

Amoxicillin (Amoxycillin)

Newborn use only

2020

Alert	S4 – High risk medicine. Antimicrobial Stewardship Team recommends this drug is listed as unrestricted.																														
Indication	Directed treatment of infections caused by <ol style="list-style-type: none"> susceptible gram positive (including <i>Streptococcus</i> species, <i>Enterococcus faecalis</i> and <i>Listeria monocytogenes</i>) and susceptible gram negative bacteria (some strains of <i>Escherichia coli</i>, non-beta-lactamase-producing <i>Haemophilus influenzae</i>, <i>Neisseria meningitidis</i>, non-penicillinase-producing strains of <i>Proteus</i> and <i>Salmonellae</i>). Empiric treatment of suspected early onset sepsis including meningitis, with an aminoglycoside.																														
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																														
Trade Name	Alphamox Suspension [Alphapharm], Amoxil Paediatric Drops [Aspen], Amoxil Parenteral [Aspen], Amoxil Syrup Forte Sugar Free [Aspen], Amoxil Syrup Sugar Free [Aspen], Amoxycillin Sandoz [Sandoz], APO-Amoxycillin [Apotex], Bgramin [Ascent Pharma], Chemmart Amoxycillin [Apotex], Cilamox Sugar Free Syrup [Aspen Pharma], Fisamox [Aspen], Ibiamox [Willow], Maxamox [Sandoz], Ranmoxy Granules [Ranbaxy], Terry White Chemists Amoxycillin [Apotex]																														
Presentation	IV: Amoxicillin sodium 500 mg and 1 g vials. Oral: Syrup 125 mg/5 mL and 250 mg/5 mL; Paediatric drops 100 mg/mL.																														
Dosage / Interval	<p>IV</p> <p>Standard infections: 50 mg/kg/dose. Meningitis: 100 mg/kg/dose.</p> <table border="1"> <thead> <tr> <th>Corrected Gestational Age/Postmenstrual Age</th> <th>Postnatal Age</th> <th>Interval</th> </tr> </thead> <tbody> <tr> <td>< 30+0 weeks</td> <td>0–28 days</td> <td>12 hourly</td> </tr> <tr> <td>< 30+0 weeks</td> <td>29+ days</td> <td>8 hourly</td> </tr> <tr> <td>30⁺⁰–36⁺⁶ weeks</td> <td>0–14 days</td> <td>12 hourly</td> </tr> <tr> <td>30⁺⁰–36⁺⁶ weeks</td> <td>15+ days</td> <td>8 hourly</td> </tr> <tr> <td>37⁺⁰–44⁺⁶ weeks</td> <td>0–7 days</td> <td>12 hourly</td> </tr> <tr> <td>37⁺⁰–44⁺⁶ weeks</td> <td>8+ days</td> <td>8 hourly</td> </tr> </tbody> </table> <p>ORAL</p> <p>Treatment: 25–50 mg/kg/dose.</p> <table border="1"> <thead> <tr> <th>Corrected Gestational Age/Postmenstrual Age</th> <th>Postnatal Age</th> <th>Interval</th> </tr> </thead> <tbody> <tr> <td>37⁺⁰–44⁺⁶ weeks</td> <td>0–7 days</td> <td>12 hourly</td> </tr> <tr> <td>37⁺⁰–44⁺⁶ weeks</td> <td>8+ days</td> <td>8 hourly</td> </tr> </tbody> </table> <p>Prophylaxis (e.g. Urinary Tract Infection): 10–15 mg/kg/dose once a day</p>	Corrected Gestational Age/Postmenstrual Age	Postnatal Age	Interval	< 30+0 weeks	0–28 days	12 hourly	< 30+0 weeks	29+ days	8 hourly	30 ⁺⁰ –36 ⁺⁶ weeks	0–14 days	12 hourly	30 ⁺⁰ –36 ⁺⁶ weeks	15+ days	8 hourly	37 ⁺⁰ –44 ⁺⁶ weeks	0–7 days	12 hourly	37 ⁺⁰ –44 ⁺⁶ weeks	8+ days	8 hourly	Corrected Gestational Age/Postmenstrual Age	Postnatal Age	Interval	37 ⁺⁰ –44 ⁺⁶ weeks	0–7 days	12 hourly	37 ⁺⁰ –44 ⁺⁶ weeks	8+ days	8 hourly
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Maximum Daily Dose	300 mg/kg/day																														
Route	IV IM (only if IV route not possible as intramuscular route is painful) ORAL																														
Preparation/Dilution	<p>IV</p> <p>Add 4.6 mL of water for injection to the 500 mg vial to make 100 mg/mL solution OR Add 9.3 mL of water for injection to the 1 g vial to make 100 mg/mL solution.</p> <p>FURTHER DILUTE</p> <p>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.</p> <p>IM</p> <p>Add 2.3 mL of water for injection to the 500 mg vial to make 200 mg/mL solution.</p> <p>ORAL</p> <ol style="list-style-type: none"> Syrup 125 mg/5 mL: Add 87 mL of water for irrigation to make a final volume of 100mL with a final concentration of 125mg/5mL of suspension. Syrup 250mg/5mL: Add 87 mL of water for irrigation to make a final volume of 100mL with a final concentration of 250mg/5mL of suspension. 																														

