

Port.: Mycostatin; **S.Afr.:** Candicide; Canstat; Mycostatin; Nystacid; **Singapore:** Mycostatin; **Spain:** Mycostatin; **Swed.:** Mycostatin; **Switz.:** Mycostatine; **Thai.:** 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; **Thai.:** 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.

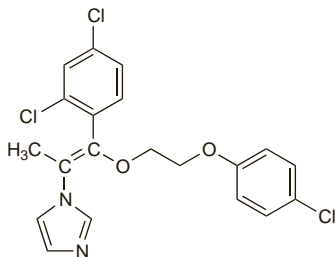
Омоконазола Нитрат

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

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.

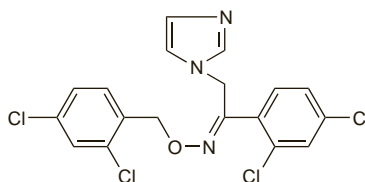
Оксиконазола Нитрат

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

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.

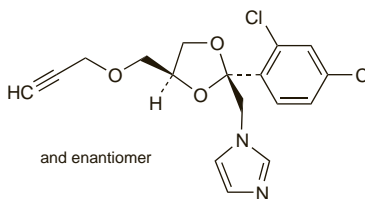
Parconazole Hydrochloride (USAN, rINNM)

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 Гидрохлорид

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

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.

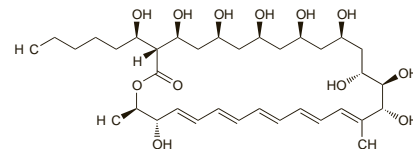
Пентамицин

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

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]-Δ²-1,2,4-triazolin-5-one.

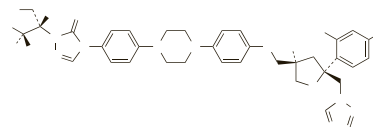
Позаконазол

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

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.

Interactions

Posaconazole is metabolised by the uridine diphosphate glucuronosyltransferase UGT1A4, and is a substrate for p-glycoprotein. The use of drugs that either inhibit (for example, clarithromycin, erythromycin, ciclosporin, and verapamil) or induce (see below) enzymes in this pathway may increase or decrease plasma-posaconazole concentrations, respectively. Rifabutin and phenytoin have been shown to decrease plasma-posaconazole concentrations and a similar effect may be expected with rifampicin, carbamazepine, primidone, and phenobarbital. Concentrations of posaconazole are reduced by cimetidine possibly due to reduced absorption of posaconazole as a result of decreased acid production and reduced posaconazole concentrations may also be expected with other H₂-antagonists and proton pump inhibitors.

Posaconazole is an inhibitor of the cytochrome P450 isoenzyme CYP3A4 and concentrations of other drugs that are metabolised by this enzyme pathway may be increased by posaconazole. Increased plasma concentrations of astemizole, cisapride, halofantrine, pimozide, quinidine, and terfenadine could be expected and concomitant use is contra-indicated because of the risk of cardiac arrhythmias including torsade de pointes. Use with ergot alkaloids such as ergotamine and dihydroergotamine is also contra-indicated because of the possible risk of ergotism. HMG-CoA reductase inhibitors such as atorvastatin, lovastatin, and simvastatin are contra-indicated as concomitant use as been associated with rhabdomyolysis. Increased plasma concentrations of sirolimus and tacrolimus have been noted; doses of sirolimus and tacrolimus may need to be reduced and concentrations monitored. Similarly, dose reduction with monitoring is recommended for ciclosporin. Close monitoring of blood glucose is necessary if posaconazole is used with oral hypoglycaemics such as the sulfonylureas. Dose reductions may be needed for calcium-channel blockers, digoxin, vinca alkaloids, and some benzodiazepines (such as alprazolam, midazolam, and triazolam). It is expected that posaconazole will increase the concentrations of HIV-protease inhibitors and NNRTIs.

Interactions may occur where both posaconazole and the other drug are affected. Examples are ciclosporin (where concentrations of both posaconazole and ciclosporin are increased) and rifabutin (where concentrations of posaconazole are reduced but those of rifabutin are increased).

For further information on interactions between drugs metabolised by the cytochrome P450 isoenzyme CYP3A and azoles, see under Itraconazole, p.537.

