

Profile

Liranafate is an antifungal related to tolnaftate (p.548) and is applied once daily as a 2% cream or solution in the treatment of superficial dermatophyte infections (p.521).

Preparations**Proprietary Preparations** (details are given in Part 3)

Jpn: Zefnart.

Mepartericin (BAN, USAN, rINN)

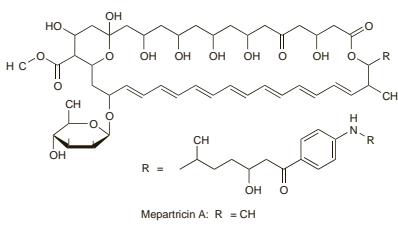
Mepartericina; Mépartericine; Mepartericinum; Methylpartricin; SN-654; SPA-S-160.

Мепартицин

CAS — 11121-32-7.

ATC — A01AB16; D01AA06; G01AA09; G04CX03.

ATC Vet — QA01AB16; QD01AA06; QG01AA09; QG04CX03.

**Profile**

Mepartericin is a mixture of the methyl esters of 2 related polyene antibiotics that may be obtained from a strain of *Streptomyces aureofaciens*. It has antifungal and antiprotozoal activity and has been used in vaginal candidiasis and trichomoniasis as pessaries or as a vaginal cream. A cream is also available for the treatment of superficial candidiasis. An oral form of mepartericin sodium laurylsulfate is also used. Oral mepartericin 40 mg daily is used in the treatment of some prostate disorders.

Prostate disorders. Studies^{1,2} have shown that mepartericin given by mouth is effective in the treatment of *benign prostatic hyperplasia* (see p.2178 for the more usual treatments); a dose of 40 mg daily is commonly used.² Mepartericin is thought to reduce cholesterol, oestrogen, and androgen binding to the prostate. Similarly, another study³ has shown that the same dose of mepartericin provides symptomatic improvement in the management of *chronic prostatitis/chronic pelvic pain syndrome* (see Prostatitis, p.2181).

1. Tosto A, et al. A double-blind study of the effects of mepartericin in the treatment of obstruction due to benign prostatic hyperplasia. *Curr Ther Res* 1995; **56:** 1270-75.
2. Denis L, et al. Double-blind, placebo-controlled trial to assess the efficacy and tolerability of mepartericin in the treatment of BPH. *Prostate* 1998; **37:** 246-52.
3. De Rose AF, et al. Role of mepartericin in category III chronic nonbacterial prostatitis/chronic pelvic pain syndrome: a randomized prospective placebo-controlled trial. *Urology* 2004; **63:** 13-16.

Preparations**Proprietary Preparations** (details are given in Part 3)

Austria: Iperplasin; Prostec; **Belg.:** Tricandil†; **Braz.:** Montricin†; **Chile:** Normoprost†; **Cz.:** Iperetrofan; **Ital.:** Iperetrofan; Tricandi; **Philippines:** Iperetrofan; **Pol.:** Iperetrofan; **Port.:** Iperplasin; Iperetrofan; Tricandi.

Multi-ingredient: **Braz.:** Tricangine†.

Micafungin Sodium (USAN, rINNM)

FK-463; Micafungina sodica; Micafungina Sodique; Natrui Micafunginum. 5-[((S,2S)-2-[(2R,6S,9S,11R,12R,14aS,15S,16S,20S,23S,25aS)-20-[(1R)-3-Amino-1-hydroxy-3-oxopropyl]-2,11,12,15-tetrahydroxy-6-[(1R)-1-hydroxyethyl]-1-6-methyl-5,8,14,19,22,25-hexaoxa-9-[(4-[4-(pentylphenoxy)phenyl]isoxazol-3-yl]benzoyl)amino]tetracosahydro-1H-dipyromolo[2,1-c'2,1'-f][1,4,7,10,13,16]hexaazacycloheicosin-23-yl]-1,2-dihydroxyethyl)-2-hydroxyphenyl sodium sulfate.

