Paediatric Medication Guideline

Intravenous Amoxicillin-Clavulanic acid

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Author/custodian	Pharmacist Advanced – Safety and Quality Pharmacist Advanced – Antimicrobial Stewardship			**Review date**	24/09/2021
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Applicable to	All Children's Health Queensland (CHQ) clinical staff				
Authorisation	Executive Director Clinical Services				

Purpose

The purpose of this guideline is to provide clinical advice around the use of Intravenous Amoxicillin-Clavulanic acid in paediatric patients at the Queensland Children's Hospital (QCH).

Scope

This guideline is intended to assist all clinical staff to prescribe and administer Intravenous Amoxicillin-Clavulanic acid appropriately to patients at QCH. It is not intended to be a substitute for specific professional or clinical advice, or to replace consultation with senior staff, which should always be sought if clinically relevant.

This material is published by Children's Health Queensland with the intention of providing a guideline for use at QCH. Anyone wishing to use this guideline outside QCH should refer to their local Medicines Committee before using.

Related documents

Procedures, Guidelines, Protocols

- CHQ-PROC-01035 Antimicrobial Restriction
- CHQ Antimicrobial Restriction list
- CHQ-PROC-01039 Medication - Administration
- CHQ-PROC-01000 Medication

Description and Indications for Use

Intravenous Amoxicillin-clavulanic acid is a broad spectrum antibiotic that covers gram-positive, gram-negative and anaerobic organisms excluding Pseudomonas. This agent does not currently feature in the Therapeutic Guidelines: Antibiotic, however there is extensive clinical experience overseas. For directed therapy against a cultured organism, consult your CHQ Infectious Diseases (ID) and Antimicrobial Stewardship team for further advice.

Table 1: IV Amoxicillin-clavulanic acid may be used empirically for the following situations for paediatric patients:

Indication	Approved duration/ ID review required
Retropharyngeal abscess	Up to 24 hours then seek ID review/ advice
Severe Animal bites/ wounds	Up to 24 hours then seek ID review/ advice
Complicated Appendicitis (e.g. perforation, appendiceal collection / abscess) and Peritonitis	Up to 4 days then seek ID review/ advice

Prescribing Instructions

Table 2: Dosing recommendations in paediatric patients with normal renal function[1]

* Dose based on actual body weight. # All doses are expressed as Amoxicillin component

Age group *	Dosing regimen #
Neonates and infants (Birth to 3 months of age)	**If less than 4kg:** 25 mg/kg/dose (amoxicillin component) IV every 12 hours
	If more than 4kg: 25 mg/kg/dose (amoxicillin component) IV every 8 hours
Infant and children (3 months to 12 years of age)	**Mild to moderate infection:** 25 mg/kg/dose (amoxicillin component) IV every 8 hourly (maximum 1000 mg amoxicillin component per dose)
	Severe infection: 25 mg/kg/dose (amoxicillin component) IV every 6 hourly (maximum 1000 mg amoxicillin component per dose) Note: Maximum 800 mg clavulanic acid per 24 hour period.
Children and adolescents (weighing more than 40 kg)	**Mild to moderate infection:** 1000 mg (amoxicillin component) IV every 8 hourly
	Severe infection: 1000 mg (amoxicillin component) IV every 6 hourly Note: Maximum 800 mg clavulanic acid per 24 hour period.
	Critically ill patient with life-threatening infection: 25 mg/kg/dose (amoxicillin component) IV every 6 hourly (maximum 2000 mg amoxicillin component per dose. Note: Maximum 800 mg clavulanic acid per 24 hour period)

Table 3: Dosing recommendations in paediatric patients with renal impairment[1]

Creatinine Clearance (calculated using modified Schwartz formula $)

Creatinine Clearance $	Dose recommendation
Serious infection and CrCl more than 30 mL/min	Dose as for normal renal function
Moderate renal impairment (CrCl 10 to 30 mL/min)	25 mg/kg/dose (amoxicillin component) IV every 8 hourly (maximum 1000 mg amoxicillin component per dose)
Severe renal impairment (CrCl less than 10 mL/min)	25 mg/kg/dose (amoxicillin component) IV every 12 hourly (maximum 1000 mg amoxicillin component per dose) Seek specialist/clinical pharmacist advice on dosing in renal replacement therapy

$ Modified Schwartz formula is used to calculate Paediatric Creatinine Clearance (CrCl):

CrCl (mL/min/1.73m^2) = **[36.5 x Height (cm)]** / **Creatinine (micromol/L)** = ... mL/min/1.73 m^2

***Not validated to be used in children <1 year of age. Cap CrCl at maximum of 150 mL/min/1.73m^2.*

Formulations[1, 2]

IV Amoxicillin-clavulanic acid is available in 500mg/100mg; 1000mg/200mg and 2000mg/200mg vials.

- Each 500/100 mg vial contains 0.5 mmoL (19.6 mg) of potassium and 1.4 mmoL (31.4 mg) of sodium (approx.).
- Each 1000/200 mg vial contains 1 mmoL (39.3 mg) of potassium and 2.7 mmoL (62.9 mg) of sodium (approx.).
- Each 2000/200 mg vial contains 1 mmoL (39.3 mg) of potassium and 5.5 mmoL (125.9 mg) of sodium (approx.).