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

Antimicrobial Action

Posaconazole is a triazole antifungal drug that in sensitive fungi inhibits the enzyme lanosterol 14 α -demethylase (CYP51) resulting in the impairment of ergosterol synthesis in fungal cell membranes. Posaconazole has activity against *Candida* spp., *Aspergillus* spp., *Coccidioides immitis*, *Fonsecaea pedrosoi*, and some species of *Fusarium* and zygomycetes.

Pharmacokinetics

Posaconazole exhibits linear pharmacokinetics after single and multiple doses with a high fat meal. No further increases in plasma concentration are seen with doses above 800 mg daily. It is slowly absorbed from the gastrointestinal tract and has a large volume of distribution. Peak plasma concentrations occur about 5 hours after an oral dose. Steady state plasma-posaconazole concentrations occur after 7 to 10 days of multiple dosage. Plasma protein binding is over 98%.

Metabolism plays only a minor role in the elimination of posaconazole; most circulating metabolites are glu-

curonide conjugates with only small amounts of oxidative metabolites. Posaconazole is slowly eliminated with a mean elimination half-life of 35 hours. The main elimination route of posaconazole is via the faeces (77%) where 66% of a dose is excreted unchanged. About 14% of a dose is excreted in the urine with only trace amounts excreted unchanged.

♦ Reviews.

1. Courtney R, *et al.* Pharmacokinetics, safety, and tolerability of oral posaconazole administered in single and multiple doses in healthy adults. *Antimicrob Agents Chemother* 2003; **47**: 2788-95.

Uses and Administration

Posaconazole is an oral triazole antifungal used in the treatment of severe oropharyngeal candidiasis. It is also indicated in the treatment of invasive aspergillosis, chromoblastomycosis, coccidioidomycosis, fusariosis, or mycetoma infections in patients who are resistant to, or intolerant of, other antifungals. Posaconazole is also given for the prophylaxis of fungal infections in patients who are at high risk for invasive fungal disease due to prolonged neutropenia.

Posaconazole is given orally as a suspension; doses should be given with a meal, or a nutritional supplement in those who cannot tolerate food, in order to enhance oral absorption and ensure adequate exposure.

For the treatment of **oropharyngeal candidiasis** posaconazole is given in a loading dose of 200 mg on the first day, followed by 100 mg daily for 13 days. In patients with oropharyngeal candidiasis refractory to itraconazole and/or fluconazole, posaconazole is given at a dose of 400 mg twice daily.

In patients with refractory **invasive systemic fungal infections**, it is given at a dose of 400 mg twice daily. Patients not tolerating food or nutritional supplements should take 200 mg four times daily.

In the **prophylaxis** of invasive fungal infections, the recommended dose is 200 mg three times daily. Treatment is continued until recovery from neutropenia or immunosuppression. In patients undergoing cytotoxic chemotherapy for haematological malignancies, or haematopoietic stem-cell transplantation, treatment should begin several days before the anticipated onset of neutropenia and continue for 7 days after the neutrophil count rises above 500 cells/mm³.

♦ References.

1. Herbrecht R. Posaconazole: a potent, extended-spectrum triazole anti-fungal for the treatment of serious fungal infections. *Int J Clin Pract* 2004; **58**: 612-24.
2. Segal BH, *et al.* Posaconazole as salvage therapy in patients with chronic granulomatous disease and invasive filamentous fungal infection. *Clin Infect Dis* 2005; **40**: 1684-8.
3. Keating GM. Posaconazole. *Drugs* 2005; **65**: 1553-67.
4. Raad II, *et al.* Safety of long-term oral posaconazole use in the treatment of refractory invasive fungal infections. *Clin Infect Dis* 2006; **42**: 1726-34.
5. Nagappan V, Deresinski S. Posaconazole: a broad-spectrum triazole antifungal agent. *Clin Infect Dis* 2007; **45**: 1610-7.
6. Frampton JE, Scott LJ. Posaconazole: a review of its use in the prophylaxis of invasive fungal infections. *Drugs* 2008; **68**: 993-1016.

Preparations

Proprietary Preparations (details are given in Part 3)

Austral.: Noxafil; **Cz.:** Noxafil; **Fr.:** Noxafil; **Gr.:** Noxafil; **Neth.:** Noxafil; **NZ:** Noxafil; **Pol.:** Noxafil; **Swed.:** Noxafil; **UK:** Noxafil; **USA:** Noxafil.

