one week after symptoms have cleared and cultures have become negative. Some infections may require several months of treatment and giving ketoconazole for such prolonged periods may increase the risk of hepatotoxicity.

A dose of 400 mg once daily for 5 days is used for the treatment of chronic vaginal candidiasis.

Ketoconazole is applied topically as a 2% cream in the treatment of candidal or dermatophyte infections of the skin, or in the treatment of pityriasis versicolor. It is used once or twice daily and continued for at least a few days after the disappearance of symptoms. A foam containing 2% ketoconazole applied twice daily for 4 weeks may be used in the treatment of seborrhoeic dermatitis. A shampoo containing 1 or 2% ketoconazole is also used; it is applied twice weekly for 2 to 4 weeks (or occasionally longer) in the treatment of dandruff or seborrhoeic dermatitis. The 2% shampoo is used once daily for up to 5 days in pityriasis versicolor. For prophylaxis of seborrhoeic dermatitis the 2% shampoo is used once every 1 to 2 weeks; for prophylaxis of pityriasis versicolor it may be used once daily for a maximum of 3 days before exposure to sunshine.

Acanthamoeba infections. Although there is currently no established treatment for granulomatous amoebic encephalitis, ketoconazole may have some activity against the *Acanthamoeba* spp. responsible for this infection and has been applied topically to skin lesions. Ketoconazole has also been suggested for *Acanthamoeba* keratitis (p.822), when it has been given orally with topical miconazole.

Acute respiratory distress syndrome. In two small double-blind, controlled trials,[1,2] the development of acute respiratory distress syndrome (ARDS—p.1498) and mortality rates were lower in high-risk patients given ketoconazole than in those given placebo. An accompanying editorial[3] commented that adequate blood concentrations appeared to be essential. The mode of action could be associated with inhibition of leukotriene and thromboxane synthesis.[2,3] Nevertheless, in a study in 234 patients,[4] ketoconazole failed to reduce mortality or improve clinical outcomes when given early in the course of ARDS. Some centres have developed guidelines for ketoconazole prophylaxis in patients at risk of ARDS.[5]

1. Slotman GJ, *et al.* Ketoconazole prevents acute respiratory failure in critically ill surgical patients. *J Trauma* 1988; **28:** 648–54.
2. Yu M, Tomasa G. A double-blind, prospective, randomized trial of ketoconazole, a thromboxane synthetase inhibitor, in the prophylaxis of the adult respiratory distress syndrome. *Crit Care Med* 1993; **21:** 1635–42.
3. Slotman GJ. Ketoconazole: maybe it isn't the magic potion, but ... *Crit Care Med* 1993; **21:** 1642–4.
4. The ARDS Network Authors. Ketoconazole for early treatment of acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. *JAMA* 2000; **283:** 1995–2002.
5. Sinuff T, *et al.* Development, implementation, and evaluation of a ketoconazole practice guideline for ARDS prophylaxis. *J Crit Care* 1999; **14:** 1–6.

Blastomycosis. Ketoconazole has largely been replaced by itraconazole as the azole of choice in the treatment of blastomycosis (p.518) because of its higher incidence of adverse effects, and lower efficacy. If used as an alternative it is given in doses of 400 to 800 mg daily.[1]

1. Chapman SW, *et al.* Clinical practice guidelines for the management of blastomycosis: 2008 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2008; **46:** 1801–12. Also available at: http://www.journals.uchicago.edu/doi/pdf/10.1086/588300 (accessed 03/07/08)

Endocrine disorders and malignant neoplasms. Ketoconazole has been reported to impair steroid hormone synthesis[1] and to blunt the response of cortisone to adrenocorticotrophic hormone (ACTH)[2] and has been tried in the management of a number of endocrine disorders.

In **Cushing's syndrome** (p.2344), ketoconazole in doses of up to 1200 mg daily has been used successfully as an alternative or adjuvant to definitive therapies such as surgery or radiotherapy.[3-6]

Treatment of **hirsutism** is usually with an anti-androgen (see under Cyproterone, p.2089), but ketoconazole has been tried in small numbers of women at a dose of 300 mg daily[7] or 400 mg daily,[8,9] with variable results.

