Flucloxacillin
Newborn use only

2019

Alert	The Antimicrobial Stewardship Team has listed this drug under the following category: Unrestricted.
Indication	Treatment of sepsis where infection by *S. Aureus* or susceptible coagulase-negative Staphylococci (CoNS) is suspected or confirmed, and other infections caused by susceptible organisms.
Action	Bactericidal agent that works by inhibiting the biosynthesis of cell wall mucopeptides. Flucloxacillin is stable against beta-lactamase producing bacteria.
Drug Type	Penicillin antibiotic.
Trade Name	Flucil, Flucloxacillin sodium monohydrate for injection (DBL), Flubiclox
Presentation	500 mg vial, 1000 mg vial, 125 mg/5 mL suspension.
Dosage/Interval	**IV, IM or IO: 50 mg/kg/dose. Dosing interval as below.** **Oral: 25–50 mg/kg/dose. Dosing interval as below.** Dosing interval for all routes **Day of life** – **Dosing interval** Days 0–7 – 12 hourly Days 8–28 – 8 hourly Day 29 + – 6 hourly
Route	IV IM (only if IV route not possible as intramuscular route is painful) IO Oral
Maximum Daily Dose	200 mg/kg/day
Preparation/Dilution	**IV/IO:** **500mg vial** Add 4.6 mL of water for injection to the 500 mg vial for reconstitution to make 100 mg/mL solution ***Further dilute*** Draw up 5 mL of solution (500 mg of flucloxacillin) and add 5 mL sodium chloride 0.9% to make a final volume of 10mL with a concentration of 50 mg/mL.[10] **1g vial** Add 4.3 mL of water for injection to the 1 g vial for reconstitution to make 200 mg/mL solution. ***Further dilute*** Draw up 2.5 mL of solution (500 mg of flucloxacillin) and add 7.5 mL sodium chloride 0.9% to make a final volume of 10mL with a concentration of 50 mg/mL.[10] **IM:** 500 mg vial: Add 1.6 mL of WFI, or lidocaine (lignocaine) 1% to 500mg powder for reconstitution (250 mg/mL)[10] OR 1000 mg vial: Add 3.3 mL of WFI, or lidocaine (lignocaine) 1% to the 1000 mg powder for reconstitution (250 mg/mL).[10] NOTE: DO NOT ADMINISTER LIDOCAINE (LIGNOCAINE) CONTAINING SOLUTIONS INTRAVENOUSLY
Administration	IV: Infuse over 30-60 minutes. Can also be given as slow injection over 3–5 minutes.[10] IM: Inject slowly into a large muscle (if administering a volume greater than 1mL, divide the dose and administer at 2 different injection sites to minimise pain). Oral: Give 30 to 60 minutes before feeds. Shake the bottle well before measuring dose. Usually reconstituted by Pharmacy. If supplied unreconstituted, reconstitute powder for oral suspension using water for injection with the volume specified on the bottle.

Monitoring	Monitor liver function tests if using high dose/long course or in existing hepatic impairment. Monitor renal function as the drug is mainly renally excreted.
Contraindications	History of flucloxacillin associated jaundice or hepatic dysfunction. History of a hypersensitivity reaction to beta-lactam antibiotics e.g., penicillins.
Precautions	Use with caution in renal or hepatic impairment. Use with caution in jaundiced or preterm infants as flucloxacillin can displace bilirubin from albumin. IM injection can cause pain and irritation – obtaining IV access as soon as possible is recommended.
Drug Interactions	Aminoglycosides, including gentamicin, should not be mixed with flucloxacillin when both drugs are given parenterally as inactivation occurs. Ensure line is adequately flushed between antibiotics.
Adverse Reactions	Transient diarrhoea – common with oral doses. Hypersensitivity (rare) – urticaria, fever, bronchospasm, anaphylaxis, eosinophilia. Phlebitis (much rarer than with dicloxacillin) – monitor injection site. Hepatitis and cholestatic jaundice (may occur up to several weeks after stopping), isolated cases of nephritis.
Compatibility	Fluids: Glucose 5%, sodium chloride 0.9%. lidocaine (lignocaine) 0.5% or 1% Y-site: Adrenaline (epinephrine), aminophylline, ampicillin, dexamethasone sodium phosphate, digoxin, heparin, hydrocortisone sodium succinate, potassium chloride, ranitidine, sodium bicarbonate.
Incompatibility	Fluids: Amino acid solutions and lipid emulsions. Y-site: Aminoglycosides (e.g., gentamicin), atropine sulfate monohydrate, benzylpenicillin, calcium gluconate monohydrate, ciprofloxacin, dobutamine, erythromycin lactobionate, midazolam, morphine sulfate pentahydrate, vancomycin.
Stability	Use immediately following reconstitution. Vial is for single use only. Reconstituted oral suspension should be discarded after 14 days.
Storage	Vial: Store below 25°C. Oral suspension: Store powder below 25°C, once reconstituted store solution at 2–8°C
Special Comments	IM administration will result in delayed peak serum concentrations compared with administration via Intravenous or intraosseous route
Evidence summary	Traditional IV dose regimens for flucloxacillin are based on a pharmacokinetic study from 1987 on 9 infants. The more recent pharmacokinetic study from 2006 suggests that traditional doses are inadequate for *S. aureus* and proposes a regimen of 25 mg/kg/dose 4 hourly for *S. aureus* infections and 10 mg/kg/dose 6 hourly for CoNS (based on Monte Carlo simulation from data obtained from 55 neonates, gestation 26 to 42 weeks), but these regimens have not been prospectively verified in a follow up study [4, 8] (Level IV). Lidocaine (Lignocaine) is used as diluent for IM preparation to reduce the pain at injection site.[10,11]
References	1. Edmund Hey (2011) Neonatal Formulary 6th Ed, page 111 2. MIMSOnline Product Information (2015) Flucloxacillin Sodium for Injection, DBL 3. Society of Hospital Pharmacists of Australia (2015) Australian Injectable Drugs Handbook, 6th Edition, Flucloxacillin Monograph 4. Pullen J. et al. (2006) Population Pharmacokinetics and Dosing of Flucloxacillin in Preterm and Term Neonates, Ther Drug Monit 28:351–358 5. Pacifici GM. et al. (2008) Clinical Pharmacokinetics of Penicillins in the Neonate: a review of the literature, European Journal of Clinical Pharmacology, 65; 191–198 6. Pullen J. et al. (2007) Protein Binding of Flucloxacillin in Neonates, Ther Drug Monit, 29:279–283 7. Gordon A., Jeffery HE. (2009) Antibiotic regimens for suspected late onset sepsis in newborn infants (Review), The Cochrane Collaboration, 2009 Issue 1 8. Herngren L. et al. (1987) Pharmacokinetics of Free and Total Flucloxacillin in Newborn Infants,

	European Journal of Clinical Pharmacology, 32; 403–409 9. Aspen (2015) Flucil Oral Liquid Product Information, MIMSOnline. 10. Australian Injectable Drugs Handbook. 7th Edition. Accessed on 19 September 2019 11. Amir J, Ginat S, Cohen YH, Marcus TE, Keller N, Varsano I. Lidocaine as a diluent for administration of benzathine penicillin G. The Pediatric infectious disease journal. 1998 Oct 1;17(10):890-3.

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