Натрий Микаfungин

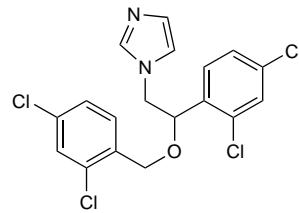
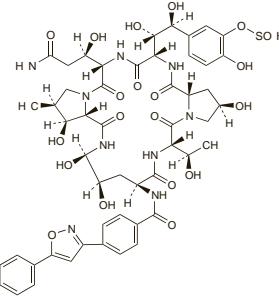
C₅₆H₇₀N₉NaO₂₃S = 1292.3.

CAS — 235114-32-6 (micafungin); 208538-73-2 (micafungin sodium).

ATC — J02AX05.

ATC Vet — QJ02AX05.

The symbol † denotes a preparation no longer actively marketed



Pharmacopoeias. In *Eur.* (see p.vii), *Jpn*, and *US*.

Ph. Eur. 6.2 (Miconazole). A white or almost white powder. It exhibits polymorphism. M.p. 83° to 87°. Very slightly soluble in water; soluble in alcohol; freely soluble in methyl alcohol. Protect from light.

USP 31 (Miconazole). A white to pale cream powder. It may exhibit polymorphism. M.p. 78° to 88°. Insoluble in water; soluble 1 in 9.5 of alcohol, 1 in 2 of chloroform, 1 in 15 of ether, 1 in 4 of isopropyl alcohol, 1 in 5.3 of methyl alcohol, and 1 in 9 of propylene glycol; freely soluble in acetone and in dimethylformamide. Store at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

Miconazole Nitrate (BANM, USAN, rINNM)

Miconazole, nitrate de; Miconazoli nitrás; Mikonatsolinitraatti; mikonazol Nitrat; Mikonazolnitrat; Mikonazol-nitrat; Mikonazolo nitratas; Mikonazolu azotan; Nitrato de miconazol; R-14889.

Миконазола Нитрат

C₁₈H₁₄Cl₄N₂O₃HNO₃ = 479.1.

CAS — 22832-87-7.

ATC — A01AB09; A07AC01; D01AC02; G01AF04; J02AB01; S02AA13.

ATC Vet — QA01AB09; QA07AC01; QD01AC02; QG01AF04; QJ02AB01; QS02AA13.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US*.

Ph. Eur. 6.2 (Miconazole Nitrate). A white or almost white powder. Very slightly soluble in water; slightly soluble in alcohol; sparingly soluble in methyl alcohol. Protect from light.

USP 31 (Miconazole Nitrate). A white or practically white, crystalline powder, with not more than a slight odour. Soluble 1 in 6250 of water, 1 in 312 of alcohol, 1 in 75 of methyl alcohol, 1 in 525 of chloroform, 1 in 1408 of isopropyl alcohol, 1 in 119 of propylene glycol; freely soluble in dimethyl sulfoxide; soluble in dimethylformamide; insoluble in ether. Protect from light.

Adverse Effects

After oral use of miconazole, nausea and vomiting have been reported, and also diarrhoea (usually on long-term treatment). There have been allergic reactions, rarely, and isolated reports of hepatitis.

Local irritation and sensitivity reactions may occur when miconazole nitrate is used topically; contact dermatitis has been reported.

After the intravenous infusion of miconazole, phlebitis, nausea, vomiting, diarrhoea, anorexia, pruritus, rash, febrile reactions, flushes, drowsiness, and hyponatraemia have been reported. Other effects include hyperlipidaemia, aggregation of erythrocytes, anaemia, and thrombocytosis. Transient tachycardia and other cardiac arrhythmias have followed the rapid intravenous injection of miconazole (but see also Effects on the Heart, below). Rare adverse effects include acute psychosis, arthralgia, and anaphylaxis. Many of these adverse effects have been associated with the injection vehicle, which contains polyoxy castor oil (p.1918).

Effects on the heart. Bradycardia, progressing to fatal ventricular fibrillation and cardiac arrest, occurred in a heart transplant patient during intravenous infusion of miconazole for an invasive fungal infection.¹

1. Coley KC, Crain JL. Miconazole-induced fatal dysrhythmia. *Pharmacotherapy* 1997; **17:** 379-82.

Overdosage. A report¹ of a generalised tonic-clonic convolution that occurred in an infant 10 to 15 minutes after the inadvertent infusion of miconazole 500 mg instead of 50 mg.