Ketoconazole has been reported to produce a beneficial response in some forms of **precocious puberty** (p.2081) that do not generally respond to gonadorelin analogues; cessation of menstruation and regression of pubertal signs in girls[10] and reduced testosterone secretion and increase in adult height in boys[11-13] has been noted in small numbers of patients studied.

The anti-androgenic effects of ketoconazole have also been found useful in the management of **prostatic cancer** (p.671) in selected patients,[14-18] although there have been some concerns about its tolerability,[17] and it is not generally used as a first-line treatment.

Ketoconazole was ineffective in suppressing **postoperative erection** in patients undergoing penile reconstructive surgery.[19]

1. Pont A, *et al.* Ketoconazole blocks adrenal steroid synthesis. *Ann Intern Med* 1982; **97:** 370–2.
2. White MC, Kendall-Taylor P. Adrenal hypofunction in patients taking ketoconazole. *Lancet* 1985; **i:** 44–5.
3. Winquist EW, *et al.* Ketoconazole in the management of paraneoplastic Cushing's syndrome secondary to ectopic adrenocorticotropin production. *J Clin Oncol* 1995; **13:** 157–64.
4. Estrada J, *et al.* The long-term outcome of pituitary irradiation after unsuccessful transsphenoidal surgery in Cushing's disease. *N Engl J Med* 1997; **336:** 172–7.
5. Berwaerts JJ, *et al.* Corticotropin-dependent Cushing's syndrome in older people: presentation of five cases and therapeutical use of ketoconazole. *J Am Geriatr Soc* 1998; **46:** 880–4.
6. Chou SC, Lin JD. Long-term effects of ketoconazole in the treatment of residual or recurrent Cushing's disease. *Endocr J* 2000; **47:** 401–6.
7. Venturoli S, *et al.* A prospective randomized trial comparing low dose flutamide, finasteride, ketoconazole, and cyproterone acetate-estrogen regimens in the treatment of hirsutism. *J Clin Endocrinol Metab* 1999; **84:** 1304–10.
8. Sonino N, *et al.* Low-dose ketoconazole treatment in hirsute women. *J Endocrinol Invest* 1990; **13:** 35–40.
9. Venturoli S, *et al.* Ketoconazole therapy for women with acne and/or hirsutism. *J Clin Endocrinol Metab* 1990; **71:** 335–9.
10. Syed FA, Chalew SA. Ketoconazole treatment of gonadotropin independent precocious puberty in girls with McCune-Albright syndrome: a preliminary report. *J Pediatr Endocrinol Metab* 1999; **12:** 81–3.
11. Bertelloni S, *et al.* Long-term outcome of male-limited gonadotropin-independent precocious puberty. *Horm Res* 1997; **48:** 235–9.
12. Soriano-Guillén L, *et al.* Adult height after ketoconazole treatment in patients with familial male-limited precocious puberty. *J Clin Endocrinol Metab* 2005; **90:** 147–51.
13. Almeida MQ, *et al.* Long-term treatment of familial male-limited precocious puberty (testotoxicosis) with cyproterone acetate or ketoconazole. *Clin Endocrinol (Oxf)* 2008; **69:** 93–98.
14. Lowe FC, Bamberger MH. Indications for use of ketoconazole in management of metastatic prostate cancer. *Urology* 1990; **36:** 541–5.
15. Mahler C, *et al.* Ketoconazole and liarozole in the treatment of advanced prostatic cancer. *Cancer* 1993; **71:** 1068–73.
16. Small EJ, *et al.* Ketoconazole retains activity in advanced prostate cancer patients with progression despite flutamide withdrawal. *J Urol (Baltimore)* 1997; **157:** 1204–7.
17. Bok RA, Small EJ. The treatment of advanced prostate cancer with ketoconazole: safety issues. *Drug Safety* 1999; **20:** 451–8.
18. Pettaway CA, *et al.* Neoadjuvant chemotherapy and hormonal therapy followed by radical prostatectomy: feasibility and preliminary results. *J Clin Oncol* 2000; **18:** 1050–7.
19. DeCastro BJ, *et al.* Oral ketoconazole for prevention of postoperative penile erection: a placebo controlled, randomized, double-blind trial. *J Urol (Baltimore)* 2008; **179:** 1930–2.

