MONOGRAPH

Amoxicillin / Clavulanic Acid Monograph - Paediatric

Scope (Staff):	Medical, Pharmacy, Nursing
Scope (Area):	All Clinical Areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

QUICKLINKS

Dosage/Dosage Adjustments	Administration	Compatibility	Monitoring

DRUG CLASS

Amoxicillin is a penicillin antibiotic with clavulanic acid, a beta-lactamase inhibitor.[1, 2]

INDICATIONS AND RESTRICTIONS

Amoxicillin with clavulanic acid should be reserved for infections due to bacteria that produce beta-lactamase enzymes including some strains of *Escherichia coli*, *Haemophilus influenzae* and *Klebsiella* species. It has good anaerobic cover.[3]

Oral: Unrestricted (green) antibiotic

This is not a restricted agent. Follow standard ChAMP guidelines where appropriate.

IV: Monitored (orange) antibiotic

Amoxicillin with clavulanic acid is indicated for use as per the indications stipulated in Formulary One. For any other use, phone approval must be obtained from ChAMP before prescribing as per the Antimicrobial Stewardship Policy.

CONTRAINDICATIONS

- Hypersensitivity to amoxicillin, clavulanic acid or any component of the formulation or in patients with a history of high-risk allergy to penicillins.[1, 2, 4-6]
- Contraindicated in patients with a history of cholestatic jaundice or hepatic dysfunction with amoxicillin/clavulanate therapy.[1, 2, 6]
- Patients with phenylketonuria note that the suspension formulations contain aspartame.[1, 4]

PRECAUTIONS

- Amoxicillin with clavulanic acid may be prescribed in selected patients with high risk allergy to another Beta-lactam sub-class (e.g. some cephalosporins, carbapenems) in discussion with immunology.[1, 4]
- In patients with a previous low risk reaction to amoxicillin or another penicillin (delayed rash [>1hr after initial exposure] without mucosal or systemic involvement) the risk of subsequent reaction is low. Re-challenge may be acceptable in discussion with immunology.[5]
- Amoxicillin with clavulanic acid is associated with a higher incidence of rash when used in patients with infectious mononucleosis, acute lymphoblastic leukaemia, chronic lymphocytic leukaemia and HIV infection.[1, 5]
- The IV preparation contains 39 mg of potassium and 63 mg of sodium per 1 gram of amoxicillin. The oral tablet contains 24 mg of potassium.[1, 5]
- Electrolyte disturbance, neurotoxicity and risk of neutropenia may be increased in renal impairment. See dose adjustments for renal impairment.[1]

FORMULATIONS

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required:

Oral (ratio 7:1)

- Amoxicillin 875 mg with clavulanic acid 12 5mg
- Amoxicillin 400 mg with clavulanic acid 57 mg per 5 mL oral powder for suspension

IV (ratio 5:1)

- Amoxicillin 1000 mg with clavulanic acid 200 mg per vial.

