

Alert	The Antimicrobial Stewardship Team listed this drug under the following category: Unrestricted. Nystatin is not suitable for the treatment of invasive fungal disease.
Indication	1) Prophylaxis in infants at high risk for invasive fungal infections. Criteria for prophylaxis should be determined by local policy. Indications may include: Infants \leq 32 weeks gestation at birth or $<$ 1500 g birth weight or larger infants with risk factors including use of broad spectrum antibiotics, having a central venous access device (PICC/UVC/CVC), receiving parenteral nutrition or inhaled steroids. 2) Treatment of mucocutaneous candidiasis.
Action	Fungicidal agent which works by combining with the sterol elements of fungal cell membranes causing cell death by producing increased cell wall permeability.
Drug Type	Polyene antibiotic.
Trade Name	Nilstat oral drops, Mycostatin oral drops. Mycostatin topical cream.
Presentation	1. Oral drops (100,000 units/mL) 2. Topical cream (for cutaneous application)
Dosage/Interval	1. Prophylaxis of invasive fungal infection: 1 mL of oral drops every 8 hours. 2. Treatment of oral candidiasis (thrush): 1 mL of oral drops every 6 hours. Can be given more frequently in severe/resistant thrush. 3. Treatment of candida dermatitis: Local application of cream twice a day. Can be applied more frequently in severe/resistant cases.
Route	1. Oral 2. Topical application on the skin
Maximum Daily Dose	
Preparation/Dilution	Not required.
Administration	1. Prophylaxis with oral drops: Shake well before withdrawing the dose. Administer after a feed (if not NBM). Use the whole dose to saturate cotton bud and paint the inside of the mouth. Alternatively, 0.5 mL can be given through the feeding tube and flushed with a bolus of air (1 mL for a 5 Fg tube, 2 mL for an 8 Fg tube). Use the other 0.5 mL to saturate a cotton bud and paint the inside of the infant's mouth. 2. Treatment of oral thrush with the oral drops: Use the entire dose to paint the inside of the infant's mouth. 3. Treatment of dermatitis: Dry the skin thoroughly and apply the cream to the affected area. Leave the skin exposed if feasible. May need to be reapplied if the cream is wiped off during skin care.
Monitoring	Not required.
Contraindications	Known hypersensitivity to nystatin or any other ingredients (sucrose, methyl hydroxybenzoate, propyl hydroxybenzoate)
Precautions	None
Drug Interactions	Not applicable
Adverse Reactions	Generally well tolerated. Large doses may produce gastrointestinal upset (vomiting, diarrhoea). Rarely, may lead to rashes e.g. urticaria. Type 4 hypersensitivity reactions have been reported in adults.
Compatibility	No information
Incompatibility	Do not mix in the syringe with any other medication.
Stability	Stable until expiry date on the bottle/tube.
Storage	At room temperature
Special Comments	Nil
Evidence summary	Efficacy <u>Prevention of invasive fungal infections</u> A systematic review of RCTs found oral nystatin to be highly effective in preventing invasive fungal infection in VLBW infants with a relative risk of 0.16 when compared to placebo. ¹ A Cochrane

	<p>meta-analysis² found a statistically significant reduction in the incidence of invasive fungal infection (typical risk ratio 0.20, 95% CI 0.14-0.27) in very preterm VLBW infants when comparing oral/topical non-absorbed antifungal prophylaxis (nystatin or miconazole) with placebo or no drug. Substantial statistical heterogeneity was present though.² (LOE 1A, GOR A)</p> <p>A study from Australian and New Zealand NICUs reported³ that prophylactic oral nystatin is associated with a significantly lower incidence of fungal infection compared with no antifungal prophylaxis.³</p> <p><u>Treatment of mucocutaneous fungal infection</u></p> <p>Boon et al reported a cure rate of 80% after 2 weeks with the dose of 400,000 units/day.⁴ In a randomised trial⁵ comparing nystatin suspension with miconazole gel in immunocompetent infants for treatment of oropharyngeal candidiasis, Hoppe reported miconazole gel to be significantly superior with regard to efficacy, rapidity of achieving cure and oropharyngeal yeast eradication. Relapses and side effects were no different between miconazole and nystatin.⁵ However, miconazole gel is contraindicated in those under 6 months of age due to risk of airway obstruction from gel.</p> <p>Safety</p> <p>Acute generalised exanthematous pustulosis has been described following oral nystatin therapy.⁶</p>
References	<ol style="list-style-type: none"> 1. Blyth CC, Barzi F, Hale K, Isaacs D. Chemoprophylaxis of neonatal fungal infections in very low birthweight infants: efficacy and safety of fluconazole and nystatin. <i>J Paediatr Child Health</i> 2012;48:846-51 2. Austin N, Cleminson J, Darlow BA, McGuire W. Prophylactic oral/topical non-absorbed antifungal agents to prevent invasive fungal infection in very low birth weight infants. <i>Cochrane Database Syst Rev</i> 2015 Oct 24;(10):CD003478 3. Howell A, Isaacs D, Halliday R. The Australasian Study Group for Neonatal Infections. Oral nystatin prophylaxis and neonatal fungal infections. <i>Arch Dis Child Fetal Neonatal Ed</i> 2009;94:F429-F433 4. Boon JM, Lafeber HN, t'Mannetje AH, et al. Comparison of ketoconazole suspension and nystatin in the treatment of newborns and infants with oral candidosis. <i>Mycoses</i> 1989;32:312-5 5. Hoppe JE. Treatment of oropharyngeal candidiasis in immunocompetent infants: a randomized multicenter study of miconazole gel vs. nystatin suspension. The Antifungals Study Group. <i>Pediatr Infect Dis J</i> 1997;16:288-93 6. Kuchler A, Hamm H, Weidenthaler-Barth B, Kampgen E, Brocker EB. Acute generalized exanthematous pustulosis following oral nystatin therapy: a report of three cases. <i>Br J Dermatol</i> 1997;137:808-11.

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