Hypercalcaemia. Ketoconazole has been used[1,2] in the treatment of hypercalcaemia (p.1668). It acts to reduce 1,25-dihydroxycholecalciferol concentrations by inhibiting cytochrome P450-dependent 1α-hydroxylation of vitamin D.

1. Yavuz H. Familiar drugs for the treatment of hypercalcemia. *J Pediatr* 1998; **133:** 311.
2. Young C, *et al.* Hypercalcaemia in sarcoidosis. *Lancet* 1999; **353:** 374.

Leishmaniasis. As discussed on p.824, ketoconazole has been tried as an alternative to conventional first- and second-line therapy for visceral leishmaniasis,[1,2] although reports of treatment have not all been favourable.[3,4]

It has also been tried in cutaneous leishmaniasis. A cure rate of 70% was reported in over 100 patients with *Leishmania major* infections treated with oral ketoconazole 200 to 400 mg daily for 4 to 6 weeks. Ketoconazole was not considered to be effective in infections due to *L. tropica*, *L. aethiopica*,[5] or *L. guyanensis*.[6] Ketoconazole 600 mg daily for 28 days has produced similar results to sodium stibogluconate intramuscularly for 20 days in patients with cutaneous leishmaniasis due to *L. panamensis*.[7] A further comparative study[8] of 96 patients being treated for cutaneous leishmaniasis, caused mainly by *L. major* or *L. tropica*, found ketoconazole given in doses of 600 mg in adults or 10 mg/kg in children for 30 days to be more effective than 6 to 8 bi-weekly intralesional injections of meglumine antimonate. In another study,[9] ketoconazole was less effective than sodium stibogluconate when cutaneous leishmaniasis was due to *L. braziliensis*, but more effective when *L. mexicana* was the cause.

1. Wali JP, *et al.* Ketoconazole in treatment of visceral leishmaniasis. *Lancet* 1990; **330:** 810–11.
2. Wali JP, *et al.* Ketoconazole in the treatment of antimony- and pentamidine-resistant Kala-azar. *J Infect Dis* 1992; **166:** 215–16.
3. Sundar S, *et al.* Ketoconazole in visceral leishmaniasis. *Lancet* 1990; **336:** 1582–3.
4. Rashid JR, *et al.* The efficacy and safety of ketoconazole in visceral leishmaniasis. *East Afr Med J* 1994; **71:** 392–5.
5. Weinrauch L, *et al.* Ketoconazole in cutaneous leishmaniasis. *Br J Dermatol* 1987; **117:** 666–7.
6. Dedet J-P, *et al.* Failure to cure Leishmania braziliensis guyanensis cutaneous leishmaniasis with oral ketoconazole. *Trans R Soc Trop Med Hyg* 1986; **80:** 176.
7. Saenz RE, *et al.* Efficacy of ketoconazole against Leishmania braziliensis panamensis cutaneous leishmaniasis. *Am J Med* 1990; **89:** 147–55.
8. Salmanpour R, *et al.* Comparative study of the efficacy of oral ketoconazole with intra-lesional meglumine antimoniate (Glucantime) for the treatment of cutaneous leishmaniasis. *J Dermatol Treat* 2001; **12:** 159–62.
9. Navin TR, *et al.* Placebo-controlled clinical trial of sodium stibogluconate (Pentostam) versus ketoconazole for treating cutaneous leishmaniasis in Guatemala. *J Infect Dis* 1992; **165:** 528–34.