1. Coulthard K, et al. Convulsions after miconazole overdose. *Med J Aust* 1987; **146:** 57-8.

Precautions

Miconazole oral gel should be avoided in patients with hepatic impairment.

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

Miconazole has been fetotoxic at high doses in *animals* and its use is generally not recommended during pregnancy. For a discussion of the caution needed when using azole antifungals during pregnancy, see under Pregnancy in Precautions of Fluconazole, p.532.

Porphyria. Miconazole is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *in-vitro* systems.

Interactions

Miconazole can inhibit the metabolism of drugs metabolised by the cytochrome P450 isoenzymes CYP3A4 and CYP2C9, and may thus have effects similar to those of fluconazole (p.532). Miconazole may enhance the activity of oral anticoagulants, sulfonylurea hypoglycaemics, or phenytoin. Adverse effects have been reported when miconazole was given with carbamazepine.

There is a risk of cardiac arrhythmias if miconazole is used with astemizole, cisapride, or terfenadine and such combinations should be avoided.

Anticoagulants. The anticoagulant activity of coumarin anticoagulants can be potentiated by miconazole given orally,¹ intravaginally,² or topically.³ As of December 2002 the Australian Adverse Drug Reactions Advisory Committee had received 18 reports of significant increases in the INR of patients previously stabilised on warfarin within 1 to 2 weeks of starting treatment with miconazole oral gel.⁴

1. Ortín M, et al. Miconazole oral gel enhances acenocoumarol anticoagulant activity: a report of three cases. *Ann Pharmacother* 1999; **33**: 175-7.

2. Lansdorp D, et al. Potentiation of acenocoumarol during vaginal administration of miconazole. *Br J Clin Pharmacol* 1999; **47**: 225-26.

3. Devaraj A, et al. Interaction between warfarin and topical miconazole cream. *BMJ* 2002; **325**: 77.

4. Australian Adverse Drug Reactions Advisory Committee (ADRAC). Miconazole oral gel elevates INR—a reminder. *Aust Adverse Drug React Bull* 2002; **21**: 14. Available at: <http://www.tga.gov.au/adr/adrdb/addr0212.pdf> (accessed 28/06/05)

Antimicrobial Action

Miconazole is an imidazole antifungal with similar antimicrobial activity to that of ketoconazole (p.539). It also has some activity against *Aspergillus* spp., *Cryptococcus neoformans*, *Pseudallescheria boydii*, and some Gram-positive bacteria including staphylococci and streptococci.

References

1. Barasch A, Griffin AV. Miconazole revisited: new evidence of antifungal efficacy from laboratory and clinical trials. *Future Microbiol* 2008; **3**: 265-9.

Microbiological interactions. A study *in vitro* indicating antimicrobial synergism of miconazole and benzoyl peroxide against *Staphylococcus* spp. and *Propionibacterium acnes*.¹

For the effect on antifungal activity of giving azoles and amphotericin B together, see p.525.

1. Vanden Bossche H, et al. Synergism of the antimicrobial agents miconazole and benzoyl peroxide. *Br J Dermatol* 1982; **107**: 343-8.

Pharmacokinetics

Miconazole is incompletely absorbed from the gastrointestinal tract. Peak plasma concentrations of 1 microgram/mL are achieved about 4 hours after a dose of 1 g daily. Over 90% is reported to be bound to plasma proteins.

Miconazole is metabolised in the liver to inactive metabolites. From 10 to 20% of an oral dose is excreted in the urine, mainly as metabolites, within 6 days. About 50% of an oral dose may be excreted unchanged in the faeces. The elimination pharmacokinetics of micona-

zole have been described as triphasic, with a biological half-life of about 24 hours.

Very little miconazole is removed by haemodialysis.

There is little absorption through skin or mucous membranes when miconazole nitrate is applied topically.

Reviews

1. Daneshmand TK, Warnock DW. Clinical pharmacokinetics of systemic antifungal drugs. *Clin Pharmacokinet* 1983; **8**: 17-42.

