has a pH of 8.0 to 9.0. Protect from light.
USP 31 (Ciclopirox Olamine). A white to slightly yellowish-white, crystalline powder. Slightly soluble in water; very soluble in alcohol and in dichloromethane; practically insoluble in cyclohexane. pH of a 1% solution in water is between 8.0 and 9.0. Store in airtight containers at a temperature of 5° to 25°. Protect from light.

Adverse Effects
Irritation and pruritus have been reported after topical application of ciclopirox.

Antimicrobial Action
Ciclopirox has a wide spectrum of antifungal activity. It inhibits most *Candida*, *Epidermophyton*, *Microsporum*, and *Trichophyton* spp. and is also active against *Malassezia furfur*. It has some antibacterial activity.

Uses and Administration
Ciclopirox is an antifungal that is applied topically in the treatment of fungal skin and nail infections, including cutaneous candidiasis (p.518), dermatophytosis, pityriasis versicolor (see Skin Infections, p.521), and seborrhoeic dermatitis (p.1584). It has also been used in the treatment of vaginal candidiasis.

It is applied twice daily for skin infections, as a cream, gel, suspension, solution, or powder; both the base and the olamine salt have been used, with products containing the equivalent of 0.77% ciclopirox base.

A lacquer containing 8% ciclopirox base is applied once daily for nail infections.

A shampoo containing 1% ciclopirox base is used twice weekly for the treatment of seborrhoeic dermatitis.

◊ References.

1. Gupta AK, Skinner AR. Ciclopirox for the treatment of superficial fungal infections: a review. *Int J Dermatol* 2003; **42** (suppl 1): 3–9.
2. Gupta AK, Nicol KA. Ciclopirox 1% shampoo for the treatment of seborrheic dermatitis. *Int J Dermatol* 2006; **45:** 66–9.

Preparations

USP 31: Ciclopirox Olamine Cream; Ciclopirox Olamine Topical Suspension.

Proprietary Preparations (details are given in Part 3)
Arg.: Dermaflor†; Loprox; Micopirox; Stieprox; ***Austral.:*** Stieprox; ***Austria:*** Batrafen; Stieprox; ***Braz.:*** Fungirox†; Gino Loprox; Loprox; Micolamina; Micoliv†; Stiprox; ***Canad.:*** Loprox; Penlac; Stieprox; ***Chile:*** Batrafen; Fungopirox; Mikium†; Stiprox; ***Cz.:*** Batrafen; Dafnegin; Stieprox; ***Denm.:*** Mycofen; Stieprox; ***Fin.:*** Stieprox; ***Fr.:*** Mycosquam; Mycoster; Sebiprox; Stiprox; ***Ger.:*** Batrafen; Ciclopoli; Inimur Myko; Nagel Batrafen; Sebiprox; ***Gr.:*** Candimyc; Dafnegin†; Myclopir; Mycomycen; Neo-botacreme; Neo-mycodermol; Rozolam; Stieprox; ***Hong Kong:*** Batrafen; Stieprox; ***Hung.:*** Batrafen; ***India:*** Olamin; Onylac; ***Indon.:*** Batrafen; Loprox; ***Irl.:*** Batrafen†; Oilatum Scalp Treatment; Stieprox; ***Israel:*** Batrafen; Cicloderm; ***Ital.:*** Batrafen; Biroxol†; Brumixol; Dafnegin; Miclast; Micomicen; Micoxolamina; Sebiprox; Stiprox; ***Malaysia:*** Stieprox; ***Mex.:*** Loprox; Stiprox; ***Neth.:*** Loprox; Sebiprox; ***Norw.:*** Stieprox; ***NZ:*** Batrafen; Stieprox; ***Philipp.:*** Stieprox; ***Pol.:*** Batrafen; Dafnegin; Hascofungin; Pirolam; Stieprox; ***Port.:*** Batrafen; Mycoster; Sebiprox; ***Rus.:*** Batrafen (Батрафен); ***Singapore:*** Stieprox; ***Spain:*** Batrafen; Ciclochem; Fungowas; Rimafungol†; Sebiprox; ***Switz.:*** Batrafen; Dafnegil Neo; ***Thai.:*** Cicloderm†; Loprox; Stieprox; ***Turk.:*** Canolen; Nibulen; ***UK:*** Oilatum Scalp Treatment; ***USA:*** Loprox; Penlac; ***Venez.:*** Batrafen.

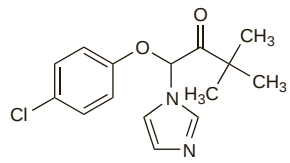
Multi-ingredient: ***Arg.:*** Derm's Shampoo; Stieproxal; ***Fr.:*** Novophane; Novophane S; Stiproxal; ***India:*** Flucort-C; ***Israel:*** Cicloderm-C; ***UK:*** Oilatum Scalp Intensive.

Climbazole *(BAN, rINN)*

Bay-e-6975; Climbazol; Climbazolum; MEB-6401. 1-(*p*-Chlorophenoxy)-1-imidazol-1-yl-3,3-dimethyl-2-butanone.

Климбазол

$C_{15}H_{17}ClN_2O_2$ = 292.8.
CAS — 38083-17-9.



Profile
Climbazole is an azole antifungal included in preparations for the topical treatment of seborrhoeic dermatitis.

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

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Arg.:*** Mencogrin; Micocert; Micodual; ***Chile:*** Eucerin Shampoo Anticaspa; Node DS; Shampoo Anticaspa; ***Fr.:*** Item Alphazole; Node DS; Node P; Sebosquam; Squaphane; Squaphane E; Squaphane Masque-Creme; Squaphane P; Squaphane S; ***Ital.:*** Derman-Shampoo AF†; Pitiren; ***Port.:*** Alphazole†; Efluvium Anti-caspa; ***Venez.:*** Node DS; Sensibio DS.