

1. NAME OF THE MEDICINAL PRODUCT

Nystatin Orifarm, 100 000 IU/ml oral suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains 100 000 IU nystatin.

Excipients with known effect:

- Methyl parahydroxybenzoate 1 mg
- Sodium 1.2 mg/ml, equivalent to 0.053 mmol/ml

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral suspension.

Light yellow, opalescent suspension with peppermint odour and flavour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Oral and intestinal candidiasis. As adjuvant treatment with other local nystatin preparations to prevent reinfection.

4.2 Posology and method of administration

Oral candidiasis

Posology

Adults, children (≥ 2 years), infants (1 month to 2 years) and neonates (from birth to 1 month): 1 ml (100,000 IU) 4 times daily. The dose may be increased if necessary.

Duration of treatment

Usual treatment duration for oral candidiasis is 1-2 weeks.

Treatment may be prolonged to 4 to 6 weeks in special circumstances, such as in immunocompromised patients.

Method of administration

The suspension is preferably taken after meals and is retained in the mouth for as long as possible before swallowing. For infants, the suspension may be administered drop by drop or diluted with water and brushed on the lesions.

The bottle should be shaken well before use.

Intestinal candidiasis

Posology

Adults: 5 ml (500,000 IU) 3 times daily. The dose may be doubled if necessary.

Children (≥ 2 years) and infants (1 month to 2 years): 1 ml (100,000 IU) 4 times daily.

Duration of treatment.

Treatment should continue for 2-3 days after symptoms have ceased, in order to prevent relapse.

When used in combination with antibiotics, nystatin treatment should be given at least as long as the antibiotic in question.

Method of administration

The suspension is swallowed directly.

The bottle should be shaken well before use.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Nystatin Orifarm oral suspension should not be used for the treatment of systemic mycoses.

If irritation or hypersensitivity reactions occur, treatment should be discontinued.

Nystatin Orifarm contains methyl parahydroxybenzoate. May cause allergic reactions (possibly delayed).

Nystatin Orifarm contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

No known.

4.6 Fertility, pregnancy and lactation

Pregnancy

It is not known whether nystatin can cause fetal harm when administered to a pregnant woman. Animal studies have shown reproductive toxicity (see section 5.3). Nystatin should only be prescribed to a pregnant woman if the potential benefit to the mother justifies the potential risk to the fetus.

Breastfeeding

It is not known whether nystatin is excreted in human milk. Although the gastrointestinal absorption is negligible, caution should be exercised when nystatin is prescribed to a nursing woman.

Fertility

No clinical data are available concerning the effect of nystatin on fertility. A study in rats did not show any negative effects on fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Nystatin is assumed not to affect the ability to drive or operate machinery.

4.8 Undesirable effects

Adverse reactions are listed by system organ class and absolute frequency. Frequencies are defined as Very Common ($\geq 1/10$), Common ($\geq 1/100$, $< 1/10$), Uncommon ($\geq 1/1000$, $< 1/100$), Rare ($\geq 1/10,000$ to $< 1/1000$) or Very rare ($< 1/10,000$), no known frequency (cannot be estimated from available data).

Immune system disorders	Very rare, not known (cannot be estimated from the available data)	Hypersensitivity and angioedema (including swelling of the face) have been reported.
Gastrointestinal disorders	Uncommon	Nausea, vomiting, dyspepsia and diarrhoea.*
Skin and subcutaneous tissue disorders	Uncommon	Rash and urticaria.
	Rare	Stevens-Johnson Syndrome.
	No known frequency	Acute Generalised Exanthematous Pustulosis (AGEP)

*Nausea and diarrhoea are dose related.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Doses 4-8 times more than recommended per day have given nausea and gastrointestinal problems such as vomiting and diarrhoea. Treatment: gastric emptying, if necessary, active carbon. Symptomatic treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antibiotic antifungal, ATC code: A07AA02

Nystatin is obtained from *Streptomyces noursei* and is constituted of a yellow powder, almost insoluble in water. Nystatin is fungistatic or fungicidal depending on the concentration achieved and the susceptibility of the fungus. Nystatin has an effect on several species of fungi, but not on bacteria, protozoa nor viruses, and does not affect the body's normal bacterial flora. Most sensitive is the yeast-like fungi and the effect on *Candida albicans* is specific.

A modified membrane permeability is achieved by binding to sterols in the fungal cell wall, resulting in leakage of cell contents. It is well tolerated, even during long-term treatment, and development of resistance by nystatin has not been observed. Nystatin prevents gastrointestinal super infections of *Candida* in antibiotic therapy.

5.2 Pharmacokinetic properties

Nystatin is absorbed to a small extent from the gastrointestinal tract and is excreted largely unchanged in the faeces.

5.3 Preclinical safety data

No studies have been made to evaluate mutagenic or carcinogenic effect of nystatin.

Fertility and developmental toxicity studies (segment I, II and III) were carried out with nystatin in rats and rabbits. Parental mortality and toxicity at the higher dose (3.0 mg/kg/day) was observed in all studies.

Nystatin did not show any effect on the incidence of foetal malformations in rabbits. Despite the parentally toxic doses, nystatin showed no effect on F0 male or female fertility or early embryonic development of F1 offspring in rats. In F1 rats, post-wean development toxicity was observed at all dosage levels. Owing to

these toxic effects on postnatal development in F1 rats, caution should be exercised when using nystatin in females of childbearing potential.

Environmental Risk Assessment (ERA)

Nystatin is potentially persistent in the environment and environmental risk is not excluded.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Xylitol
Carmellose sodium
Methyl parahydroxybenzoate (E218)
Peppermint oil
Purified water
Sodium hydroxide (for pH adjustment)
Hydrochloric acid (for pH adjustment)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened bottle: 3 years.
Opened bottle: 2 months.

6.4 Special precautions for storage

Unopened bottle: store below 25° C.

Opened bottle: store below 25° C.

6.5 Nature and contents of container

Amber glass bottle, 100 ml with PP cap.

6.6 Special precautions for disposal <and other handling>

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD month YYYY}

Date of latest renewal: {DD month YYYY}

10. DATE OF REVISION OF THE TEXT

2025-04-16