

**Natamycin** (BAN, USAN, pINN)

Antibiotic A-5283; CL-12625; E235; Natamycin; Natamycinum; Natamycyna; Natamysiini; Pimaricin; Pimarisin.

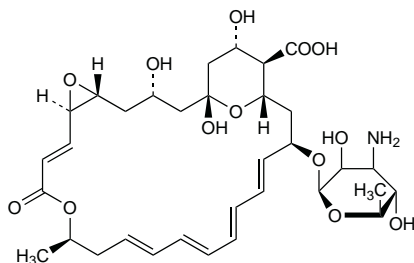
Натамицин

C<sub>33</sub>H<sub>47</sub>NO<sub>13</sub> = 665.7.

CAS — 7681-93-8.

ATC — A01AB10; A07AA03; D01AA02; G01AA02; S01AA10.

ATC Vet — QA01AB10; QA07AA03; QD01AA02; QG01AA02; QS01AA10.



**Pharmacopoeias.** In *Jpn*, *Pol*, and *US*.

**USP 31** (Natamycin). An off-white to cream-coloured powder. It may contain up to 3 moles of water. Practically insoluble in water; soluble in glacial acetic acid and in dimethylformamide; slightly soluble in methyl alcohol. A 1% suspension in water has a pH of 5.0 to 7.5. Store in airtight containers. Protect from light.

**Adverse Effects and Precautions**

Gastrointestinal disturbances have occurred after oral use of natamycin. Local application has sometimes produced irritation.

**Porphyria.** Natamycin has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

**Antimicrobial Action**

Natamycin is a polyene antifungal active against *Candida* and *Fusarium* spp. In addition it is active against the protozoan *Trichomonas vaginalis*.

**Pharmacokinetics**

Natamycin is poorly absorbed from the gastrointestinal tract. It is not absorbed through the skin or mucous membranes when applied topically. After ocular use, natamycin is present in therapeutic concentrations in corneal stroma but not in intra-ocular fluid; systemic absorption does not usually occur.

**Uses and Administration**

Natamycin is a polyene antifungal antibiotic produced by the growth of *Streptomyces natamensis*. It is used for the local treatment of candidiasis (p.518) and fungal keratitis (see Eye Infections, p.519). It has also been used in vaginal trichomoniasis (p.827).

A 5% ophthalmic suspension or a 1% ointment of natamycin is used in the treatment of blepharitis, conjunctivitis, or keratitis due to susceptible fungi, including *Fusarium solani*.

Natamycin lozenges are used for the treatment of oral candidiasis in a dose of 10 mg every 4 to 6 hours. Tablets have been given orally for the treatment of intestinal candidiasis. Natamycin has also been used topically for fungal skin infections and for candidal and trichomonal infections of the vagina.

**Preparations**

**USP 31:** Natamycin Ophthalmic Suspension.

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

**Arg.:** Natacyn; **Cz.:** Pimafucin; **Fin.:** Pimafucin; **Ger.:** Deronga Heilpaste†; Pima Bicon N; Pimafucin; **Hung.:** Pimafucin; **India:** Natadrops; **Indon.:** Fukricin; **Ital.:** Natafucin†; **Malaysia:** Natacyn; **Mex.:** Miconasina; **Neth.:** Pimafucin; **Pol.:** Pimafucin; **Rus.:** Pimafucin (Пимафуцин)†; Pimafucin (Пимафуцин); **S.Afr.:** Natacyn; **Singapore:** Natacyn; **Thai.:** Natacyn; **Turk.:** Pimafucin; **USA:** Natacyn.

**Multi-ingredient:** **Cz.:** Pimafucort; **Fin.:** Pimafucort; **Hung.:** Pimafucort; **Neth.:** Pimafucort; **NZ:** Pimafucort; **Pol.:** Pimafucort; **Port.:** Pimafucort; **Rus.:** Pimafucort (Пимафукурт).

**Neticonazole Hydrochloride** (rINN)

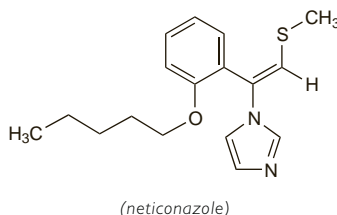
Hidrocloruro de neticonazol; Néticonazole, Chlorhydrate de; Neticonazoli Hydrochloridum; SS-717. (E)-1-{2-(Methylthio)-1-[o-(pentyloxy)phenyl]vinyl}imidazole hydrochloride.

