Ketoconazole *(BAN, USAN, rINN)*

Ketoconazol; Kétoconazole; Ketoconazolum; Ketokonatsoli; Ketokonazol; Ketokonazolas; R-41400. (±)-*cis*-1-Acetyl-4-{4-[2-(2,4-dichlorophenyl)-2-imidazol-1-ylmethyl-1,3-dioxolan-4-ylmethoxy]phenyl}piperazine.

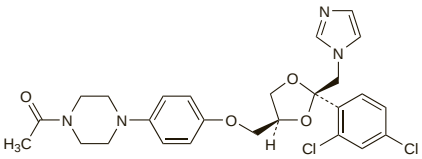
Кетоконазол

$C_{26}H_{28}Cl_2N_4O_4$ = 531.4.

CAS — 65277-42-1.

ATC — D01AC08; G01AF11; J02AB02.

ATC Vet — QD01AC08; QG01AF11; QJ02AB02.



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

Ph. Eur. 6.2 (Ketoconazole). A white or almost white powder. Practically insoluble in water; sparingly soluble in alcohol; freely soluble in dichloromethane; soluble in methyl alcohol. Protect from light.

Adverse Effects

Gastrointestinal disturbances are the most frequently reported adverse effect after the oral use of ketoconazole. Nausea and vomiting have been reported in about 3% of patients, and abdominal pain in about 1%. These adverse effects are dose-related and may be minimised by giving ketoconazole with food. Asymptomatic, transient elevations in serum concentrations of liver enzymes may occur in about 10% of patients. Hepatitis has been reported and the risk appears to increase if treatment with ketoconazole is continued for longer than 2 weeks; it is usually reversible on stopping ketoconazole but fatalities have occurred. Ketoconazole interferes with steroid biosynthesis and adverse endocrine effects include gynaecomastia, oligospermia, menstrual irregularities, and adrenal cortex suppression, especially at high doses.

Other adverse effects include allergic reactions such as urticaria and angioedema, and rare cases of anaphylaxis after the first dose have been reported. Pruritus, rash, alopecia, headache, dizziness, impotence, and somnolence may also occur. Thrombocytopenia, paraesthesia, raised intracranial pressure, and photophobia have been reported rarely.

After topical use of ketoconazole, irritation, dermatitis, or a burning sensation has occurred.

Effects on the blood. A case of fatal aplastic anaemia was reported[1] in a 23-year-old woman who had taken ketoconazole for 4 days for the treatment of vaginal discharge.

1. Duman D, *et al*. Fatal aplastic anemia during treatment with ketoconazole. *Am J Med* 2001; **111:** 737.

Effects on endocrine function. Oral ketoconazole blocks testosterone synthesis and adrenal response to corticotropin, resulting in azospermia and oligospermia, gynaecomastia, impotence and decreased libido, and adrenal insufficiency.[1-8] As an inhibitor of steroid production, ketoconazole is valuable in controlling hypercortisolism and is used therapeutically in some endocrine disorders and prostatic cancer. For further discussion see under Uses and Administration, below.

1. DeFelice R, *et al.* Gynecomastia with ketoconazole. *Antimicrob Agents Chemother* 1981; **19:** 1073–4.
2. Pont A, *et al.* High-dose ketoconazole therapy and adrenal and testicular function in humans. *Arch Intern Med* 1984; **144:** 2150–3.
3. White MC, Kendall-Taylor P. Adrenal hypofunction in patients taking ketoconazole. *Lancet* 1985; **i:** 44–5.
4. Dandona P, *et al.* Non-suppression of cortisol secretion by long term treatment with ketoconazole in patients with acute leukaemia. *J Clin Pathol* 1985; **38:** 677–8.
5. Pillans PI, *et al.* Hyponatraemia and confusion in a patient taking ketoconazole. *Lancet* 1985; **i:** 821–2.
6. McCance DR, *et al.* Acute hypoadrenalism and hepatotoxicity after treatment with ketoconazole. *Lancet* 1987; **i:** 573.
7. Best TR, *et al.* Persistent adrenal insufficiency secondary to low-dose ketoconazole therapy. *Am J Med* 1987; **82:** 676–80.
8. Khosla S, *et al.* Adrenal crisis in the setting of high-dose ketoconazole therapy. *Arch Intern Med* 1989; **149:** 802–4.

