Alert
High risk medicine. 
Antimicrobial Stewardship Team recommends this drug is listed as unrestricted.

Indication
Treatment
1. Susceptible gram positive (including Streptococcus species, Enterococcus faecalis and Listeria monocytogenes),
2. Susceptible gram-negative bacteria (some strains of Escherichia coli, non-beta-lactamase-producing Haemophilus influenzae, Neisseria meningitidis, non-penicillinase-producing strains of Proteus and Salmonellae).
3. Empiric treatment of suspected early onset sepsis including meningitis, with an aminoglycoside.

Prophylaxis
1. Urinary Tract Infection (UTI) prophylaxis
2. Asplenia/hyposplenism prophylaxis

Action
Bactericidal – inhibits synthesis of the bacterial cell wall. Amoxicillin is hydrolysed by beta-lactamases and therefore not effective against penicillinase-producing bacteria.

Drug Type
Antibacterial – semi-synthetic, bactericidal aminopenicillin

Presentation
IV: Amoxicillin 1 g vial.
Oral: Syrup 125 mg/5 mL and 250 mg/5 mL; Paediatric drops 100 mg/mL.

Dosage
Treatment - IV
Standard infections: 50 mg/kg/dose.
Meningitis: 100 mg/kg/dose.

<table>
<thead>
<tr>
<th>Corrected gestational age/postmenstrual age*</th>
<th>Day of life</th>
<th>Interval</th>
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<tr>
<td>&lt; 300 weeks</td>
<td>0–28 days</td>
<td>12 hourly</td>
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<td>&lt; 300 weeks</td>
<td>29+ days</td>
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<td>300–36 weeks</td>
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*Also referred to as "current gestational age"

Treatment - ORAL
Treatment: 25–50 mg/kg/dose.

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Prophylaxis - ORAL
Urinary Tract Infection: 10–15 mg/kg/dose once a day
Asplenia/hyposplenism: 20 mg/kg/dose once a day (14)

Maximum Daily Dose
300 mg/kg/day

Route
IV
IM (only if IV route not possible as intramuscular route is painful)
ORAL

Preparation
IV
Add 9.2 mL of water for injection to the 1 g vial to make 100 mg/mL solution.

FURTHER DILUTE
Draw up 5 mL (500 mg of amoxicillin) of the above solution and add 5 mL sodium chloride 0.9% to make a final volume of 10mL with a final concentration of 50 mg/mL.
Use immediately as concentrated solution >30 mg/mL is not stable.(9)
IM
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**ORAL**
Manufacturer’s recommendations should guide reconstitution of the oral suspension as multiple brands of amoxicillin are available.

**Administration**
- IV: Infuse over 30 minutes into the proximal cannula site. Separate from aminoglycosides by clearing the lines with a flush as penicillins inactivate them. IM injection: Only if IV route is not possible.
- PO: The liquid preparation should be shaken well. After mixing, administer immediately. The dose may be mixed with milk.

**Monitoring**
Monitoring is not required. Follow infectious disease/microbiology advice in case of poor therapeutic response.

**Contraindications**
Hypersensitivity to penicillins (unlikely to be an issue in neonates).

**Precautions**
Hypersensitivity to cephalosporins (unlikely to be an issue in neonates). In renal impairment, the excretion of amoxicillin will be delayed. In infants with severe renal impairment, it may be necessary to reduce the total daily dose.

**Drug Interactions**
- IV: Aminoglycosides, including gentamicin, should not be mixed with amoxicillin when both drugs are given parenterally as inactivation of the aminoglycoside occurs. Ensure line is adequately flushed between antibiotics.
- PO: No significant drug-drug interaction found for neonates on oral amoxicillin.

**Adverse Reactions**
Common: Diarrhoea, skin rash (erythematous maculopapular), phlebitis at the injection site, superinfection with resistant organisms during prolonged therapy.
Uncommon/rare: Neurotoxicity, electrolyte disturbances e.g. hypernatraemia due to the sodium content (2.6 mmol per gram in Fisamox IV and 3.3 mmol per gram in Ibiamox IV), erythema multiforme, exfoliative skin lesions, *C. difficile* diarrhoea, pancytopenia, raised liver enzymes. Amoxicillin may result in a false positive for glucose in the urine due to excessive amounts of urinary amoxicillin.

**Compatibility**
Fluids: Glucose 5%, glucose 5% in sodium chloride 0.45% (less stable in carbohydrate solutions, it is preferable to avoid adding it to them) (13), sodium chloride 0.9%, water for injection (WFI)

- Y site: No information.

**Incompatibility**
Fluids: Blood products, dextran, fat emulsions, amino acid solutions

- Y site: Amikacin, ciprofloxacin, gentamicin, imipenem-cilastatin, midazolam, potassium chloride, rocuronium, sodium bicarbonate, tobramycin.

**Stability**
- IV: The reconstituted solution should be administered immediately; discard unused portion. A transient pink or slight opalescence may appear during reconstitution. Do NOT administer if reconstituted solution is pink.
- PO: The medication mixed with milk should be administered immediately.