Preparations

USP 31: Ketoconazole Oral Suspension; Ketoconazole Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: C-86; Cetonil; Eumicel; Faction; Fangan; Fitonal; Fungicil†; Grenfung; Keduo; Ketogel†; Ketolef; Ketonazol; Ketozol†; Krol†; Micoespec K; Micoral; Orifungal; Perative; Quadion; Socosep; Tersoderm Plus†; Tikl; Triatop†; ***Austral.:*** Daktagold†; Hexal Konazol Shampoo; Nizoral; Sebizole; ***Austria:*** Fungoral; Nizoral; ***Belg.:*** Docketoral; Nizoral; ***Braz.:*** Aciderm; Arcolan; Candiderm; Candoral; Cetocona†; Cetoconalab; Cetohexal†; Cetomed; Cetomicoss†; Cetomizol; Cetonax; Cetoneo; Cetonil; Cetonin; Cetozan; Cetozaz†; Cetozol; Fungoral†; Ketomicol†; Ketonan†; Ketonazol; Lozan; Miconan; Micoral; Nizoral; Nizoretic; Noriderm; Noronal; Sioconazol†; Tonazox†; Zanoc; Zolmicol; ***Canad.:*** Ketoderm; Nizoral; ***Chile:*** Arcolane; Biogel; Eprofil†; Fungarest; Fungium; Ketonil†; Soridermal; TKC; ***Cz.:*** Asquam; Nizoral; Orozanol†; ***Denm.:*** Kezoral; Nizoral; ***Fin.:*** Nizoral; ***Fr.:*** Ketoderm; Ketolium; Nizoral; ***Ger.:*** Nizoral; Terzolin; ***Gr.:*** Abba; Adenosan; Aquarius; Botaderm; Cezolin; Ebersept; Flidaphen; Fungoral; Ilgem; Libroman; Mycofebrin; Neo-egmol; Nyoxep; Scalpin; Sostatin; Vafluson†; ***Hong Kong:*** Diazon; Fluzoral; Fungazol; Ketozol; Ketozole; Larry; Nizoral; Pristine; Pristinex; Sebizole†; Stada K; Synizoral; ***Hung.:*** Ketospor; Nizoral; ***India:*** Arcolane; Danfree; Danruf; Funazole; Fungicide; Hyphoral; Keto; ***Indon.:*** Anfuhex; Dermaral; Dexazol; Dysfungal; Fexazol; Formyco; Funet; Fungasol; Fungoral; Interzol; Ketomed; Lusanoc; Micoticum; Muzoral; Mycoderm; Mycoral; Mycozid; Nizol; Nizoral; Nofung; Picamic; Profungal; Solinfec; Sporex; Thicazol; Wizol; Zoloral; Zoralin; Zumazol; ***Irl.:*** Nizoral; ***Israel:*** Nizoral; ***Ital.:*** Nizoral; Triatop; ***Malaysia:*** Dezor; Fungazol; Funginox; Ketozole†; Kezoral; Larry; Nizoral; Pristine†; Pristinex†; Sebizole†; Sunazol†; Yucomy; Ziconal†; ***Mex.:*** Akorazol; Apo-Kesol†; Biozoral; Conazol; Cremosan; Ergomicon; Eurolat; Fungipar; Fungoral; Fungosine; Honzil; Keprobiozol†; Kestomicol†; Ketofar; Ketomed; Ketomizol; Ketoril; Konaderm; Konaturil; Lemyken†; Lizovag; Lornazol†; Messelzol; Mi-Ke-Sons; Micoser; Micozol; Mycodib; Nastil; Nazolfarm; Nazoltec; Nizoral; Onofin-K; Prenalon; Remecon; Strizole; Termizol; Tiniasil; Tiniazol; Tocomizol†; Toconal; Tolcrem; Tomiko; Triatop; ***Neth.:*** Nizoral; ***Norw.:*** Fungoral; Konazal; ***NZ:*** Daktagold; Ketopine; Nizoral; Sebizole; ***Philipp.:*** Ketovid; Nizoral; ***Pol.:*** Fungores; Nizoral; Noell; ***Port.:*** Farmorol; Frisol†; Frisolac; Micopar; Nizale; Nizoral; Rapamic; Tedol; ***Rus.:*** Livarole (Ливарол); Mycosoral (Микозорал); Nizoral (Низорал); ***S.Afr.:*** Adco-Dermed; Ketazol; Kez; Nizcreme; Nizoral; Nizorelle; Nizovules; Nizshampoo; ***Singapore:*** Antanazol; Beatoconazole; Dezor; Dezoral†; Diazon; Ketozole; Kezoral; Nicozone; Nitozol; Nizoral; Pristine; Pristinex; Profungal†; Sebizole; Yucomy; ***Spain:*** Fungarest; Fungo Farmasierra; Fungo Zeus; Keto-Cure; Ketoderma; Ketoisdin; Medezol; Micoticum; Panfungol; ***Swed.:*** Fundan; Fungoral; Ketoson; ***Switz.:*** Ketozol; Nizoral; Terzolin; ***Thai.:*** AC-FA; Chintaral; Dezor; Diazon; Fungazol; Fungiderm-K; Funginox; Kara†; Katsin; Kazinal; Kenalyn; Kenazol; Kenazole†; Kenoral; Ketazol†; Ketazon; Ketocine; Ketolan; Ketomed; Ketonazole; Ketoral†; Ketosil; Ketozal; Kezon; Konazol†; Lama; Larry; Manoketo; Masarol; Mizoron; Mycella; Myco; Mycoral; Ninazol; Nizoral; Nora†; Pasalen; Sporaxyl; Sporoxyl; Triatop†; ***Turk.:*** Fungoral; Ketoral; Konazol; Nizoral; ***UK:*** Daktarin Gold; Dandrazol; Dandrid; Nizoral; ***USA:*** Extina; Nizoral; Xolegel; ***Venez.:*** Arcolane; Danfree†; Freetop; Kenazol; Ketazol; Ketocoval†; Ketomed; Napox†; Nizoral; Noractin†; Topstar†.