Effects on the liver. Hepatic adverse reactions to oral ketoconazole are well known.[1-4] Transient minor elevations of liver enzymes without clinical signs or symptoms of hepatic disease occur in about 10% of patients and may occur at any stage of treatment. Although this reaction is not usually clinically important it may signal the onset of more serious hepatic injury and indicates the need for close monitoring of liver function. Symptomatic hepatic reactions are much rarer (less than 0.1% of patients) but are potentially fatal. There is usually a hepatocellular pattern of damage and sometimes cholestasis. Patients at increased risk of hepatic injury include those with a history of liver disease, those aged over 50, especially women, and those requiring prolonged treatment. It is important to monitor liver function during treatment as well as to limit the length of treatment. If liver enzyme values continue to rise or jaundice or hepatitis occur, ketoconazole should be withdrawn immediately since fatalities have occurred in patients who continued treatment after signs of hepatic injury developed.

1. Janssen PA, Symoens JE. Hepatic reactions during ketoconazole treatment. *Am J Med* 1983; **74:** 80–5.
2. Lewis JH, *et al*. Hepatic injury associated with ketoconazole therapy. *Gastroenterology* 1984; **86:** 503–13.
3. Lake-Bakaar G, *et al*. Hepatic reactions associated with ketoconazole in the United Kingdom. *BMJ* 1987; **294:** 419–21.
4. García Rodríguez LA, *et al*. A cohort study on the risk of acute liver injury among users of ketoconazole and other antifungal drugs. *Br J Clin Pharmacol* 1999; **48:** 847–52.

Precautions

Since ketoconazole has been reported to cause hepatotoxicity it should not be given to patients with pre-existing liver disease. Patients given ketoconazole should be monitored for symptoms of hepatitis; also, liver function tests should be performed before starting oral treatment with ketoconazole lasting for more than 14 days and then at least monthly throughout therapy.

Ketoconazole has been shown to be teratogenic in *animal* studies 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.

Hypochlorhydria, which may be present in patients with AIDS, can reduce absorption of ketoconazole. In this case absorption may be improved by giving ketoconazole with an acidic drink, such as a cola beverage.

Breast feeding. Ketoconazole is excreted in breast milk and licensed product information states that oral use should be avoided during breast feeding. However, no adverse effects were seen in a breast-fed infant whose mother was receiving ketoconazole;[1] it was calculated that the infant was exposed to about 0.4% of the usual therapeutic dose of ketoconazole for this age group. The American Academy of Pediatrics considers[2] that use of ketoconazole is therefore usually compatible with breast feeding.

1. Moretti ME, *et al*. Disposition of maternal ketoconazole in breast milk. *Am J Obstet Gynecol* 1995; **173:** 1625–6.
2. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 28/06/05)

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

Interactions

Use of drugs that reduce stomach acidity, such as antimuscarinics, antacids, histamine H_2-antagonists, and proton pump inhibitors, may reduce the absorption of ketoconazole. Absorption of ketoconazole may also be reduced by sucralfate. Enzyme-inducing drugs such as rifampicin, isoniazid, efavirenz, nevirapine, or phenytoin may reduce plasma-ketoconazole concentrations. Concentrations of isoniazid and rifampicin may also be reduced by ketoconazole.

Ketoconazole inhibits certain hepatic oxidase enzymes, especially the cytochrome P450 isoenzyme CYP3A4, in a similar way to itraconazole (p.537) and similar care should be taken to avoid adverse effects due to increased plasma concentrations of the interacting drugs.

A disulfiram-like reaction may occur in patients taking ketoconazole after drinking alcohol. The efficacy of oral contraceptives may be reduced.

◊ For reviews of drug interactions with azole antifungals, see Itraconazole, p.537.