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

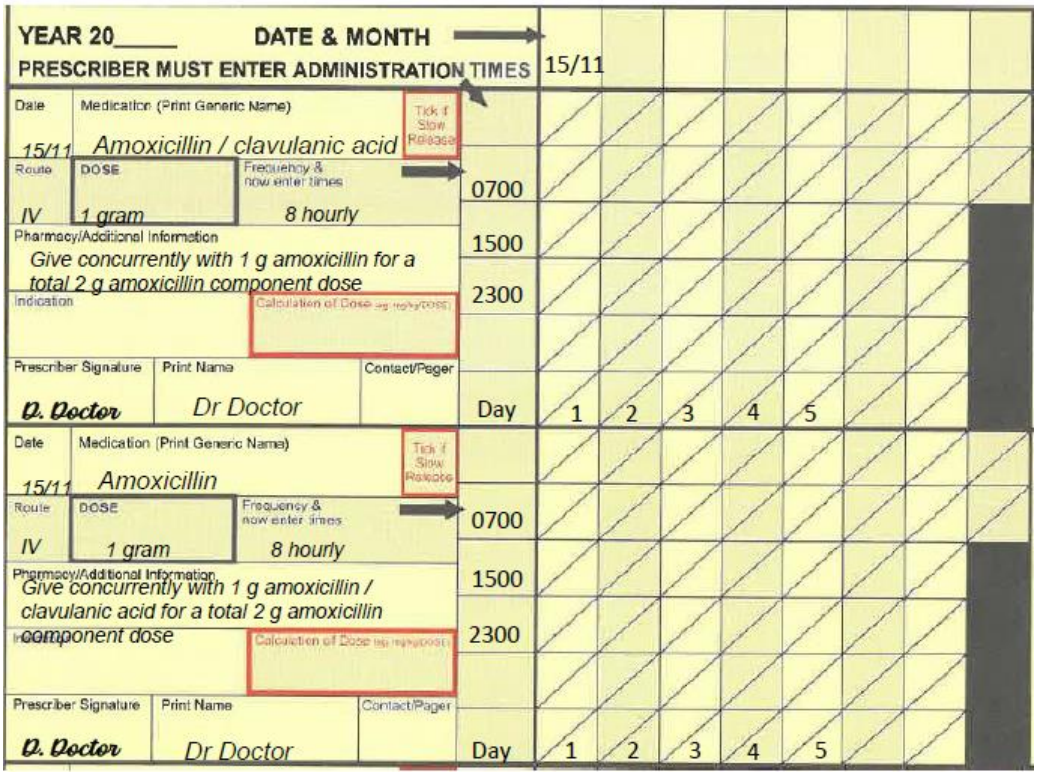
Neonates: **Refer to Neonatal Medication Protocols** for oral dosing. IV dosing for term neonates is outlined below. There is limited information for IV dosing in premature neonates, please consult Infectious Diseases or Clinical Microbiology.

All doses are expressed and should be prescribed as the amoxicillin component (oral doses refer to the 7:1 ratio of amoxicillin/ clavulanic acid preparations).

IV: Change to oral route when possible

- **Birth (term) to 3 months and <4kg:** 25 mg/kg/dose 12 hourly[1, 7]
- **Birth (term) to 3 month and ≥4kg:** 25 mg/kg/dose 8 hourly[1, 7]
- **≥3 months and <40kg:** 25 mg/kg/dose (to a maximum of 1 gram) 8 hourly. The dose may be increased to 25 mg/kg/dose (to a maximum of 1 gram) 6 hourly in severe infections.[1, 7]
- **≥40kg:** 1 gram every 8 hours. The dose may be increased to up to 2 grams every 6 to 8 hours in severe infections.[1, 7]

PCH only stocks the 1 g/200 mg vials of amoxicillin/ clavulanic acid. Where the 2 gram amoxicillin component is required, a 1 gram dose of amoxicillin with clavulanic acid should be prescribed in combination with a 1 gram dose of amoxicillin to give the final 2 gram amoxicillin dose which avoids administration of the additional clavulanic acid and its associated adverse effects.[1, 2] See below for a prescribing example.



Oral (>4 weeks to 18 years): (Products with amoxicillin component of 400mg/5mL or 875mg per tablet – 7:1 ratio).

Usual dose: 25mg/kg/dose (to a maximum of 875mg) twice daily.[8]

Dosing in Overweight and Obese Children: Dose based on measured body weight.

Renal impairment:

- eGFR calculator

For IV Administration:

- eGFR ≥30 mL/minute/1.73m^2 – use normal dose.[2, 4, 9]
- eGFR 10-30 mL/minute/1.73m^2 - use normal initial dose and then use half normal dose every 12 hours.[2, 4, 9]
- eGFR <10 mL/minute/1.73m^2 - use normal initial dose and then use half normal dose every 24 hours.[2, 4, 9]
- Monitor for accumulation of electrolytes (potassium and sodium) contained in the IV preparation.[5]

For Oral Administration:

- Dosage adjustment may be required in cases of impaired renal function (with creatinine clearance of less than 30 mL/minute/1.73m^2) due to the increased risk of crystalluria.[5]
- For patients with a creatinine clearance of less than 30mL/minute, the higher strength preparations (i.e. the 7:1 ratio, 875mg/125mg tablets and 400mg/57mg per 5mL suspension) should be avoided due to the clavulanic acid component and the risk of crystalluria.[9]

