Natamycin *(BAN, USAN, pINN)*

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

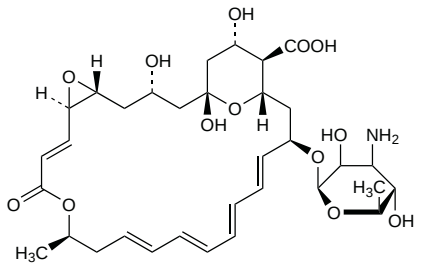
Натамицин

$C_{33}H_{47}NO_{13}$ = 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 natalensis*. 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 Biciron N; Pimafucin; ***Hung.:*** Pimafucin; ***India:*** Natadrops; ***Indon.:*** Fukricin; ***Ital.:*** Natafucin†; ***Malaysia:*** Natacyn; ***Mex.:*** Miconacina; ***Neth.:*** Pimafucin; ***Pol.:*** Pimafucin; ***Rus.:*** Piamfucin (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 (Пимафукорт).

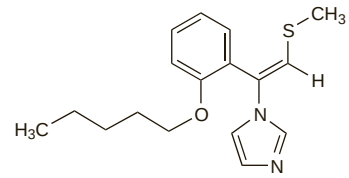
Neticonazole Hydrochloride *(rINNM)*

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

Нетиконазола Гидрохлорид

$C_{17}H_{22}N_2OS,HCl$ = 338.9.

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



(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)*

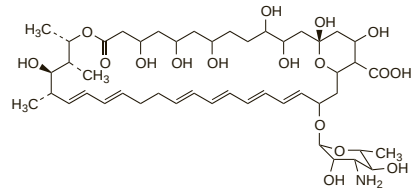
Fungicidin; Nistatin; Nistatina; Nistatinas; Nisztatin; Nystatiini; Nystatine; Nystatinum; Nystatyna.

Нистатин

CAS — 1400-61-9.

ATC — A07AA02; D01AA01; G01AA01.

ATC Vet — QA07AA02; QD01AA01; QG01AA01.



(nystatin A_1)

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_1. 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.[1] 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[1] 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. Gøtzsche 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.: Candermil; Candidias; Dipni; Micostatin; Neostatin; Nistagrand; Nistamed; Nistat; ***Austral.:*** Mycostatin; N-Statin†; Nilstat; ***Austria:*** Candio; Mycostatin; Nystaderm; ***Belg.:*** Nilstat; Sterostatine†; ***Braz.:*** Albistin; Candistatin†; Canditrat; Hidrotiazida†; Inofungin; Kandistat; Kolpazol†; Micostal; Micostalab; Micostatin; Neo Mistatin; Neostatin; Nicostat; Nidazolin; Nifatin†; Nistagen†; Nistagyn; Nistanil†; Nistatin; Nistaval; Nistax†; Nistomic; Tricocet; ***Canad.:*** Candistatin; Mycostatin; Nadostine†; Nilstat†; Nyaderm; ***Chile:*** Micostatin; Nistoral; ***Cz.:*** Fungicidin; ***Denm.:*** Mycostatin; ***Fin.:*** Mycostatin; ***Fr.:*** Mycostatine; ***Ger.:*** Adiclair; Biofanal; Candio; Fungireduct†; Lederlind; Moronal; Mykoderm Heilsalbe; MykoPosterine N†; Mykundex; Mykundex mono; Nystaderm; ***Gr.:*** Mycostatin; Nystamont†; Nystamysyn; ***Hong Kong:*** Lystin; Mycostatin; ***India:*** Mycostatin; ***Indon.:*** Candistin; Enystin; Fungatin; Kandistatin; Mycostatin; Nymiko; ***Irl.:*** Mycostatin; ***Ital.:*** Mycostatin; ***Malaysia:*** Mikostat; Mycostatin; Uphastatin†; ***Mex.:*** Aponistan V; Bistatin V; Mibesan-S; Micostatin; Nistan; Nistaquim; Nizin-V; ***Norw.:*** Mycostatin; ***NZ:*** Mycostatin; Nilstat; ***Philipp.:*** Afunginal; Mycostatin;