Нетиконазола Гидрохлорида

C<sub>17</sub>H<sub>22</sub>N<sub>2</sub>OS.HCl = 338.9.

CAS — 130726-68-0 (neticonazole); 130773-02-3 (neticonazole hydrochloride).

The symbol † denotes a preparation no longer actively marketed



(neticonazole)

**Profile**

Neticonazole is an imidazole antifungal that has been used topically as the hydrochloride in the treatment of superficial fungal infections.

**Preparations**

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

**Jpn:** Atolant.

**Nystatin** (BAN, USAN, rINN)

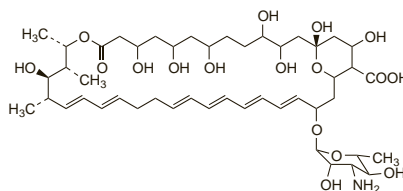
Fungicidin; Nistatin; Nistatina; Nistatinas; Nisztatin; Nystatini; Nystatine; Nystatinum; Nystatyna.

Нистатин

CAS — 1400-61-9.

ATC — A07AA02; D01AA01; G01AA01.

ATC Vet — QA07AA02; QD01AA01; QG01AA01.



(nystatin A<sub>1</sub>)

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

**Ph. Eur. 6.2** (Nystatin). An antifungal substance obtained by fermentation using certain strains of *Streptomyces noursei*. It contains mainly tetraenes, the principal component being nystatin A<sub>1</sub>. The potency is not less than 4400 units/mg and not less than 5000 units/mg if intended for oral use, calculated with reference to the dried substance. It is a yellow or slightly brownish hygroscopic powder. Practically insoluble in water and in alcohol; freely soluble in dimethylformamide and in dimethyl sulfoxide; slightly soluble in methyl alcohol. Store in airtight containers. Protect from light.

**USP 31** (Nystatin). A substance, or a mixture of two or more substances, produced by the growth of *Streptomyces noursei* (Streptomycetaceae). It has a potency of not less than 4400 units/mg, or, where intended for use in extemporaneous preparation of oral suspensions, not less than 5000 units/mg. A yellow to light tan, hygroscopic powder, with an odour suggestive of cereals; it is affected by long exposure to light, heat, and air. Practically insoluble in water and in alcohol; insoluble in chloroform and in ether; freely soluble in dimethylformamide and in dimethyl sulfoxide; slightly to sparingly soluble in methyl alcohol, in *n*-butyl alcohol, and in *n*-propyl alcohol. A 3% suspension in water has a pH of 6.0 to 8.0. Store in airtight containers. Protect from light.

**Adverse Effects**

Nausea, vomiting, and diarrhoea have occasionally been reported after oral use of nystatin. Oral irritation or sensitisation may occur. Rashes, including urticaria, have occurred and Stevens-Johnson syndrome has been reported rarely. Irritation may occur rarely after the topical use of nystatin.

**Effects on the skin.** Generalised pustular eruptions were reported in 3 patients after oral nystatin.<sup>1</sup> Subsequent sensitivity testing revealed delayed (type IV) hypersensitivity to nystatin.

1. Küchler A, *et al.* Acute generalized exanthematous pustulosis following oral nystatin therapy: a report of three cases. *Br J Dermatol* 1997; **137**: 808–11.

**Precautions**

Some intravaginal preparations of nystatin may damage latex contraceptives and additional contraceptive precautions may be necessary during treatment.

**Antimicrobial Action**

Nystatin is a polyene antifungal antibiotic that interferes with the permeability of the cell membrane of sensitive fungi by binding to sterols, chiefly ergosterol. Its main action is against *Candida* spp.

**Pharmacokinetics**

Nystatin is poorly absorbed from the gastrointestinal tract. It is not absorbed through the skin or mucous membranes when applied topically.

**Uses and Administration**

Nystatin is a polyene antifungal antibiotic used for the prophylaxis and treatment of candidiasis of the skin and mucous membranes (see p.518). It has been used with antibacterials in various regimens to suppress the overgrowth of gastrointestinal flora and as part of selective decontamination regimens (see Intensive Care, p.175).

For the treatment of intestinal or oesophageal candidiasis, nystatin is given in oral doses of 500 000 or 1 000 000 units, as a tablet or capsule, 3 or 4 times daily. In infants and children a dosage of 100 000 units or more may be given 4 times daily, as an oral suspension.

