Metronidazole
Newborn use only

2020

Alert	High risk medicine. There are few data from prospective trials on the safety and efficacy of metronidazole in newborn infants.
Indication	Anaerobic bacterial and protozoal infections including meningitis. Necrotising enterocolitis.
Action	Bactericidal against anaerobic bacteria and an antiprotozoal agent.
Drug type	Antibacterial — nitromethylimidazole
Trade name	Metronidazole Sandoz IV Solution for infusion, DBL Metronidazole Intravenous Infusion, Metronidazole Intravenous Infusion (Baxter) Solution for infusion, Metronidazole-Claris Solution for infusion, Metronidazole Kabi solution fort Infusion. Flagyl S oral Suspension
Presentation	500 mg/100 mL IV solution 200 mg/5 mL Oral Suspension
Dose	IV or Oral Postmenstrual age/Corrected age* — Loading dose — Maintenance dose to commence — Maintenance < 27 weeks — 15 mg/kg — 24 hours after loading — 7.5 mg/kg 24 hourly 27^{+0}–33^{+6} weeks — 15 mg/kg — 12 hours after loading — 7.5 mg/kg 12 hourly 34^{+0}–40^{+6} weeks — 15 mg/kg — 8 hours after loading — 7.5 mg/kg 8 hourly ≥ 41^{+0} weeks — 15 mg/kg — 6 hours after loading — 7.5 mg/kg 6 hourly * Also referred to as "current gestational age"
Dose adjustment	
Maximum dose	
Total cumulative dose	
Route	IV, oral
Preparation	Use undiluted.
Administration	IV Infusion over 30 minutes. Oral: Give **1 hour before feeds.**
Monitoring	Full blood count if patient is on therapy > 1 week. Liver and renal function tests.
Contraindications	Hypersensitivity to metronidazole or other nitroimidazoles.
Precautions	Patients with seizures or peripheral neuropathy, blood dyscrasias, renal or hepatic impairment – dose reduction may be required.
Drug interactions	Co-administration with phenobarbital (phenobarbitone) and phenytoin may reduce metronidazole concentrations and increase phenytoin concentrations. Monitor anticonvulsant concentrations. Concurrent use with QT-prolonging drugs may result in increase of QT interval resulting in arrhythmias (torsades de pointes).
Adverse reactions	More common: GI upset, stomatitis and candida overgrowth. Drug metabolite may cause brownish discolouration of urine. Rare: Convulsive seizures and peripheral neuropathy characterised mainly by numbness or paraesthesia of an extremity have been reported in adults. May cause reversible leucopenia and/or thrombocytopenia.
Compatibility	Fluids: Glucose 5%, glucose 10% (not recommended due to high osmolarity of the resulting solution), sodium chloride 0.9%, glucose/sodium chloride fluids. Y-site: Amino acid solution, aciclovir, dopamine, esmolol, fluconazole, labetalol, lipid emulsion, magnesium sulfate, methylprednisolone sodium succinate, midazolam, morphine sulfate, piperacillin-tazobactam (EDTA-free), remifentanil.
Incompatibility	Amphotericin, aztreonam, cefepime, ganciclovir
Stability	Once removed from original container, use as soon as practicable.
Storage	IV: Store below 25°C. Do NOT refrigerate. Oral suspension: Store below 25°C. Protect from light.
Excipients	Injection: Citric acid, dibasic sodium phosphate, sodium chloride. Suspension: Aluminium magnesium silicate, ethanol, methyl hydroxybenzoate, monobasic sodium phosphate, natural soluble lemon flavour, orange oil terpeneless, propyl hydroxybenzoate, sucrose.

Special comments	Metronidazole oral suspension is best absorbed on an empty stomach.
Evidence	**Efficacy and Safety** There is a lack of data from prospective trials on the safety and efficacy of metronidazole in newborn infants. A retrospective study reported broad-spectrum antibiotics plus metronidazole may not prevent the deterioration of NEC in full-term and near-term infants. (1) (LOE III-3 GOR D) **Pharmacokinetics** Metronidazole principally undergoes hepatic metabolism with clearance increasing with weight and post-menstrual age (PMA). Cohen-Wolkowiez et al evaluated the pharmacokinetics of metronidazole in 32 infants born at ≤ 32 weeks' gestation and less than 120 days old. The study correlated metronidazole clearance with PMA and developed a PK model using nonlinear mixed-effect modeling (NONMEM). Monte Carlo simulations were performed and the study gives dosing recommendations based on PMA separated into < 34 weeks, 34 weeks to 40 weeks, and > 40 weeks. (2,3) Suyagh et al evaluated the pharmacokinetics of 32 infants born at ≤ 37 weeks gestation and less than 55 days old. A 1-compartment model was developed using NONMEM. Monte Carlo simulations were performed and dose recommendations are given based on PMA separated into < 26 weeks, 26–27 weeks, 28–33 weeks, and ≥ 34 weeks. (4) (LOE IV GOR C)
Practice points	
References	1. Luo LJ, Li X, Yang KD, Lu JY, Li LQ. Broad-spectrum antibiotic plus metronidazole may not prevent the deterioration of necrotizing enterocolitis from stage II to III in full-term and near-term infants: A propensity score-matched cohort study. Medicine. 2015;94(42). 2. Cohen-Wolkowiez M, Ouellet D, Smith PB, et al. Population pharmacokinetics of metronidazole evaluated using scavenged samples from preterm infants. Antimicrob Agents Chemother 2012;56:1828–37. 3. Cohen-Wolkowiez M, Sampson M, Bloom BT, et al. Determining population and developmental pharmacokinetics of metronidazole using plasma and dried blood spot samples from premature infants. Pediatr Infect Dis J 2013;32:956–61. 4. Suyagh M, Collier PS, Millership JS, Iheagwaram G, Millar M, Halliday HL, McElnay JC. Metronidazole population pharmacokinetics in preterm neonates using dried blood-spot sampling. Pediatrics. 2011 Feb 1;127(2):e367-74.1. 5. MIMS Product Information (2014) DBL Metronidazole Intravenous Infusion, Hospira 6. Australian Injectable Drugs Handbook, 6th Edition 2016. 7. Micromedex. Metronidazole monograph, accessed on 10/10/2016 8. MIMS Product Information (2016) Flagyl S Suspension, Sanofi-Aventis

VERSION/NUMBER	DATE
Original 1.0	29/12/2016
Version 2.0	11/12/2020
Current 2.1	17/05/2021
REVIEW	17/05/2026

Authors Contribution

Original author/s	Jing Xiao, Srinivas Bolisetty
Evidence Review	David Osborn
Expert review	Tony Lai, Brendan McMullan, Pamela Palasanthiran
Nursing Review	Eszter Jozsa, Kirsty Minter
Pharmacy Review	Michelle Jenkins
ANMF Group contributors	Chris Wake, Nilkant Phad, Bhavesh Mehta, John Sinn, Jessica Mehegan, Thao Tran, Helen Huynh, Carmen Burman, Jessica Mehegan
Final editing and review of the original	Ian Whyte
Electronic version	Cindy Chen, Ian Callander
Facilitator	Srinivas Bolisetty