Ampicillin
Newborn use only

2021

Alert	The Antimicrobial Stewardship Team recommends this drug is listed under the following category: Unrestricted.
Indication	Directed treatment of infections caused by susceptible gram positive (including *Streptococcus* species, *Enterococcus faecalis* and *Listeria monocytogenes*) and susceptible gram-negative bacteria (some strains of *Escherichia coli*, many strains of *Haemophilus influenzae, Neisseria meningitidis, Proteus mirabilis* and *Salmonellae*). Empiric treatment of suspected early onset sepsis including meningitis, with an aminoglycoside.
Action	Bactericidal - inhibits the synthesis of the bacterial cell wall. Ampicillin is hydrolysed by beta-lactamases and therefore not effective against penicillinase producing bacteria.
Drug Type	Antibacterial - Penicillin
Trade Name	Ampicyn, Austrapen, Ibimicyn
Presentation	Ampicillin 500 mg vial Ampicillin 1000 mg vial
Dosage	**Standard infections: 50 mg/kg/dose. Dosing interval as per table below** **Meningitis: 100 mg/kg/dose. Dosing interval as per table below**

Method		Interval
Corrected Gestational Age/Postmenstrual Age	**Postnatal Age**	
< 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
≥ 45^{+0} weeks	0+ days	6 hourly

Maximum Daily Dose	400 mg/kg/day
Route	IV IM (only if IV route not possible as intramuscular route is painful)
Preparation	**IV (Ampicyn, Austrapen):** Add 4.7 mL of water for injection to the 500 mg vial for reconstitution to make 100 mg/mL solution OR Add 9.3 mL of water for injection to the 1 g vial for reconstitution to make 100 mg/mL solution. **FURTHER DILUTE:** - Draw up 5 mL (500 mg of ampicillin) of solution and add 5 mL sodium chloride 0.9% to make a final volume of 10mL with a concentration of 50 mg/mL solution OR - Draw up 3 mL (300 mg of ampicillin) of solution and add 7 mL sodium chloride 0.9% to make a final volume of 10mL with a concentration of 30 mg/mL solution **IV (Ibimicyn):** Add 4.7 mL of water for injection to the 500 mg vial for reconstitution to make 100 mg/mL solution OR Add 7.4 mL of water for injection to the 1 g vial for reconstitution, draw up the entire content of the vial and make up the volume to 10 mL with WFI to make 100 mg/mL solution. **FURTHER DILUTE** - Draw up 5 mL (500 mg of ampicillin) of solution and add 5 mL sodium chloride 0.9% to make a final volume of 10mL with a concentration of 50 mg/mL solution OR - Draw up 3 mL (300 mg of ampicillin) of solution and add 7 mL sodium chloride 0.9% to make a final volume of 10mL with a concentration of 30 mg/mL solution **IM:** Add 1.7 mL of water for injection to the 500 mg vial for reconstitution to make 250 mg/mL solution OR Add 3.3 mL of water for injection to the 1 g vial for reconstitution to make 250 mg/mL solution.
Administration	IV: Infusion over 30 minutes. Separate from aminoglycosides by clearing the lines with a flush as ampicillin inactivates them. Higher doses (meningitis) should be diluted to 30 mg/mL and infused over 30 minutes.

Monitoring	Plasma concentrations not usually required; however may be useful for infections caused by bacteria with high Minimum Inhibitory Concentration (MIC).
Contraindications	Hypersensitivity reactions can occur in ampicillin-treated infants younger than 6 months of age but are rarely reported in neonates.
Precautions	Hypersensitivity to penicillin derivatives. In renal impairment the excretion of ampicillin will be delayed. In infants with severe renal impairment it may be necessary to reduce the total daily dose.
Drug Interactions	Aminoglycosides including gentamicin should not be mixed with ampicillin when both drugs are given parenterally as inactivation occurs. Ensure line is adequately flushed between antibiotics.
Adverse Reactions	Allergic reactions – maculopapular or urticarial rash, fever (rare in neonates). Other: Diarrhoea; CNS excitation or seizures with very large doses reported in adults; and prolonged bleeding time with repeated doses.
Compatibility	Fluids: Sodium chloride 0.9%. Y site: Aciclovir, amifostine, anidulafungin, aztreonam, bivalirudin, dexmedetomidine, esmolol, filgrastim, foscarnet, granisetron, heparin sodium, labetalol, linezolid, magnesium sulfate, morphine sulfate, pethidine, potassium chloride, remifentanil.
Incompatibility	Fluids: Glucose and glucose containing solutions, fat emulsions. Y site: Amino acid solutions, adrenaline hydrochloride, aminoglycosides – amikacin, gentamicin, tobramycin; aminophylline, atropine, buprenorphine, caspofungin, chlorpromazine, clindamycin, dobutamine, dolasetron, dopamine, ergometrine, fluconazole, ganciclovir, haloperidol lactate, hydralazine, ketamine, lincomycin, metoclopramide, midazolam, mycophenolate mofetil, ondansetron, pentamidine, prochlorperazine, promethazine, protamine, sodium bicarbonate, tranexamic acid, verapamil.
Stability	Administer immediately; discard unused portion of reconstituted solution.
Storage	Store below 25°C Protect from light.
Special Comments	Clearance is primarily by the renal route. Clearance increases with increasing gestational age and postnatal age. Serum half-life is longer in premature infants and infants younger than 7 days.
Evidence	**Effectiveness** A 2 hospital crossover study comparing ampicillin versus penicillin combined with gentamicin in the empiric therapy of extremely low-birth weight neonates at risk of early onset sepsis showed similar effectiveness in change of antibiotics at 72 hours and/or 7-day all-cause mortality. 11, 12 A systematic review comparing the effectiveness and safety of penicillin or ampicillin-chloramphenicol versus third generation cephalosporin in patients with community-acquired suspected acute bacterial meningitis found 12 trials enrolling infants under 1 year of age. There were no significant differences between the groups in the risk of death, deafness, or treatment failure; there were significantly decreased risks of culture positivity of CSF after 10 to 48 hours and increases in the risk of diarrhoea between the groups (RD 8%; 95% CI 3% to 13%) with third generation cephalosporin. 13 **Dose:** There are no clinical trials comparing standard versus high dose ampicillin in neonates with sepsis or meningitis. Clinical trials reporting effectiveness of regimens including ampicillin for meningitis reported use of daily doses of ampicillin ≥ 200 mg/kg/day.13 Doses of ampicillin of 200 mg/kg/day result in adequate CSF concentrations for treatment of enterococcus and Listeria monocytogenes.10, 14 **Recommendation** When ampicillin 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 (Level of evidence III-2, Grade of recommendation B).
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