Uses and Administration

Miconazole is an imidazole antifungal used as miconazole base or nitrate in the treatment of superficial candidiasis (p.518), and of the skin infections dermatophytosis and pityriasis versicolor (p.521). It has also been given intravenously by infusion in the treatment of disseminated fungal infections, but other azoles are now more commonly used.

Miconazole may be given orally as a gel containing 20 mg/g (24 mg/mL) for the treatment of oropharyngeal and intestinal candidiasis. The usual adult dose is 5 to 10 mL four times daily (equivalent to a total of about 15 mg/kg daily). Children under the age of 2 years may be given the oral gel in a dose of 2.5 mL twice daily; those aged between 2 and 6 years, 5 mL twice daily; and those aged over 6 years, 5 mL four times daily. For the treatment of oral lesions the oral gel is applied directly.

Miconazole nitrate is usually applied twice daily as a 2% cream, lotion, or powder in the treatment of fungal infections of the skin including candidiasis, dermatophytosis, and pityriasis versicolor. In the treatment of vaginal candidiasis, 5 g of a 2% intravaginal cream is inserted into the vagina once daily for 10 to 14 days or twice daily for 7 days. Miconazole nitrate pessaries may be inserted in dosage regimens of 100 mg once daily for 7 or 14 days, 100 mg twice daily for 7 days, 200 or 400 mg daily for 3 days, or in a single dose of 1200 mg.

Acanthamoeba keratitis. Miconazole has been applied topically in *Acanthamoeba* keratitis (p.822) in combination with systemic treatment with either ketoconazole or itraconazole.

Skin disorders. Topical preparations containing an imidazole such as ketoconazole or miconazole, usually with hydrocortisone, are used in the management of *seborrhoeic dermatitis* (p.1584). A cream containing miconazole nitrate 2% and benzoyl peroxide 5% has been used topically in the treatment of acne (p.1577).

Preparations

BP 2008: Miconazole and Hydrocortisone Acetate Cream; Miconazole and Hydrocortisone Cream; Miconazole and Hydrocortisone Ointment; Miconazole Cream; Miconazole Oromucosal Gel;

USP 31: Miconazole Injection; Miconazole Nitrate Cream; Miconazole Nitrate Topical Powder; Miconazole Nitrate Vaginal Suppositories.

Proprietary Preparations

(details are given in Part 3)

Arg.: Daktarin; Deralbine; Gynotran; Miconol; Micotral; Micotrim S[†]; Monizol; Nedit; Salcrem; Miconazol[†]; **Austral.:** Daktarin; Eulactol; Hairscience Anti-Dandruff; Monistat; Resolve; Resolve Thrush; **Austria:** Daktarin; Gyno-Daktarin; **Belg.:** Daktarin; Gyno-Daktarin; Zymycan; **Braz.:** Anfugiton; Bioldol[†]; Ciconazol; Daknax[†]; Daktarin; Daktazol; Ginedak; Gino-Daczel; Ginotran; Gyno-Daktarin; Micofin; Micotran; Micosen; Mycosin; Vodol; **Canad.:** Micatin; Micozole; Monazole[†]; Monistat; **Chile:** Daktarin; Fungos; ZeaSorb AF; **Cz.:** Daktarin[†]; **Denn.:** Bremadol[†]; Brentani; **Fin.:** Daktarin; Gyno-Daktarin; Medizol[†]; **Frl.:** Daktarin; Gyno-Daktarin; **Ger.:** Amykon[†]; Castellani mit Miconazol[†]; Daktarin; Decomyk; Derma-Mykotal; Fungur M; Gyno-Mykotal; InfestoSoor; Micobeta; Micotar; Mykoderm; Mykoderm Mund-Gel; Mykotin; Vobamyk; **Gr.:** Daktarin; Fantersol; Medacter; Mezolian; Uhtano; **Hong Kong:** Daktarin; Zole; **Indon.:** Daktarin; Fungares; Micoskin; Micrem; Moladerm; Mycorine; Sporene; **Irl.:** Daktarin; Gyno-Daktarin; **Israel:** Daktarin; Fungiderm; Gyno-Daktarin; Hifa Femme K-Mizol; Lotrimin AF; Micoffen; Mindosan V[†]; Nacomic; Neomic; Nilmic; Nisicam; Oz Crema; Piat[†]; Vigasil; **Neth.:** Daktarin; Dermacure; Gyno-Daktarin; Kruidvat; Antischimmelcreme; Zymycan; **Norw.:** Daktarin; **Nz.:** Daktarin; Fungo; Hairsience Anti-dandruff[†]; Micozole; Micreme; Monistat; **Philipp.:** Daktarin; De-Ol; Defungin; Fungtopic; Monistat; **Pol.:** Daktarin; Gyno-Femidazol; Miconal; **Port.:** Daktarin; Gyno-Daktarin; Mican; Zymycan; **Rus.:** Daktarin (Дактарин); Gynezel (Гинезел); **S.Afr.:** Covarex; Daktarin; Dermazole; Gyno-Daktarin; Gynospor; **Singapore:** Antifungal; Daktarin; Decozol; Fungot; Hairscience[†]; Liconar; Micon; Minazol; Mycoban; Resolve; Zarin; **Spain:** Daktarin; Fungisidin; Pasedon;