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	3. Paediatric drops 100 mg/mL: Add 18 mL water for injection to make a final volume of 21mL with a final concentration of 100mg/mL.
Administration	<p>IV: Infuse over 30 minutes into the proximal cannula site.</p> <p>Separate from aminoglycosides by clearing the lines with a flush as penicillins inactivate them.</p> <p>IM injection: Only if IV route is not possible.</p> <p>PO: The liquid preparation should be shaken well After mixing, administer immediately. . The dose may be mixed with milk.</p>
Monitoring	<p>Monitoring is not required.</p> <p>Follow infectious disease/microbiology advice in case of poor therapeutic response.</p>
Contraindications	Hypersensitivity to penicillins (unlikely to be an issue in neonates).
Precautions	<p>Hypersensitivity to cephalosporins (unlikely to be an issue in neonates).</p> <p>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.</p>
Drug Interactions	<p>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.</p> <p>PO: No significant drug-drug interaction found for neonates on oral amoxicillin.</p>
Adverse Reactions	<p>Common: Diarrhoea, skin rash (erythematous maculopapular), phlebitis at the injection site, superinfection with resistant organisms during prolonged therapy</p> <p>Uncommon/rare: Neurotoxicity, electrolyte disturbances e.g. hypernatraemia due to the sodium content (3.3 mmol per gram in Amoxil IV and 2.6 mmol per gram in Fisamox IV), erythema multiforme, exfoliative skin lesions, <i>C. difficile</i> diarrhoea, pancytopenia, raised liver enzymes. Amoxicillin may result in a false positive for glucose in the urine due to excessive amounts of urinary amoxicillin.</p>
Compatibility	<p>Fluids: Sodium chloride 0.9%, sterile water for injection</p> <p>Y site: No information⁹</p>
Incompatibility	<p>Fluids: Glucose and glucose-containing solutions, fat emulsions</p> <p>Y site: Aminoglycosides, ciprofloxacin, imipenem-cilastatin, midazolam, potassium chloride, sodium bicarbonate⁹</p>
Stability	<p>IV: The reconstituted solution should be administered immediately; discard unused portion</p> <p>PO: The medication mixed with milk should be administered immediately.</p>
Storage	<p>IV: Store below 25°C. Protect from light.</p> <p>PO: Store unconstituted powder for oral suspension at 20–25 °C. Reconstituted suspension is stable for 14 days at room temperature or if refrigerated. Refrigeration is preferred.</p>
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.
Evidence	<p>Effectiveness:</p> <p>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 mortality¹. Subgroup analysis in ELBW neonates showed similar results, though NICU mortality was lower in the ampicillin group in < 26 weeks gestation neonates².</p> <p>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 infection³. 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 breathing⁴.</p>

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 organisms⁵. Amoxicillin achieves higher serum and CSF concentrations than ampicillin⁶. 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 children⁵. Oral medication can nearly always be used to complete any sustained course of treatment.¹³

Pharmacokinetics:

Study of amoxicillin pharmacokinetics in preterm infants⁷ has shown that a q12h schedule in the first week achieves serum concentrations well above the MIC for major micro-organisms in neonatal infections. Another study⁸ in neonates older than 1 week showed that amoxicillin clearance was related to post-conceptual age and not to postnatal age with a rapid linear increase in clearance after 34 weeks post-conceptual age.

In a study¹⁰, early switching to the oral route in asymptomatic full-term newborns with early onset GBS disease maintained serum amoxicillin concentrations within the therapeutic range. 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).

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