**Storage**
- IV: Store below 25°C. Protect from light.
- PO: Store unreconstituted powder for oral suspension at 20–25°C. Reconstituted suspension is stable for 14 days at room temperature or if refrigerated. Refrigeration is preferred.

**Special Comments**
Clearance is primarily by the renal route. Clearance increases with increasing gestational age and postmenstrual age. Serum half-life is longer in premature infants and infants younger than 7 days. Fisamox and Ibiamox 1g vial powder displacement volume ~ 0.8 mL.

**Evidence**
Efficacy
There are few studies of amoxicillin in the neonatal population to study effectiveness and the majority of the information is derived from studies of ampicillin. A study in two Estonian NICUs comparing ampicillin + gentamicin versus penicillin + gentamicin in the empiric therapy of neonates at risk of early-onset sepsis showed similar effectiveness in need to change antibiotics at 72 hours and/or 7-day all-cause mortality. (1) Subgroup analysis in ELBW neonates showed similar results, though NICU mortality was lower in the ampicillin group in < 26 weeks gestation neonates. (2)
In an RCT of amoxicillin prophylaxis for prevention of catheter-related infections in newborn infants with central venous catheters, bacterial contamination of the catheter tip at removal was significantly reduced in the amoxicillin group. No significant difference was found in the incidence of invasive related infections in newborn infants.
Amoxicillin
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infection.\(^3\) In a randomised, open-label, equivalence trial in Africa, oral amoxicillin was found to be equivalent to injectable procaine penicillin plus gentamicin in the treatment of neonates and young infants with fast breathing.\(^4\)

IV amoxicillin has similar properties to ampicillin and there is little to choose between the two when given by the IV route to treat susceptible organisms.\(^5\) Amoxicillin achieves higher serum and CSF concentrations than ampicillin.\(^6\) Oral amoxicillin has similar properties to ampicillin. Both the antibiotics are well absorbed when given by mouth, widely distributed in body tissues (including bronchial secretions) and rapidly excreted in the urine. Oral amoxicillin has better bioavailability but can be variable in young children.\(^5\) Oral medication can nearly always be used to complete any sustained course of treatment.\(^12\)

**Pharmacokinetics:**

Study of amoxicillin pharmacokinetics in preterm infants\(^7\) has shown that a q12h schedule in the first week achieves serum concentrations well above the MIC for major micro-organisms in neonatal infections.\(^7\) Another study in neonates older than 1 week showed that amoxicillin clearance was related to post-conceptional age and not to postnatal age with a rapid linear increase in clearance after 34 weeks post-conceptional age.\(^8\)

In a study\(^9\), early switching to the oral route in asymptomatic full-term newborns with early onset GBS disease maintained serum amoxicillin concentrations within the therapeutic range.\(^10\) The dose used in that study was 200–300 mg/kg/day in 4 divided doses. All the concentrations were in the therapeutic range with the lower dose. Another pharmacokinetic study in 6–13 days old neonates concluded that amoxicillin should be useful for oral treatment of neonatal infections caused by susceptible micro-organisms in infants who are not critically ill. The dose used was 50 mg/kg twice a day.\(^11\)

**Recommendation:**

Amoxicillin can be used as a substitute for benzylpenicillin or ampicillin for suspected, early-onset, neonatal sepsis in combination with an aminoglycoside. When amoxicillin is used in combination with an aminoglycoside for the treatment of meningitis, it is recommended that the dose be doubled from 50 to 100 mg/kg/dose.\(^12\) This is in keeping with similar recommendations for benzylpenicillin and ampicillin based on high minimum bactericidal concentration of group B streptococci and high inocula of the organisms in neonatal meningitis. (Level of evidence 5, Grade of recommendation D).

**References**


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**Authors Contribution**

<table>
<thead>
<tr>
<th>Role</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original author/s</td>
<td>Rajesh Maheshwari</td>
</tr>
<tr>
<td>Evidence Review - original</td>
<td>David Osborn</td>
</tr>
<tr>
<td>Expert review</td>
<td>Brendan McMullan, Alison Kesson, Tony Lai, Pam Palasanthiran</td>
</tr>
<tr>
<td>Nursing Review</td>
<td>Eszter Jozsa, Kirsty Minter, Priya Govindaswamy</td>
</tr>
<tr>
<td>Pharmacy Review</td>
<td>Ushma Trivedi, Jing Xiao, Michelle Jenkins, Cindy Chen, Carmen Burman, Joanne Malloy, Hannah Bell, Simarjit Kaur</td>
</tr>
<tr>
<td>ANMF Group contributors</td>
<td>Nikant Phad, Himanshu Popat, Anna Gill, Catherine Allgood, Rahul Prasad, Bhavesh Mehta, John Sinn, Thao Tran, Wendy Huynh, Helen Huynh</td>
</tr>
<tr>
<td>Final editing and review of the original</td>
<td>Ian Whyte</td>
</tr>
<tr>
<td>Electronic version</td>
<td>Cindy Chen, Ian Callander</td>
</tr>
<tr>
<td>Facilitator</td>
<td>Srinivas Bolisetty</td>
</tr>
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**Amoxicillin**

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