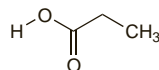
Propionic Acid

E280; E283 (potassium propionate); Kwas propionowy; Propanoic acid, ácido. Propanoic acid.

Пропионовая Кислота

C₂H₅CO₂H = 74.08.

CAS — 79-09-4.



Pharmacopoeias. In *Fr.* Also in *USNF*.

USNF 26 (Propionic Acid). An oily liquid having a slight pungent, rancid odour. Miscible with water, with alcohol, and with various other organic solvents. Store in airtight containers.

Calcium Propionate

E282. Calcium propionate.

Пропионат Кальция

(C₃H₅O₂)₂Ca = 186.2.

CAS — 4075-81-4 (anhydrous calcium propionate); 56744-45-7 (calcium propionate monohydrate).

Sodium Propionate

E281; Natrii propionas; Natrio propionatas; Natriumpropionaat; Natriumpropionat; Nátrium-propionát; Propionan sodný; Propionato de sodio; Sodium, propionate de. Sodium propionate.

Пропионат Натрия

C₃H₅NaO₂ = 96.06.

CAS — 137-40-6 (anhydrous sodium propionate); 6700-17-0 (sodium propionate hydrate).

ATC — S01AX10.

ATC Vet — QA16QA02; QS01AX10.

Pharmacopoeias. In *Eur.* (see p.vii). Also in *USNF*.

Ph. Eur. 6.2 (Sodium Propionate). Slightly hygroscopic colourless crystals or white or almost white powder. Freely soluble in water; sparingly soluble in alcohol; practically insoluble in dichloromethane. A 2% solution in water has a pH of 7.8 to 9.2. Store in airtight containers.

USNF 26 (Sodium Propionate). Colourless transparent crystals or a granular crystalline powder; odourless or with a faint acetic-butyric odour. Deliquescent in moist air. Soluble 1 in 1 of water, 1 in 0.65 of boiling water, and 1 in 24 of alcohol; practically insoluble in chloroform and in ether. Store in airtight containers.

Profile

Propionic acid and its salts are antifungals. Calcium and sodium propionate have been used topically, usually with other antimicrobials for the treatment of dermatophyte infections. Eye drops containing sodium propionate have also been used.

Propionic acid and its calcium, sodium, and potassium salts are used in the baking industry as inhibitors of moulds.

Preparations

Proprietary Preparations (details are given in Part 3)

Ital.: Propionat.

Multi-ingredient: **Arg.:** Cicatrol; Fam-X; Fungicidaf; Hipoglos Cicatrizante; Novo Miconol; Picidex; Plusderm; **Austral.:** Mycoderm; **Austria:** Dermowund; **Braz.:** Andriodermol; Colpagex N; Gynax-N; Micotox; Vagitrin-N; **Canad.:** Amino-Cerv; **Chile:** Fittig; **Fr.:** Dermacide; Otoralgyl a la phenylephrine; **Hong Kong:** Mycoderm; **Indon.:** Declyne; **Israel:** Otomylin; **Malaysia:** Mycoderm; **S.Afr.:** Neopan; **USA:** Amino-Cerv; Propyllin; **Venez.:** Diodonator.

Pyrolnitrin (USAN, rINN)

52230; NSC-107654; Pirrolnitrina; Pyrrolnitrine; Pyrrolnitrinum. 3-Chloro-4-(3-chloro-2-nitrophenyl)pyrrole.

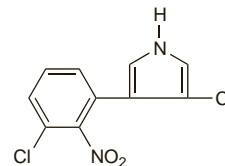
Пирролнитрин

C₁₀H₆Cl₂N₂O₂ = 257.1.

CAS — 1018-71-9.

ATC — D01AA07.

ATC Vet — QD01AA07.



Pharmacopoeias. In *Jpn.*

Profile

Pyrolnitrin is an antifungal antibiotic isolated from *Pseudomonas pyrocinia* and applied topically in the treatment of superficial fungal infections.

Preparations

Proprietary Preparations (details are given in Part 3)

Ital.: Micutrin.

Multi-ingredient: **Ital.:** Micutrin Beta†; **Port.:** Pirrolfungin†.