

NDA 50-514/S-009

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Natacyn®

(natamycin
ophthalmic suspension)5%
Sterile

DESCRIPTION: NATAcYN® (natamycin ophthalmic suspension) 5% is a sterile, antifungal drug for topical ophthalmic administration. Each mL of the suspension contains: **Active:** natamycin 5% (50mg). **Preservative:** benzalkonium chloride 0.02%. **Inactive:** sodium hydroxide and/or hydrochloric acid (neutralized to adjust the pH), purified water. The active ingredient is represented by the chemical structure:
Established name: Natamycin

Chemical Structure

Molecular Formula: C₃₃H₄₇NO₁₃

Molecular Weight: 665.73

Chemical name: Stereoisomer of 22-[(3-amino-3,6-dideoxy- β-D-mannopyranosyl)oxy]-1,3,26-trihydroxy-12- methyl-10-oxo-6,11,28-trioxatricyclo[22.3.1.05,7] octacos-8,14,16,18,20-pentaene-25-carboxylic acid.

Other: Pimaricin

The pH range is 5.0 – 7.5.

CLINICAL PHARMACOLOGY: Natamycin is a tetraene polyene antibiotic derived from *Streptomyces natalensis*. It possesses *in vitro* activity against a variety of yeast and filamentous fungi, including *Candida*, *Aspergillus*, *Cephalosporium*, *Fusarium* and *Penicillium*. The mechanism of action appears to be through binding of the molecule to the sterol moiety of the fungal cell membrane. The polyenesterol complex alters the permeability of the membrane to produce depletion of essential cellular constituents. Although the activity against fungi is dose-related, natamycin is predominantly fungicidal.* Natamycin is not effective *in vitro* against gram-positive or gram-negative bacteria. Topical administration appears to produce effective concentrations of natamycin within the corneal stroma but not in intraocular fluid. Systemic absorption should not be expected following topical administration of NATAcYN® (natamycin ophthalmic suspension) 5%. As with other polyene antibiotics, absorption from the gastrointestinal tract is very poor. Studies in rabbits receiving topical natamycin revealed no measurable compound in the aqueous humor or sera, but the sensitivity of the measurement was no greater than 2 mg/mL.

INDICATIONS AND USAGE: NATAcYN® (natamycin ophthalmic suspension) 5% is indicated for the treatment of fungal blepharitis, conjunctivitis, and keratitis caused by susceptible organisms including *Fusarium solani* keratitis. As in other forms of suppurative keratitis, initial and sustained therapy of fungal keratitis should be determined by the clinical diagnosis, laboratory diagnosis by smear and culture of corneal scrapings and drug response. Whenever possible the *in vitro* activity of natamycin against the responsible fungus should be determined. The effectiveness of natamycin as a single agent in fungal endophthalmitis has not been established.

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CONTRAINDICATIONS: NATACYN® (natamycin ophthalmic suspension) 5% is contraindicated in individuals with a history of hypersensitivity to any of its components.

PRECAUTIONS: General. FOR TOPICAL OPHTHALMIC USE ONLY — NOT FOR INJECTION. Failure of improvement of keratitis following 7-10 days of administration of the drug suggests that the infection may be caused by a microorganism not susceptible to natamycin.

Continuation of therapy should be based on clinical re-evaluation and additional laboratory studies.

Adherence of the suspension to areas of epithelial ulceration or retention of the suspension in the fornices occurs regularly.

Use only if the container is undamaged.

Information for Patients: Do not touch dropper tip to any surface, as this may contaminate the suspension. Patients should be advised not to wear contact lenses if they have signs and symptoms of fungal blepharitis, conjunctivitis, and keratitis.

Carcinogenesis, Mutagenesis, Impairment of Fertility: There have been no long term studies done using natamycin in animals to evaluate carcinogenesis, mutagenesis, or impairment of fertility.

Pregnancy: Pregnancy Category C. Animal reproduction studies have not been conducted with natamycin. It is also not known whether natamycin can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. NATACYN® (natamycin ophthalmic suspension) 5% should be given to a pregnant woman only if clearly needed.

Nursing Mothers: It is not known whether these drugs are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when natamycin is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established.

Geriatric Use: No overall differences in safety or effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS:-The following events have been identified during post-marketing use of NATACYN® in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The events, which have been chosen for inclusion due to their seriousness, frequency of reporting, possible causal connection to NATACYN®, or a combination of these factors include: allergic reaction, change in vision, chest pain, corneal opacity, dyspnea, eye discomfort, eye edema, eye hyperemia, eye irritation, eye pain, foreign body sensation, paresthesia, and tearing.

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DOSAGE AND ADMINISTRATION: SHAKE WELL BEFORE USING. The preferred initial dosage in fungal keratitis is one drop of NATACYN® (natamycin ophthalmic suspension) 5% instilled in the conjunctival sac at hourly or two-hourly intervals. The frequency of application can usually be reduced to one drop 6 to 8 times daily after the first 3 to 4 days. Therapy should generally be continued for 14 to 21 days or until there is resolution of active fungal keratitis. In many cases, it may be helpful to reduce the dosage gradually at 4 to 7 day intervals to assure that the replicating organism has been eliminated. Less frequent initial dosage (4 to 6 daily applications) may be sufficient in fungal blepharitis and conjunctivitis.

HOW SUPPLIED: NATACYN® (natamycin ophthalmic suspension 5%) is a 15mL fill packaged in a 15 mL amber glass bottle with a black phenolic closure. A flint glass dropper with a red plastic closure and a black rubber bulb are packaged separately in a clear plastic blister with Tyvek backing.

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STORAGE: Store between 2-24°C (36-75°F). *Do not freeze.* Avoid exposure to light and excessive heat.

Rx Only

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ALCON LABORATORIES, INC.

Fort Worth, Texas 76134 USA