Tremix; **Swed.:** Daktar; **Switz.:** Daktarin; Dumicoat[†]; Monistat; **Thail.:** Daktarin; Dermor; Funcort[†]; Fungi-M; Fungisil; Liconar[†]; Micazin; Misone[†]; Mycoscot; Nican; Noraxin; Podakin; Ranozol; Skindure; Tara; **Turk.:** Fun-gut; Mikro-Penetrant; **UAE:** Gyno-Mikozal; Mikozal; **UK:** Daktarin; Gyno-Daktarin; Loramy[†]; **USA:** Absorbine Antifungal Foot Powder[†]; Breezee Mist Antifungal[†]; Fungoid; Lotrimin AF; M-Zole; Maximum Strength Desenex Antifungal[†]; Micatin; Monistat; Neosporin AF; Podactin; Prescription Strength Desenex; Ting; Vagistat-3; ZeaSorb AF; **Venez.:** Canidazol[†]; Daktarin; Drinax[†]; Gyno-Daktarin.

Multi-ingredient: **Arg.:** Adenil; Betacort Plus; Blamy; Ciprocort; Cuta Crema; Daktozin; Delisan; Denvercrem; Dermizol Trio; Dermosana; Factor Dermico; Gentasol; Ginal Cent; Ginkan; Gynormal; Hifamoren; Crema; La-dylen; Lazar-Cort Complex; Linfol Cicatrizante; Macril; Mailen; Miklogen; Monizol Cort; Monizol Cort Crema; Ovumix; Pentol; Protiderm; Septigen; Triboicort; Triliver; Triplex; Vagical Plus; **Austral.:** Daktozin; Resolve; Resolve Plus; Resove Tinea; **Austria:** Acne Plus; **Belg.:** Acneplus; Daktacort; Daktozin; **Braz.:** Ampilim-G; Anfugine; Daktozin; Facyl M; Gino Pleti; Ginosutin M; Tizonil M[†]; Tizonol M[†]; **Chile:** Doxifem; Famidal; Famidal Ad[†]; Ginecapat; Ginecopast Dual; Ginedazol Dual; Medidos; Mizonase; **Cz.:** Daktozin[†]; Klon-D; Mycosolon[†]; **Denn.:** Bremacet; **Fin.:** Daktacort; **Fr.:** Squaphane Squaphane E; Squaphane Masque-Creme; Squaphane P; Squaphane S; **Ger.:** Acne Plus; Decoderm tri; InfectoSoor; Micotar ZP; Vobaderm; **Gr.:** Antimycotic; Catigel; Combi; Conazol; Daktor; Doromycin; Edmuco; Expertine; Feminella; Finicort; Flenezol; Fluniprol; Flunovon; Fosemyk; Fumicon; Micoflup; Micogen; Miller; Oxygen; Pandem; Panmyk; Sarmel; Verdal; **Hong Kong:** Conazole; Daktacort; Fungo Soothing Balm; Hydro-Funga; Micosone; Klon-D; Mycosolon; **Ind.:** Bataim-GM; Betnovate-M; Candizole-T; Cloderm GM; Daktacort; Eumosone-M; Flucort-MZ; Flucreme NM; Lobate-GM; Lobate-M; Micogel F; Stecto-NM; Tenovate M; Valbet; Zole-It; **Indon.:** Benosol M; Brentan; Daktarin; Diaper; Theoret; Zolacat; **Irl.:** Daktacort; **Israel:** Daktacort; **Ital.:** Acnidazil; **Malaysia:** Beca-cort; Daktacort; Decocort; Miconazole H[†]; Neo-Penorat; Setarin H[†]; Zaricort[†]; **Mex.:** Bebetin; Daktacort; Gynotran; **Neth.:** Acnecare; Acne-re[†]; Acnidazil[†]; Daktacort; **Norw.:** Daktacort; Daktacort; **NZ.:** Daktacort; Daktozin[†]; Fungocort[†]; Micrem H; Daktacort; Neo-Penorat; **Pol.:** Daktacort; Mycosolon (Микозолон); Neo-Penorat (Нено-Пенорат); **Swed.:** Cirtimyx; Daktacort; Decocort; Micon-H; Neo-Penorat; Tri-Micon; Zaricort; **Spain:** Bexicort; Blastoestimulina; Brentan; Dermisdin[†]; Nutracel; **Swed.:** Cirtimyx; Daktacort; **Switz.:** Acne Creme Plus; Daktacort; Decoderm bivalent; **Thail.:** Daktacort; Decocort; Fungisil-T; Kelaplus; Ladocort; Tira-Plus; Timi; Trimicon; **Turk.:** Neo-Penorat; Nidazol-M; **UK:** Daktozin; Daktacort; Daktacort HC; **USA:** Fungoid HC; **Venez.:** Daktozin.