For the treatment of lesions of the mouth, pastilles or a suspension may be given in a dosage of 100 000 units 4 times daily. Higher doses of, for example, 500 000 units 4 times daily, may be needed in immunocompromised patients (but see also Candidiasis, below). The formulation should be kept in contact with the affected area for as long as possible, and patients should avoid taking food or drink for one hour after a dose. In the USA, doses of 400 000 to 600 000 units 4 times daily of the suspension, or 200 000 to 400 000 units 4 or 5 times daily as lozenges, are used.

For prophylaxis of intestinal candidiasis in patients given broad-spectrum antibacterials, tablets to a total dose of 1 000 000 units daily may be given. A prophylactic dose for infants born to mothers with vaginal candidiasis is 100 000 units daily of the oral suspension.

For the treatment of vaginal infections, nystatin is given in a dosage of 100 000 to 200 000 units daily for 14 days or longer as pessaries or vaginal cream. For cutaneous lesions, ointment, gel, cream, or dusting powder containing 100 000 units/g may be applied 2 to 4 times daily.

A liposomal formulation of nystatin for *parenteral* use is under investigation.

**Candidiasis.** A systematic review<sup>1</sup> of 14 studies (12 of prophylaxis, 2 of treatment) considered that nystatin could not be recommended for prophylaxis or treatment of *Candida* infections in patients with immunosuppression. In practice, fluconazole is usually preferred in such patients (see p.518).

1. Göttsche PC, Johansen HK. Nystatin prophylaxis and treatment in severely immunodepressed patients. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2002 (accessed 28/06/05).

**Preparations**

**BP 2008:** Nystatin Ointment; Nystatin Oral Suspension; Nystatin Pastilles; Nystatin Pessaries; Nystatin Tablets;

**USP 31:** Nystatin and Triamcinolone Acetonide Cream; Nystatin and Triamcinolone Acetonide Ointment; Nystatin Cream; Nystatin for Oral Suspension; Nystatin Lotion; Nystatin Lozenges; Nystatin Ointment; Nystatin Oral Suspension; Nystatin Tablets; Nystatin Topical Powder; Nystatin Vaginal Suppositories; Nystatin Vaginal Tablets; Nystatin, Neomycin Sulfate, Gramicidin, and Triamcinolone Acetonide Cream; Nystatin, Neomycin Sulfate, Gramicidin, and Triamcinolone Acetonide Ointment; Oxytetracycline and Nystatin Capsules; Oxytetracycline and Nystatin for Oral Suspension; Tetracycline Hydrochloride and Nystatin Capsules.

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

**Arg.:** Candemil; Candias; Dipni; Micostatin; Neostatin; Nistagrand; Nistamed; Nistat; **Austral.:** Mycostatin; N-Statini†; Nilstat; **Austria:** Candio; Mycostatin; Nystaderm; **Belg.:** Nilstat; Sterostatine†; **Braz.:** Albistin; Candistatin†; Canditrat; Hidrotiazida†; Inofungin; Kandistat; Kolpazol†; Micostat; Micostalab; Micostatin; Neo Mistatin; Neostatin; Nicostat; Nidazoln; Nifatin†; Nistagen†; Nistagen; Nistalini†; Nistatin; Nistavil; Nistax†; Nistomic; Tricocet; **Canad.:** Candistatin; Mycostatin; Nadostine†; Nilstat†; Nyaderm; **Chile:** Micostatin; Nistoral; **Cz.:** Fungicidin; **Denm.:** Mycostatin; **Fin.:** Mycostatin; **Fr.:** Mycostatine; **Ger.:** Adiclar; Biofanel; Candio; Fungireduct†; Lederlind; Moronal; Mykoderm Heilsalbe; MykoPosterine N†; Mykundes; Mykundes mono; Nystaderm; **Gr.:** Mycostatin; Nystamont†; Nystamysyn; **Hong Kong:** Lystin; Mycostatin; **India:** Mycostatin; **Indon.:** Candistin; Erystin; Fungatin; Kandistatin; Mycostatin; Nymiko; **Irl.:** Mycostatin; **Ital.:** Mycostatin; **Malaysia:** Mikostat; Mycostatin; Uphastatin†; **Mex.:** Apontan V; Bistatin V; Mibesan-S; Micostatin; Nistat; Nistagum; Nizini-V; **Norw.:** Mycostatin; **NZ:** Mycostatin; Nilstat; **Philipp.:** Afungal; Mycostatin;

**Port.:** Mycostatin; **S.Afr.:** Candicide; Canstat; Mycostatin; Nystacid; **Singapore:** Mycostatin; **Spain:** Mycostatin; **Swed.:** Mycostatin; **Switz.:** Mycostatine; **Thal.:** Lystin; Mycostatin; **Turk.:** Fungostatin; Mikostatin; **UAE:** Mikostat; **UK:** Nystamont; Nystan; **USA:** Mycostatin; Nilstat; Nystop; Pedi-Dri; **Venez.:** Micostatin; Nistafesa; Romalinaj.