- The lower strength preparations (i.e. 500mg/125mg and 125mg/31.25mg per 5 mL suspension) may be suitable.[5]

Hepatic impairment:

- Amoxicillin with clavulanic acid is contraindicated in patients with a history of cholestatic jaundice or hepatic dysfunction associated with its use.[1, 2, 6]
- Care should be taken when using amoxicillin with clavulanic acid in patients with hepatic impairment due to other causes, although no specific dose reductions are recommended.[2, 6, 9]

RECONSTITUTION & ADMINISTRATION

Reconstitution - Oral suspension (Duo® 400mg/57mg per 5mL):

- Reconstitute with water as follows: Tap the bottle until all the powder flows freely; add approximately half the amount of water as per the manufacturer's instructions for reconstitution and shake well to suspend the powder.[4]
- Add the remainder of the water and again shake well. Store the reconstituted suspension between 2°C and 8°C and discard any remaining suspension after 7 days, or as otherwise stated on manufacturer instructions.[4]

Oral administration:

- Amoxicillin with clavulanic acid preparations should be taken at the start of a light meal to minimise gastrointestinal intolerance and to optimise absorption.[1, 6, 10]
- The suspension should be shaken well prior to measuring dose.[4, 6]

Reconstitution - IV:

- Reconstitute the 1 gram/200mg vial with 19.1mL of water for injection to give a 50mg/mL solution of amoxicillin component.[11]
- Powder volume is 0.9mL for the 1gram vial.[11]
- Use reconstituted 50mg/mL solution immediately as it is only stable for 20 minutes at room temperature. When diluted in sodium chloride 0.9%, the solution is stable for 4 hours at 25°C [11]

IV administration:

IV push (Children > 3 months):

- Doses ≤1 gram may be given via a slow IV push over 3 to 4 minutes, at a final concentration of 50mg/mL or weaker. [2, 5, 11]

IV infusion:

- Dilute the required dose to a final concentration of 10mg/mL or weaker and infuse over 30 minutes.[5, 11]

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

- Sodium chloride 0.9%
- Ringer's
- Hartmann's[11]

Compatible at Y-site:

Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.

MONITORING

Renal, hepatic and haematological function should be monitored weekly with prolonged therapy (i.e. longer than 10 days).[2, 6]

ADVERSE EFFECTS

Common: pain and inflammation at injection site, diarrhoea, nausea, transient increases in liver enzymes and bilirubin, rash.[1, 5]

Infrequent: vomiting, *Clostridioides difficile*-associated disease, dizziness, dyspepsia, headache.[1, 5]

Rare: pustular drug eruption, cholestatic hepatitis (mainly due to clavulanic acid and is usually reversible), black tongue, neurotoxicity (e.g. drowsiness, hallucinations, coma or seizures – usually associated with high doses), bleeding, blood dyscrasias (e.g. neutropenia, thrombocytopenia), electrolyte disturbances, crystalluria (high IV doses).[1]

Immunologic reactions: include rash (usually maculopapular), erythema, urticaria, contact dermatitis, fever, anaphylactic shock, angioedema, bronchospasm, interstitial nephritis, haemolytic anaemia, eosinophilia, serum sickness-like syndrome, exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis.[1]

STORAGE

Oral preparations:

- **Tablet:** Store below 25°C. Protect from moisture and light.[4]
- **Suspension:** Store the dry powder below 25°C, after reconstituting, store in the refrigerator between 2°C and 8°C and discard after 7 days, or as otherwise stated on manufacturer instructions.[4]

IV preparations:

- **Vial:** store below 25°C. Protect from light.[11]

INTERACTIONS

This medication may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

Please note: The information contained in this guideline is to assist with the preparation and administration of **amoxicillin / clavulanic acid**. Any variations to the doses recommended should be clarified with the prescriber prior to administration

Related CAHS internal policies, procedures and guidelines
Antimicrobial Stewardship Policy
ChAMP Empiric Guidelines and Monographs
KEMH Neonatal Medication Protocols

References

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