## Alert
The Antimicrobial Stewardship Team has listed this drug under the following category: Unrestricted.

## Indication
Treatment of sepsis where infection by *Staphylococcus 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 *Staphylococci*.

## 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
- 250 mg/5 mL suspension

## Dose/interval
**IV, IM or Intraosseous:**
Recommended for infants with moderate to severe infection, with *Staphylococcus aureus* and susceptible coagulase negative staphylococcus infections: **25 mg/kg/dose every 4 hours** [1]

### Alternate dosing regimen:
**50 mg/kg/dose. Dosing interval as below:**

<table>
<thead>
<tr>
<th>Day of life</th>
<th>Dosing interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 0–7</td>
<td>12 hourly</td>
</tr>
<tr>
<td>Days 8–20</td>
<td>8 hourly</td>
</tr>
<tr>
<td>Day 21+</td>
<td>6 hourly</td>
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</table>

**Oral: 25 mg/kg/dose. Dosing interval as below:**

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## Dose adjustment
- Therapeutic hypothermia: No information.
- ECMO: May need increased dosing. [2]
- Renal: Use with caution.
- Hepatic: Use with caution.

## Maximum dose
200 mg/kg/day

## Total cumulative dose

## Route
- **IV**
- IM (only if IV route not possible as intramuscular route is painful).
- Intraosseous
- **Oral**

## Preparation
**IV / Intraosseous:**

- **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. [3]

- **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. [3]

- **IM:**
  - 500 mg vial: Add 1.6 mL of water for injection, or lidocaine (lignocaine) 1% to 500mg powder for reconstitution (250 mg/mL) [3] OR
  - 1000 mg vial: Add 3.3 mL of water for injection, or lidocaine (lignocaine) 1% to the 1000 mg powder for reconstitution (250 mg/mL). [3]

**NOTE:** DO NOT ADMINISTER LIDOCAINE (LIGNOCAINE) CONTAINING SOLUTIONS INTRAVENOUSLY
### Flucloxacillin

**Newborn use only**

| Administration | IV: Infuse over 30 to 60 minutes. May be given as an IV injection over 3–5 minutes however pain and phlebitis are common and can be severe. [4]  
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. Consider dosage adjustment in renal 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), amiodarone, atropine sulfate monohydrate, benzylpenicillin, calcium gluconate monohydrate, ciprofloxacin, dobutamine, erythromycin, metoclopramide, midazolam, morphine sulfate, 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 |
| Excipients | Powder displacement values of 500 mg and 1 g vials are 0.4 mL and 0.7 mL respectively. [5]  
IM administration will result in delayed peak serum concentrations compared with administration via Intravenous or Intramuscular route. |
| Special comments | **Efficacy:**  
**Infants with suspected late onset sepsis:** A small single RCT in 24 infants with suspected sepsis comparing flucloxacillin 25 mg/kg 12 hourly and gentamicin 2.5 mg/kg 12 hourly versus ticarcillin-clavulanate (Timentin) 80 mg/kg 12 hourly or 8 hourly reported no difference in mortality, treatment failure or antibiotic resistance. No infant in the flucloxacillin group had a sterile site positive culture. [6]  
There are no RCTs of oral treatment using flucloxacillin for newborn infections including skin (impetigo) or soft tissue infections (see pharmacokinetics/pharmacodynamics). [7]  
Recommendation: Therapeutic Guidelines (eTG) recommends flucloxacillin 50 mg/kg 4 to 6 hourly (child). Use a 4-hourly flucloxacillin dosing interval for critically ill patients with severe sepsis or septic shock. [8]  
Alternate IV Dosing regimen: An alternate dosing regimen in this formulary is proposed which has been recommended by British National Formulary [9] and has been commonly used in Australia without any report of lack of efficacy (personal communication).  
**Infants with newly diagnosed cystic fibrosis:** A small RCT in 38 infants with newly diagnosed CF [mean (range) age of diagnosis 5–7 weeks (1–14 weeks)] treated with continuous oral flucloxacillin 250 mg/day versus episodic antimicrobials as clinically indicated reported reduced clinical symptoms, reduced Staphylococcus aureus colonisation and reduced hospitalisation in the first 2 years. Continuous
prophylactic flucloxacillin from early diagnosis of cystic fibrosis is associated with improved clinical progress during the first two years of life. [10] (LOE II, GOR C)

**Pharmacokinetics / pharmacodynamics:**

There has been considerable variation in dosing recommendations for neonates regarding flucloxacillin. [11] Herngren et al in 9 newborn infants (gestational age 33-41 weeks) reported flucloxacillin 50 mg/kg 12 hourly resulted in plasma concentrations substantially above MIC for Staphylococcus aureus (0.2 mg/L). The average t½ 4.6 hours in infants 33-41 weeks was inversely correlated with gestational age. Plasma protein binding 86% affected by bilirubin/albumin ratio. Bioavailability oral flucloxacillin was 48%.

Conversely, Pullen et al reported 235 flucloxacillin total (free + protein bound) plasma concentrations in 55 neonates (gestation 26 to 42 weeks, postnatal age 0 to 44 days). Mean flucloxacillin elimination t½ was 2.6±1.6 hours. CoNS and Staphylococcus aureus breakpoint MIC values of flucloxacillin were 0.25 and 2.0 mg/L, respectively, equivalent to a 10 fold different MIC for Staphylococcus aureus compared with Herngren et al. The dosage regimen 25 or 50 mg/kg every 8 or 12 hours did not result in effective plasma concentrations for the treatment of Staphylococcus aureus in 31% of neonates. Recommend initial dose of 25 mg/kg/4 hourly for all neonates. [1] (LOE IV GOR C).

Adrianzen Vargas 2004 reported that in 11 infants undergoing cardiopulmonary bypass the mean serum concentration of flucloxacillin decreased by 42.5% and the t½ was 2.64 (±0.23) hours. [2] (LOE IV)

**Oral administration:**

Bioavailability oral flucloxacillin was reported to be 48% in neonates. [12] Peak plasma levels after flucloxacillin 25 mg/kg were delayed when given orally (2 hours) compared to IV, but subsequent plasma levels were adequate to achieve levels in excess of MIC of Staphylococcus aureus. [13]

Lidocaine (lignocaine) has been used as diluent for IM penicillin preparations to reduce the pain at injection site. [3]

**Practice points**

For the treatment of Staphylococcus aureus, the recommend initial dose of 25 mg/kg/4 hourly for all neonates. [1] (LOE IV GOR C).

The bioavailability oral flucloxacillin was 48% in neonates. [12] Oral flucloxacillin 25 mg/kg produced peak plasma levels after 2 hours that were adequate to achieve levels in excess of MIC of Staphylococcus aureus. [13]

**References**


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<td>REVIEW (5 years)</td>
<td>29/05/2025</td>
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