**Multi-ingredient:** **Arg.:** Bacticrot Complex; Bexon; Biotaer Gamma; Biotaer Nebulizable; Dermadex NN; Farm-X Duo; Fasigin Nistatina; Flagystatin; Kenacomb; Linfol; Min O; Naxo TV; Neocolpoben; Nistinol; O-Biol; O-Biol P; Pelvicilin NF; Polygnax; Terra-Cortril Nistatina; Tratomax; **Austral.:** Kenacomb; Otocomb Otic; **Austria:** Mycostatin V; Mycostatin-Zinkoxid; Topsym polyvalent; **Belg.:** Eolinef; Mycolog; Polygnax; **Braz.:** Benzevit; Bio-Vagin; Colpagex N; Colpatrin; Colpist; Colpastar; Colpastatin; Colpalase; Dermodex; Dermokin; Donnagel; Flagyl Nistatina; Fungimax; Ginec; Ginestatin; Gynax-N; Londerm-N; Minegyl C/Nistatina; Mud; Naxogin Composto; Neolon-D; Nistazol; Omiclon A M; Oncipus; Oxyderme; Poliginax; Tricoplex; Tricomax; Trivagel N; Vagi Biotic; Vagimax; Vagitrin-N; **Canad.:** Flagystatin; Kenacomb; ratio-Triacomb; Triacomb; Viaderm-KC; **Chile:** Multilind; Naxogin Compositum; Naxogin Dost; Nistaglos; **Cz.:** Macmiror Complex; Polygnax; **Denm.:** Kenalog Comp med Mycostatin; **Fin.:** Flagyl Comp; **Fr.:** Auricularum; Mycolog; Polygnax; Polygnax Virgo; Tergynan; **Ger.:** Aureomycin NH; Candio-Hermal Plus; Halog Trii; Jellin polyvalent; Lokalisol-antimikrobiell Creme N; Moronal V; Multilind; Mykoproct sine; Mykundes Heilsalbe; Nystaderm comp; Nystalocal; Penanyst; Polygnax; Topsym polyvalent; Volonimat Plus N; **Gr.:** Kenacomb; **Hong Kong:** Kenacomb; Macmiror Complex; Polygnax; Triacomb; **India:** Kena-comb; **Indon.:** Fasigin-Nystatin; Fladystin; Flagystatin; Gynoxa; Myco-Z; Naxogin Complex; New Kenacomb; Trichostatic; Vagistin; **Irl.:** Kenacomb; Nystaform-HC; Nystaform; Timodine; Tinaderm-M; **Israel:** Auricularum; Dermacombin; Kenacomb; **Ital.:** Assocort; Fasigin N; Macmiror Complex; **Malaysia:** Kenacomb; **Mex.:** Acenil; Bidrozil; Decadron con Nistatina; Dermalog-C; Flagystatin V; Kenacomb; Macmiror Complex V; Metrofur; Micostatin Baby; Novageon; Nysmosons-V; Promibasal-Plus; Vagitol-V; **Neth.:** Mycolog; **NZ:** Kenacomb; Viaderm-KC; **Philipp.:** Dermovate-NN; Flagystatin; Kenacomb; Lidex NGN; **Pol.:** Macmiror Complex; Triacomb; **Port.:** Dafnigil; Dermovate-NN; Kenacomb; **Rus.:** Macmiror Complex (Макмирор Комплекс); Polygnax (Полигнакс); Tergynan (Тержинан); **S.Afr.:** Duoderm; Hiconcil-NS; Kenacomb; Ristostat; Tetrex-F; **Singapore:** Flagystatin; Kenacomb; Polygnax; **Spain:** Interderm; Intradermo Cort Ant Fung; Milrosina Nistatina; Positon; **Swed.:** Kenacombin Novum; **Switz.:** Dermovate-NN; Multilind; Mycolog N; Mycolog; Nystacortonef; Nystalocal; Topsym polyvalent; **Thal.:** Dermacombin; Gynecon; Gynecon-T; Gynoco; Gynova; Gyracon; Kenacomb; Nystin; Quinradon-N; Vagicin; **UAE:** Mikostat Baby Ointment; Panderm; **UK:** Dermovate-NN; Gregoderm; Nystaform; Nystaform-HC; Timodine; Tinaderm-M; Tri-Adcortyl; Trimovate; **USA:** Myco-Biotic II; Myco-Triacet II; Mycogen II; Mycolog-II; Myconel; Mytrex; NGT; Tri-Statlin II; **Venez.:** Halcicom; Kenacomb.

