Amoxicillin-clavulanate

Newborn use only

2020

Alert	Amoxicillin-clavulanate should be reserved for treatment of infections where amoxicillin alone is ineffective. Not for intramuscular administration. The pharmacokinetics of clavulanate has not been evaluated in neonates. Dose and frequency are product specific and the products are not interchangeable. **In neonates, a 5:1 and 4:1 ratios of amoxicillin: clavulanate are currently used for intravenous and oral administrations respectively.**
Indication	Directed treatment of susceptible bacterial infections covered by amoxicillin but producing beta-lactamase including skin infection, ear infection, sinusitis, urinary tract infection, upper and lower respiratory tract infection, and animal bites.[1, 2]
Action	Amoxicillin is a semi-synthetic penicillin and has similar antibacterial spectrum as ampicillin. It is bactericidal against both gram-positive and gram-negative bacteria but is destroyed by beta-lactamase produced by many of these bacteria. Clavulanate binds irreversibly with beta-lactamases produced by a variety of gram-positive and gram-negative microorganisms and protects amoxicillin from degradation. Thus extending the spectrum of amoxicillin.[1] Amoxicillin is better-absorbed than ampicillin, following oral administration.[1]
Drug type	Antimicrobial agent – Beta-lactam aminopenicillin and Beta-lactamase inhibitor combination
Trade name	Oral: Curam 125mg/31.25mg Powder for Suspension IV: Amoxiclav Juno 1000/200, Curam 500/100, Curam 1000/200
Presentation	**IV** 500mg/100mg vial contains 500 mg of amoxicillin and 100 mg of clavulanic acid powder for injection (5:1 ratio). Each vial contains 1.4 mmol (31.4 mg) of sodium and 0.5 mmol (19.6mg) of potassium. 1000mg/200mg vial contains 1000 mg of amoxicillin and 200 mg of clavulanic acid powder for injection (5:1 ratio). Each vial contains 2.7 mmol (62.9 mg) of sodium and 1.0 mmol (39.3mg) of potassium. Vials containing alternative ratios have not been included in this formulary. **Oral** Suspension (reconstituted) contains 125 mg amoxicillin and 31.25 mg clavulanate per 5 mL (4:1 ratio).
Dosage	**Doses are based on amoxicillin component** **IV:** 25 mg (of amoxicillin component)/kg/dose, 12 hourly. [1-4] **Oral:** 15-20 mg (of amoxicillin component)/kg/dose, 12 hourly. [5]
Dose adjustment	Therapeutic hypothermia: Insufficient information to recommend any specific dose adjustment. ECMO: 25 to 50 mg/kg every 6 hours in paediatric intensive care patients after cardiac surgery may not be adequate. Renal impairment: Consider alternate antibiotic in moderate to severe renal impairment. Hepatic: No dose adjustment required. Monitor hepatic function closely. [3]
Maximum dose	ORAL –90 mg/kg/day.
Total cumulative dose	
Route	IV Oral
Preparation	IV Add 9.5 mL of water for injection to the 500mg/100mg vial to make a concentration of 50mg/mL amoxicillin equivalent OR Add 19.1mL of water for injection to the 1000mg/200mg vial to make a concentration of 50mg/mL amoxicillin equivalent.[6] **FURTHER DILUTE WITHIN 20 MINUTES OF RECONSTITUTION**

	Draw up 2mL (100mg) and add 8mL of sodium chloride 0.9% to make a final volume of 10mL with a concentration of 10mg/mL of amoxicillin equivalent.[6] **ORAL** Reconstitute powder for oral suspension with 71mL of water and shake vigorously until suspended. Final reconstituted suspension volume is 75mL (25 mg amoxicillin component per 1 mL)
Administration	**IV infusion**: over 30 to 40 minutes.[4] **Oral**: Administer at the start of a feed (to increase absorption and decrease stomach upset); administer around-the-clock to promote less variation in peak and trough serum levels. Shake suspension well before measuring the dose. The dose may be mixed with milk. After mixing, administer immediately.
Monitoring	Renal and hepatic function and full blood count if on prolonged therapy.
Contraindications	Hypersensitivity to penicillins, cephalosporins and carbapenems. Previous history of jaundice/hepatic dysfunction associated with the combination or amoxicillin or clavulanic acid. Severe renal impairment (creatinine clearance less than 30 mL/minute). Note: infants <7 days, very preterm infants and sick infants frequently have a creatinine clearance <30 mL/minute.
Precautions	In moderate renal impairment: increase the dosing interval and maintain adequate fluid intake, especially with IV doses, to reduce the possibility of amoxicillin crystalluria. Hepatic dysfunction: monitor liver function tests. Concurrent use in CMV infection increases risk of rash. Oral suspension - contains aspartame (source of phenylketonuria), therefore use with caution in patients with phenylketonuria.
Drug interactions	Warfarin: increased risk of bleeding. Tetracycline: reduction of efficacy.
Adverse reactions	Mucositis, oral candidiasis, mild to life-threatening Clostridium difficile-associated diarrhoea, life-threatening hepatic dysfunction, and skin rashes including Stevens-Johnson syndrome, Toxic epidermal necrolysis and severe hypersensitivity reactions such as anaphylaxis have been reported.
Compatibility	Fluids: sodium chloride 0.9%, glucose 5% (by Y-site only), Hartmann's, Ringer's. Y-site: No information.
Incompatibility	Fluids : Glucose 5% Drugs: amikacin, gentamicin, tobramycin, amiodarone, ciprofloxacin, metronidazole, sodium bicarbonate.
Stability	IV: the reconstituted solution is stable for 20 minutes at 25 °C. Diluted IV solution: stable in sodium chloride 0.9% for 4 hours and in Hartmann's and Ringer's for 3 hours at 25 °C. Stable in sodium chloride 0.9% for 8 hours at 2 to 8 °C when added to a pre-refrigerated bag. Oral: The medication mixed with milk should be administered immediately.
Storage	Vial: store below 25 °C. Protect from light. Oral: Store dry powder for oral suspension at 20 to 25°C. Store reconstituted suspension at 2 to 8 °C. Discard unused suspension after 7 days.
Excipients	Oral Curam Powder for Suspension: Lemon Flavouring , Peach-Apricot Flavouring, citric acid, sodium citrate, aspartame, purified talc, Orange Flavouring, Guar Gum and silicon dioxide. Contains sulfites. When reconstituted as directed, Curam 125/31.25 contains aspartame 8.5mg/5mL. Each 5mL of suspension contains 0.16mmol of potassium.
Special comments	
Evidence	Refer to full version.
Practice points	The pharmacokinetics of clavulanate has not been evaluated in neonates. Further trials are needed to establish the safety and efficacy of iv-to-oral switch therapy in neonates although some efficacy data exist for infants >1 month age. [9] [LOE I GOR C] Amoxicillin-clavulanic acid should be considered a 2nd line agent for infants with WHO defined non-severe community-acquired pneumonia. There are no data for infants <3 months age. [LOE I, GOR B]

	Amoxicillin-clavulanate should be considered a 2nd line agent for infants with a urinary tract infection or for oral to IV switch therapy for pyelonephritis with a sensitive organism for infants >1 month age. [LOE I GOR B]
References	Refer to full version.

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Original	22/06/2020
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