Multi-ingredient: ***Arg.:*** Aeromicrosona C†; Bactisona; Ciprocort; Dercotex; Duo Minoxi†; Gentacler; Gynerium; Ketohair†; Linfol Dermico; Micozol Compuesto†; Microsona C; Ovogin; Prurisedan Biotic†; Start NP†; Torgyn Duo; Tricur; Tridermal; Triefect†; ***Braz.:*** Betazol Cort; Candicort; Capel; Celocort; Cetobeta; Cetocort; Cetocorten; Cimecort; Emscort; Naderm; Novacort; Trok; Trok-N; ***Chile:*** KPL†; ***India:*** Hyphoral; Scalpe; ***Ital.:*** Keto Z; Ketomousse; ***Malaysia:*** Ketoplus; ***Mex.:*** Femisan; Gynoclin-V; Trexen Duo; ***Philipp.:*** Scalpex; ***Rus.:*** Keto Plus (Кето Плюс); ***USA:*** Xolegel Duo.

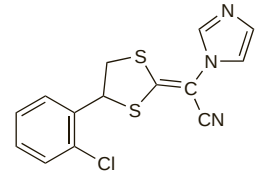
Lanoconazole *(rINN)*

Lanoconazol; Lanoconazolum; Latoconazole; NND-318; TJN-318. (±)-α-[(*E*)-4-(*o*-Chlorophenyl)-1,3-dithiolan-2-ylidene]imidazole-1-acetonitrile.

Ланоконазол

$C_{14}H_{10}ClN_3S_2$ = 319.8.

CAS — 101530-10-3.



Profile

Lanoconazole is an imidazole antifungal used topically in the treatment of fungal skin infections as a 1% cream, ointment, or solution, applied once daily. 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)

Jpn: Astat; ***Port.:*** Micoder.

Liranaftate *(rINN)*

Liranaftato; Liranaftatum; M-732; Piritetrate. *O*-5,6,7,8-Tetrahydro-2-naphthyl 6-methoxy-*N*-methylthio-2-pyridinecarbamate.

Лиранафтат

$C_{18}H_{20}N_2O_2S$ = 328.4.

CAS — 88678-31-3.

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)*

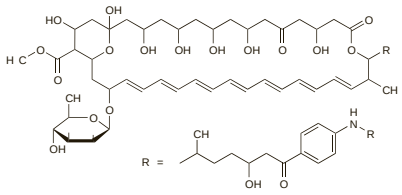
Mepartricina; Mépartricine; Mepartricinum; Methylpartricin; SN-654; SPA-S-160.

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.

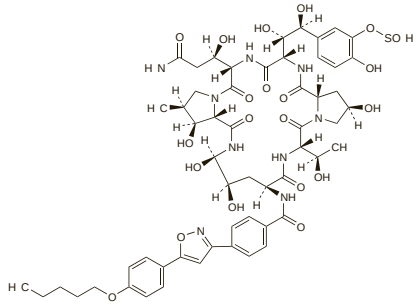
Натрий Микафунгин

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

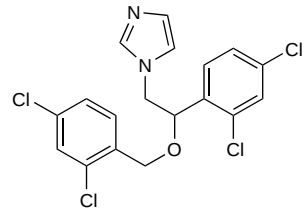
Миконазол

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