Antimicrobial Action

Ketoconazole is an imidazole antifungal that interferes with ergosterol synthesis and therefore alters the permeability of the cell membrane of sensitive fungi. It is reported to be fungistatic at concentrations achieved clinically. Ketoconazole has a wide spectrum of antimicrobial activity including activity against *Blastomyces dermatitidis*, *Candida* spp., *Coccidioides immitis*, *Epidermophyton floccosum*, *Histoplasma capsulatum*, *Malassezia* spp., *Microsporum canis*, *Paracoccidioides brasiliensis*, *Trichophyton mentagrophytes*, and *T. rubrum*. Some strains of *Aspergillus* spp., *Cryptococcus neoformans*, and *Sporothrix schenckii* are sensitive.

Ketoconazole has activity against some Gram-positive bacteria and some antiprotozoal activity against *Leishmania* spp.

There are rare reports of *Candida albicans* acquiring resistance to ketoconazole.

Microbiological interactions. For the effect of imidazoles and amphotericin B on each other's antimicrobial activity, see Amphotericin B, p.525.

Resistance. For a discussion of increasing resistance of *Candida* spp. to azoles see Fluconazole, Antimicrobial Action, p.533.

Pharmacokinetics

The absorption of ketoconazole from the gastrointestinal tract is variable and increases with decreasing stomach pH. Mean peak plasma concentrations of about 3.5 micrograms/mL have been obtained 2 hours after an oral dose of 200 mg. Systemic absorption after topical or vaginal application in healthy subjects is minimal. Ketoconazole is more than 90% bound to plasma proteins, mainly albumin. It is widely distributed and appears in breast milk. Penetration into the CSF is poor. The elimination of ketoconazole is reported to be biphasic, with an initial half-life of 2 hours and a terminal half-life of about 8 hours.

Ketoconazole is metabolised in the liver to inactive metabolites. It is excreted as metabolites and unchanged drug chiefly in the faeces; some is excreted in the urine.

◊ References.

1. Daneshmend TK, Warnock DW. Clinical pharmacokinetics of ketoconazole. *Clin Pharmacokinet* 1988; **14:** 13–34.
2. Lelawongs P, *et al*. Effect of food and gastric acidity on absorption of orally administered ketoconazole. *Clin Pharm* 1988; **7:** 228–35.
3. Lake-Bakaar G, *et al*. Gastropathy and ketoconazole malabsorption in the acquired immunodeficiency syndrome (AIDS). *Ann Intern Med* 1988; **109:** 471–3.
4. Daneshmend TK. Diseases and drugs but not food decrease ketoconazole 'bioavailability'. *Br J Clin Pharmacol* 1990; **29:** 783–4.
5. Hurwitz A, *et al*. Gastric function in the elderly: effects on absorption of ketoconazole. *J Clin Pharmacol* 2003; **43:** 996–1002.

Uses and Administration

Ketoconazole is an imidazole antifungal used topically or orally. It is given orally in chronic mucocutaneous or vaginal candidiasis, in fungal infections of the gastrointestinal tract, in dermatophyte infections of the skin and fingernails not responding to topical treatment, and in systemic infections including blastomycosis, candidiasis, coccidioidomycosis, histoplasmosis, and paracoccidioidomycosis. It has been given for the prophylaxis of fungal infections in immunocompromised patients, although fluconazole or itraconazole are usually preferred. It has been recommended that, because of its erratic absorption and slow therapeutic response, ketoconazole should not be used for the treatment of life-threatening fungal infections, including fungal meningitis, or for severe infections in immunocompromised patients. Also, because of the risk of hepatotoxicity the use of ketoconazole in nonsystemic fungal infections tends to be restricted to serious infections resistant to other treatment.

The place of ketoconazole in the treatment of fungal infections is discussed in the various sections under Choice of Antifungal, p.517.

The usual oral dose for treatment and prophylaxis of fungal infections is 200 mg once daily taken with food. This may be increased to 400 mg daily if an adequate response is not obtained; in some infections even higher doses have been used. Children may be given about 3 mg/kg daily, or 50 mg for those aged 1 to 4 years and 100 mg for children aged 5 to 12 years. Treatment should usually be continued for 14 days and for at least

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.

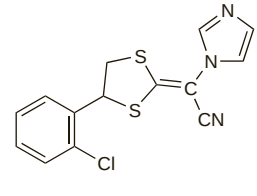
Lanoconazole *(rINN)*

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.