Powder volume:

- 500 mg/ 100 mg vial (0.5mL)
- 1000 mg/ 200 mg vial (0.9mL)
- 2000 mg/ 200 mg vial (0.9mL)

Reconstitution/Dilution[1, 2]

IV Amoxicillin-clavulanic acid 500/100mg vial:

Reconstitute contents of 500 mg/100 mg Amoxicillin/Clavulanic acid vial with 9.5 mL Water for Injection B.P. (final volume 10 mL; final concentration 50 mg/mL amoxicillin component).

Dilute dose further with a compatible fluid to a final concentration of 10 mg/mL amoxicillin component, before administering.

Note: Reconstituted solution is only stable for 20 minutes at room temperature (25 °C).

IV Amoxicillin-clavulanic acid 1000/200 mg vial:

Reconstitute contents of 1000 mg/200 mg Amoxicillin/Clavulanic acid vial with 19.1 mL Water for Injection B.P. (final volume 20 mL; final concentration 50 mg/mL amoxicillin component).

Dilute dose further with a compatible fluid to a final concentration of 10 mg/mL amoxicillin component, before administering.

Note: Reconstituted solution is only stable for 20 minutes at room temperature (25 °C).

IV Amoxicillin-clavulanic acid 2000/200 mg vial:

Reconstitute contents of 2000 mg/200 mg Amoxicillin/Clavulanic acid vial with 19.1 mL Water for Injection B.P. (final volume 20 mL; final concentration 100 mg/mL amoxicillin component).

Dilute dose further with a compatible fluid to a final concentration of 10 mg/mL amoxicillin component, before administering.

Note: Reconstituted solution is only stable for 20 minutes at room temperature (25 °C).

Stability[1, 2]

Vial: store below 25 °C. Protect from light.

Reconstituted solution: stable for 20 minutes at room temperature (25 °C).

Diluted solution:
Stable in sodium chloride 0.9% for 4 hours and in Hartmann's and Ringer's for 3 hours at room temperature (25 °C).
Stable in sodium chloride 0.9% for 8 hours at 2 to 8 °C when added to a pre-refrigerated bag.

Compatibility[1-3]

Table 4: IV Amoxicillin/Clavulanic acid compatibility/incompatibility

	Compatible	Incompatible
Fluids	Hartmann's (3 hours only) Ringer's lactate (3 hours only) Sodium chloride 0.9% (4 hours only)	Glucose 5% Total parenteral nutrition (TPN) Lipids (SMOF, Clinoleic, Intralipid etc) Blood products
Medications	No information available	Amiodarone Amikacin Ciprofloxacin Gentamicin Hydrocortisone Methylprednisolone Metronidazole Midazolam Sodium bicarbonate Tobramycin

Route and Method of Administration[1]

Intravenous slow Injection

- NOT suitable for children aged less than 3 months
- In infants and children older than 3 months: Infuse the reconstituted solution over 3 to 5 minutes
- Caution: May cause thrombophlebitis if administered via peripheral intravenous cannula.

Intravenous Infusion

- Dilute dose in Sodium Chloride 0.9% to a final concentration of 20 mg/mL (amoxicillin component) and infuse over 30 to 40 minutes. Stable in sodium chloride for 4 hours at room temperature (25 °C)
- Caution: May cause thrombophlebitis if administered via peripheral intravenous cannula.
- Infusion is not stable for use as a continuous infusion. Seek pharmacy advice for more details.
- Protect medication/infusion from light.
- NOT suitable for Intramuscular (IM) injection
- NOT compatible with Glucose 5%

Contraindications/Precautions[1]

- Confirmed allergy to penicillin's beta-lactam/beta-lactamase inhibitor combinations precluding their use
- History of cholestatic jaundice or hepatic dysfunction associated with beta-lactam/beta-lactamase inhibitor combinations. (Note: Pre-existing hepatic impairment is not a contraindication)
- Please seek advice from local pharmacy department for further specific information regarding adverse effects, other precautions and monitoring required for prolonged therapy.

Clinical Considerations

- For directed therapy against a cultured organism, consult your Infectious diseases/AMS team for further advice.
- Consider if your patient may be suitable for Early IV to Oral switch (refer to CHQ-GDL-01057 Antimicrobial treatment: Early intravenous to oral switch - Paediatric Guideline).
- Dosing: Amoxicillin-clavulanic 22.5 mg/kg/dose (Max 875mg amoxicillin component) orally, 12-hourly

Consultation

Key stakeholders who reviewed this version:

- Pharmacist Advanced - Antimicrobial Stewardship, CHQ
- Pharmacist Advanced – Medication Safety and Quality, CHQ
- Director, Infection Management and Prevention service, Immunology and Rheumatology, CHQ
- Director of Pharmacy, CHQ
- Senior Clinical Pharmacist (Critical care), CHQ
- Clinical Pharmacy team leader (Medical and Surgical), CHQ

References and suggested reading

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Guideline revision and approval history

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1.0 12/10/2017	Antimicrobial Stewardship Pharmacist	Director of Pharmacy Director of Infection Management and Prevention Services	Executive Director Medical services
2.0 24/09/2019	Pharmacist Advanced – Antimicrobial Stewardship	CHQ Medicines Advisory Committee	Executive Director Clinical services

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