Naftifine Hydrochloride (BANM, USAN, rINN)

AW-105-843; Hidrocloruro de naftifina; Naftifin; Hidroklorür; Naftifine, Chlorhydrate de; Naftifini Hydrochloridum; Naftifungin Hydrochloride; SN-105-843 (naftifine). (E)-N-Cinnamyl-N-methyl(1-naphthylmethyl)amine hydrochloride.

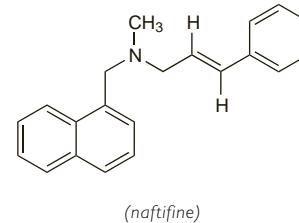
Нафтифина Гидрохлорид

$C_21H_{21}N \cdot HCl = 323.9$

CAS — 65472-88-0 (naftifine); 65473-14-5 (naftifine hydrochloride).

ATC — D01AE22.

ATC Vet — QD01AE22.



(naftifine)

Pharmacopoeias. In US.

USP 31 (Naftifine Hydrochloride). Store in airtight containers.

Profile

Naftifine hydrochloride is an allylamine derivative (see Terbinafine, p.546) which is fungicidal against dermatophytes, but only fungistatic against *Candida* spp.

Naftifine hydrochloride 1% is applied topically once or twice daily for fungal skin infections, particularly dermatophytosis (see Skin Infections, p.521).

Local reactions such as burning or stinging may occur.

Reviews

1. Gupta AK, et al. Naftifine: a review. *J Cutan Med Surg* 2008; **12**: 51-8.

Preparations

USP 31: Naftifine Hydrochloride Cream; Naftifine Hydrochloride Gel.

Proprietary Preparations

(details are given in Part 3)

Austria: Beneut; Exoderil; **Canad.:** Naftin; **Cz.:** Exoderil; **Ger.:** Exoderil; **Hong Kong:** Exoderil; **Hung.:** Exoderil; **Indon.:** Exoderil; **Israel:** Exoderil; **Ital.:** Sudian; **Malaysia:** Exoderil; **Pol.:** Exoderil; **Rus.:** Exoderil (Экодерил); **Singapore:** Exoderil[†]; **Spain:** Micosona; **Turk.:** Exoderil; **USA:** Naftin.