<table>
<tr><td>Alert</td><td>There are few data from prospective trials on the safety and efficacy of metronidazole in newborn infants.</td></tr>
<tr><td>Indication</td><td>Treatment of anaerobic bacterial (including meningitis) and protozoal infections. Treatment of necrotising enterocolitis.</td></tr>
<tr><td>Action</td><td>Metronidazole is bactericidal against anaerobic bacteria and an antiprotozoal agent.</td></tr>
<tr><td>Drug Type</td><td>Antibacterial — nitroimidazole</td></tr>
<tr><td>Trade Name</td><td>Flagyl, Metronidazole Sandoz IV Solution for infusion, DBL Metronidazole Intravenous Infusion, Metronidazole Intravenous Infusion (Baxter) Solution for infusion, Metronidazole-Claris Solution for infusion

Flagyl S Suspension</td></tr>
<tr><td>Presentation</td><td>500 mg/100 mL IV solution
200 mg/5 mL Oral Suspension</td></tr>
<tr><td>Dosage/Interval</td><td>IV or PO

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<tr><td>Postmenstrual age/Corrected age</td><td>Loading dose</td><td>Maintenance</td></tr>
<tr><td>< 27 weeks</td><td>15 mg/kg</td><td>7.5 mg/kg 24 hourly</td></tr>
<tr><td>27^{+0}–33^{+6} weeks</td><td>15 mg/kg</td><td>7.5 mg/kg 12 hourly</td></tr>
<tr><td>34^{+0}–40^{+6} weeks</td><td>15 mg/kg</td><td>7.5 mg/kg 8 hourly</td></tr>
<tr><td>$\geq 41^{+0}$ weeks</td><td>15 mg/kg</td><td>7.5 mg/kg 6 hourly</td></tr>
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<tr><td>Maximum daily dose</td><td></td></tr>
<tr><td>Route</td><td>IV or PO</td></tr>
<tr><td>Preparation/Dilution</td><td>IV: Use undiluted.</td></tr>
<tr><td>Administration</td><td>IV Infusion: Over 30 minutes with a syringe pump.
Oral: Give 1 hour before feeds preferably.</td></tr>
<tr><td>Monitoring</td><td>Full blood count if patient is on therapy > 1 week. Liver and renal function tests.</td></tr>
<tr><td>Contraindications</td><td>Hypersensitivity to metronidazole or other nitroimidazoles.</td></tr>
<tr><td>Precautions</td><td>Patients with seizures or peripheral neuropathy, blood dyscrasias, renal or hepatic impairment – dose reduction may be required.</td></tr>
<tr><td>Drug Interactions</td><td>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).</td></tr>
<tr><td>Adverse Reactions</td><td>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.</td></tr>
<tr><td>Compatibility</td><td>Fluids: Glucose 5%, glucose 10%, sodium chloride 0.9%
Drugs via 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</td></tr>
<tr><td>Incompatibility</td><td>Amphotericin, aztreonam, cefepime, ganciclovir</td></tr>
<tr><td>Stability</td><td>Once removed from original container, use as soon as practicable</td></tr>
<tr><td>Storage</td><td>IV: Store below 25°C. Do NOT refrigerate.
Oral suspension: Store below 25°C. Protect from light.</td></tr>
<tr><td>Special Comments</td><td>Metronidazole oral suspension is best absorbed on an empty stomach.</td></tr>
<tr><td>Evidence summary</td><td>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)</td></tr>
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	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)
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

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