Profile
Liranaftate 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.

Mepartricin *(BAN, USAN, rINN)*

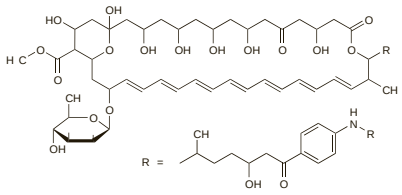
Mepartricina; Mépartricine; Mepartricinum; Methylpartricin; SN-654; SPA-S-160.

Мепартрицин

CAS — 11121-32-7.

ATC — A01AB16; D01AA06; G01AA09; G04CX03.

ATC Vet — QA01AB16; QD01AA06; QG01AA09; QG04CX03.



Mepartricin A: R = CH
Mepartricin B: R = H

Profile
Mepartricin 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 mepartricin sodium laurilsulfate is also used. Oral mepartricin 40 mg daily is used in the treatment of some prostate disorders.

Prostate disorders. Studies[1,2] have shown that mepartricin 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] Mepartricin is thought to reduce cholesterol, oestrogen, and androgen binding to the prostate. Similarly, another study[3] has shown that the same dose of mepartricin 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 mepartricin 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 mepartricin in the treatment of BPH. *Prostate* 1998; **37:** 246–52.
3. De Rose AF, *et al.* Role of mepartricin 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.:*** Ipertrofan; ***Ital.:*** Ipertrofan; Tricandil; ***Philipp.:*** Ipertrofan; ***Pol.:*** Ipertrofan; ***Port.:*** Iperplasin; Ipertrofan; Tricandil.

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

Micafungin Sodium *(USAN, rINNM)*

FK-463; Micafungina sódica; Micafungine Sodique; Natrii Micafunginum. 5-((1*S*,2*S*)-2-{(2*R*,6*S*,9*S*,11*R*,12*R*,14a*S*,15*S*,16*S*,20*S*,23*S*,25a*S*)-20-[(1*R*)-3-Amino-1-hydroxy-3-oxopropyl]-2,11,12,15-tetrahydroxy-6-[(1*R*)-1-hydroxyethyl]-16-methyl-5,8,14,19,22,25-hexaoxo-9-[(4-{5-[4-(pentyloxy)phenyl]isoxazol-3-yl}benzoyl)amino]tetracosahydro-1*H*-dipyrrolo[2,1-*c*:2′,1′-*l*][1,4,7,10,13,16]hexaazacyclohenicosin-23-yl}-1,2-dihydroxyethyl)-2-hydroxyphenyl sodium sulfate.

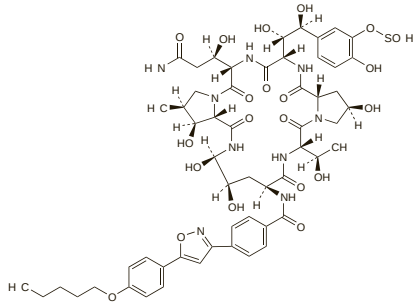
Натрий Микафунгин

$C_{56}H_{70}N_9NaO_{23}S$ = 1292.3.

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

ATC — J02AX05.

ATC Vet — QJ02AX05.



Adverse Effects
As for Caspofungin, p.528. Isolated cases of renal dysfunction or acute renal failure have also occurred in patients taking micafungin.

Precautions
Patients who develop abnormal liver or renal function tests while taking micafungin should be monitored for deterioration in hepatic or renal function respectively.

Interactions
Micafungin may increase the area under the concentration-time curve for nifedipine and sirolimus.

Antimicrobial Action
As for Caspofungin, p.528.

Pharmacokinetics
Micafungin is absorbed from the gastrointestinal tract after oral doses. It is more than 99% bound to plasma proteins, mainly albumin.

Micafungin is metabolised by arylsulfatase to its catechol form and further metabolised to the methoxy form by catechol-*O*-methyltransferase. Some hydroxylation to micafungin via cytochrome P450 isoenzymes also occurs.

After 28 days about 71% of a dose is recovered in the faeces and 12% in the urine. Mean half-lives of 14.0 to 17.2 hours have been reported.

Uses and Administration
Micafungin is an echinocandin antifungal with general properties similar to those of caspofungin (p.528). It is used for the treatment and prophylaxis of candidiasis and also in the treatment of aspergillosis. It is given as the sodium salt by intravenous infusion in doses of 50 mg once daily for candidiasis. For the treatment of oesophageal candidiasis the recommended dose is 150 mg daily. For aspergillosis 50 to 150 mg is given once daily. Doses up to 300 mg daily have been used in severe or refractory disease. A dose of 50 mg daily is used for prophylaxis of candidiasis in patients undergoing haematopoietic stem cell transplantation.

◊ Reviews.

1. Denning DW. Echinocandin antifungal drugs. *Lancet* 2003; **362:** 1142–51.
2. Jarvis B, *et al.* Micafungin. *Drugs* 2004; **64:** 969–84.
3. Carver PL. Micafungin. *Ann Pharmacother* 2004; **38:** 1707–21.
4. van Burik JA, *et al.* Micafungin versus fluconazole for prophylaxis against invasive fungal infections during neutropenia in patients undergoing hematopoietic stem cell transplantation. *Clin Infect Dis* 2004; **39:** 1407–16.
5. Chandrasekar PH, Sobel JD. Micafungin: a new echinocandin. *Clin Infect Dis* 2006; **42:** 1171–8.
6. Fritz JM, *et al.* Micafungin for the prophylaxis and treatment of Candida infections. *Expert Rev Anti Infect Ther* 2008; **6:** 153–62.

Preparations
Proprietary Preparations (details are given in Part 3)
Jpn: Funguard; ***UK:*** Mycamine; ***USA:*** Mycamine.

Miconazole *(BAN, rINN)*

Miconazol; Miconazolum; Mikonatsoli; Mikonazol; Mikonazolas; R-18134. 1-[2,4-Dichloro-β-(2,4-dichlorobenzyloxy)phenethyl]imidazole.

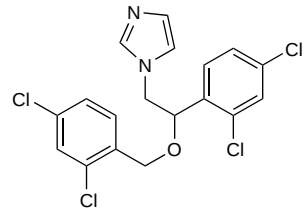
Миконазол

$C_{18}H_{14}Cl_4N_2O$ = 416.1.

CAS — 22916-47-8.

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

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



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 nitras; Mikonatsolinitraatti; mikonazol Nitrat; Mikonazolnitrat; Mikonazol-nitrát; Mikonazolo nitratas; Mikonazolu azotan; Nitrato de miconazol; R-14889.

Миконазола Нитрат

$C_{18}H_{14}Cl_4N_2O,HNO_3$ = 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 polyoxyl 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 report[1] of a generalised tonic-clonic convulsion 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.