### Omoconazole Nitrate (USAN, rINNM)

10-80-07; Nitrate de omoconazol; Omoconazole, Nitrate d'; Omoconazoli Nitras. (Z)-1-[2,4-Dichloro-β-[2-(p-chlorophenoxy)ethoxy]-α-methylstyryl]imidazole nitrate.

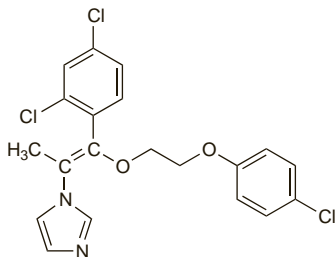
Омоконазола Нитрат

$C_{20}H_{17}Cl_3N_2O_2 \cdot HNO_3 = 486.7$ .

CAS — 74512-12-2 (omoconazole); 83621-06-1 (omoconazole nitrate).

ATC — D01AC13; G01AF16.

ATC Vet — QD01AC13; QG01AF16.



(omoconazole)

### Profile

Omoconazole is an imidazole antifungal used locally for fungal skin infections (p.521) and for vaginal candidiasis (p.518). It is applied topically as the nitrate as a 1% cream, powder, or solution in the treatment of cutaneous candidiasis, dermatophytosis, and pityriasis versicolor. For vaginal candidiasis, omoconazole nitrate is given as pessaries in doses of 150 mg daily for 6 days, 300 mg daily for 3 days, or 900 mg as a single dose.

Intravaginal preparations of azoles may damage latex contraceptives.

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)

**Austria:** Afongan; **Fr.:** Fongamil; Fongarex; **Gr.:** Fongamil; **Hung.:** Mikogal; **Mex.:** Afongan; **Port.:** Afongan; Fongamil; **Rus.:** Mikogal (Микогал).

### Oxiconazole Nitrate (BANM, USAN, rINNM)

Nitrato de oxiconazol; Oxiconazole, Nitrate d'; Oxiconazoli Nitras; Ro-13-8996; Ro-13-8996/001; Ro-13-8996/000 (oxiconazole); SGD-301-76; ST-813. 2',4'-Dichloro-2-imidazol-1-ylacetophenone (Z)-O-(2,4-dichlorobenzyl)oxime mononitrate.

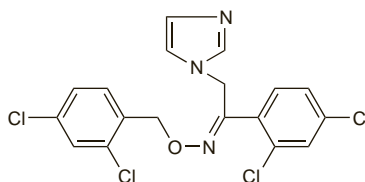
Оксиконазола Нитрат

$C_{18}H_{13}Cl_4N_3O \cdot HNO_3 = 492.1$ .

CAS — 64211-45-6 (oxiconazole); 64211-46-7 (oxiconazole nitrate).

ATC — D01AC11; G01AF17.

ATC Vet — QD01AC11; QG01AF17.



(oxiconazole)

### Profile

Oxiconazole is an imidazole antifungal applied topically as the nitrate as a cream, solution, or powder equivalent to oxiconazole 1% in the treatment of fungal infections of the skin (p.521). It is also given as a pessary in a single dose equivalent to 600 mg of oxiconazole in the treatment of vaginal candidiasis (p.518).

Local reactions including burning and itching have been reported. Intravaginal preparations of azoles may damage latex contraceptives.

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

◇ Reviews.

1. Jegasothy BV, Pakes GE. Oxiconazole nitrate: pharmacology, efficacy, and safety of a new imidazole antifungal agent. *Clin Ther* 1991; **13**: 126-41.

