Nystatin
Newborn use only

2022

Alert	The Antimicrobial Stewardship Team recommends this drug is listed as unrestricted. Nystatin is not suitable for the treatment of invasive fungal disease.
Indication	1. Prophylaxis against invasive fungal infections. a. Criteria for prophylaxis should be determined by local policy. b. Indications may include: Infants ≤ 32 weeks gestation at birth or < 1500 g birth weight or infants with risk factors including use of broad-spectrum antibiotics, central venous access device (PICC/UVC/CVC), parenteral nutrition or inhaled steroids. 2. Treatment of mucocutaneous candidiasis.
Action	Fungicidal agent. Combines with the sterol elements of fungal cell membranes causing cell death.
Drug type	Polyene antibiotic.
Trade name	Nilstat oral drops, Mycostatin oral drops, Pharmacy Action Nystatin Oral Drops, Trust Nystatin Oral Drops.
Presentation	Oral drops (100,000 units/mL) Topical cream (for cutaneous application) (100,000 units/g) - Discontinued
Dose	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.
Dose adjustment	Not applicable
Maximum dose	
Total cumulative dose	
Route	Oral
Preparation	
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 oral drops: Use the entire dose to paint the inside of the infant's mouth.
Monitoring	
Contraindications	Known hypersensitivity to nystatin or any other ingredients.
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.
Storage	Store at room temperature.
Excipients	Nilstat and Mycostatin oral drops: bentonite, sodium calcium edetate, sucrose, methyl and propyl hydroxybenzoates, polysorbate 80, cherry flavour F-1242, quinoline yellow (104) and purified water.
Special comments	
Evidence	**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 meta-analysis[2] 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) A study from Australian and New Zealand NICUs reported[3] that prophylactic oral nystatin is associated with a significantly lower incidence of fungal infection compared with no antifungal prophylaxis.[3] <u>Treatment of mucocutaneous fungal infection</u>

	Boon et al reported a cure rate of 80% after 2 weeks with the dose of 400,000 units/day.[4] In a randomised trial[5] 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. **Safety** Acute generalised exanthematous pustulosis has been described following oral nystatin therapy.[6]
Practice points	
References	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. J Paediatr Child Health 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. Cochrane Database Syst Rev 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. Arch Dis Child Fetal Neonatal Ed 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. Mycoses 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. Pediatr Infect Dis J 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. Br J Dermatol 1997; 137:808-11.

VERSION/NUMBER	DATE
Original 1.0	05/12/2016
Version 2.0	17/05/2017
Version 3.0	14/05/2021
Version 4.0	16/09/2021
Current 5.0	20/10/2022
REVIEW	20/10/2027

Authors Contribution

Original author/s	Nicholas Evans, Srinivas Bolisetty
Evidence Review	David Osborn
Current version author/s	Srinivas Bolisetty
Expert review of the original version	Brendan McMullan, Tony Lai, Alison Kesson
Nursing Review	Eszter Jozsa, Kirsty Minter, Priya Govindaswamy
Pharmacy Review	Cindy Chen
ANMF Group contributors	Nilkant Phad, Bhavesh Mehta, John Sinn, Michelle Jenkins, Jessica Mehegan, Helen Huynh, Simarjit Kaur, Sarah Woodland, Joanne Malloy, Hannah Bell, Rebecca Barzegar, Ian Callander, Eszter Jozsa, Mohammad Irfan Azeem, Renae Gengaroli, Rebecca O'Grady, Stephanie Halena, Thao Tran
Final editing and review of the original	Ian Whyte
Electronic version	Cindy Chen, Ian Callander
Facilitator	Srinivas Bolisetty