### Preparations

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

**Arg.:** Oxistat; **Austria:** Gyno-Liderman; Liderman; Oceral; **Braz.:** Micotin; Oceral; Oxipelle; Oxitrat; **Canad.:** Oxizole; **Cz.:** Gyno-Myfungar; Myfungar; **Fr.:** Fonx; **Ger.:** Myfungar; Oceral GB; **Mex.:** Gyno-Myfungar; Myfungar; Oxistat; **Rus.:** Myfungar (Мифунгар); **Spain:** Salongo; **Switz.:** Oceral; **Turk.:** Oceral; **USA:** Oxistat.

**Multi-ingredient:** **India:** Zoderm.

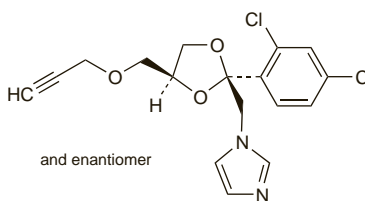
### Parconazole Hydrochloride (USAN, rINNM)

Hydrocloruro de parconazol; Parconazole, Chlorhydrate de; Parconazoli Hydrochloridum; R-39500. *cis*-1-[[2-(2,4-Dichlorophenyl)-4-[[2-(propyloxy)methyl]-1,3-dioxolan-2-yl]methyl]-1H-imidazole hydrochloride.

Парконазола Гидрохлорида

$C_{17}H_{16}Cl_2N_2O_3 \cdot HCl = 403.7$ .

CAS — 61400-59-7 (parconazole); 68685-54-1 (parconazole); 62973-77-7 (parconazole hydrochloride).



and enantiomer

(parconazole)

### Profile

Parconazole is an antifungal that has been used as the hydrochloride in the treatment of gastrointestinal candidiasis in veterinary medicine.

### Pentamycin

Fungichromin; Lagosin; Pentamicina.

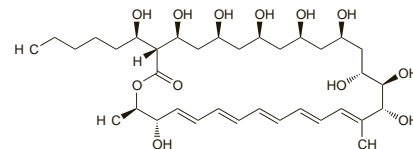
Пентамицин

$C_{35}H_{58}O_{12} = 670.8$ .

CAS — 6834-98-6.

ATC — G01AA11.

ATC Vet — QG01AA11.



### Profile

Pentamycin is a polyene antifungal antibiotic obtained from *Sireptomycetes pentaticus*. It has been used in the treatment of vaginal candidiasis and for the protozoal infection trichomoniasis.

### Posaconazole (BAN, USAN, rINN)

Posaconazol; Posaconazolium; Sch-56592. 4-[p-[4-(p-[[[(3R,5R)-5-(2,4-Difluorophenyl)tetrahydro-5-(1H-1,2,4-triazol-1-ylmethyl)-3-furyl]methoxy]phenyl)-1-piperazinyl]phenyl]-1-[[[1S,2S)-1-ethyl-2-hydroxypropyl]-Δ<sup>2</sup>-1,2,4-triazolin-5-one.

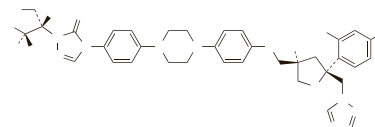
Позаконазол

$C_{37}H_{42}F_2N_8O_4 = 700.8$ .

CAS — 171228-49-2.

ATC — J02AC04.

ATC Vet — QJ02AC04.



### Adverse Effects

The most commonly reported adverse effects with posaconazole are headache and nausea. Other common adverse effects include abdominal pain, anorexia, asthenia, back pain, diarrhoea, dyspepsia, dizziness, dry mouth, dry skin, fatigue, fever, flatulence, hot flushes, insomnia, neutropenia, paraesthesia, pruritus, rash, somnolence, and vomiting. An increase in liver enzyme values has occurred in some patients, especially in those with serious underlying disease. Hypersensitivity and allergic reactions, including Stevens-Johnson syndrome, have occurred rarely.

### Precautions

Some azoles have been associated with QT interval prolongation and licensed product information therefore advises that posaconazole should be used with caution in patients with potentially proarrhythmic conditions. Patients who develop abnormal liver function tests while being treated with posaconazole should be routinely monitored for the development of more serious liver injury.

**Breast feeding.** Breast feeding while taking posaconazole is not recommended by licensed product information.

**Pregnancy.** Posaconazole has been shown to be teratogenic and embryotoxic 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. Licensed product information recommends that women of child-bearing potential should use effective contraception during treatment with posaconazole.