Waikato District Health Board	Type: **Drug Guideline**	Document reference: **0582**	Manual Classification: **Waikato DHB Drug Guidelines**
Title: **Amoxicillin/clavulanic acid for NICU**			Effective date: **20 July 2018**
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1. Purpose and scope

To facilitate the safe administration of amoxicillin/clavulanic acid within the Neonatal Intensive Care Unit (NICU).

2. Drug

Drug	**Amoxicillin/clavulanic acid, Co-amoxiclav, Augmentin®**
Drug action	Amoxicillin is a broad spectrum penicillin with antibacterial activity against certain gram negative and gram positive organisms. It is bactericidal against sensitive organisms during the stage of active multiplication, inhibiting the biosynthesis of cell wall mucopeptides. Clavulanic acid binds and inhibits beta-lactamases that inactivate amoxicillin resulting in amoxicillin having an expanded spectrum of activity.[1,2,3,4] Both amoxicillin and clavulanic acid are widely distributed to most body tissues and fluids.[1,3] The half-life of amoxicillin in full-term neonates is approximately 3.7 hours[2]. Amoxicillin is excreted mostly unchanged in the urine (60%), whereas clavulanic acid has both renal and non-renal elimination (is extensively metabolised) [1,2,3] If renal impairment exists reduce the total daily dose.[1,2] Low protein binding (amoxicillin 20% and clavulanic acid 25%). [1,2,3,4]
Indications	Bacterial infections due to beta-lactamase producing strains (where amoxicillin alone is not appropriate), including respiratory tract, bone and joint, genitourinary and abdominal infections, cellulitis, animal bites
Presentation	**IV**: Amoxicillin/clavulanic acid 600 mg vial (amoxicillin 500 mg plus clavulanic acid 100 mg) • White to off-white powder • Reconstituted solution ranges from transient pink to pale yellow.[5] • Contains 1.4 mmol (31.6 mg) of sodium per 600 mg [5] **Oral**: Amoxicillin/clavulanic acid powder for oral liquid for the preparation of 100 ml, available in two strengths • Amoxicillin 125 mg plus clavulanic acid 31.25 mg per 5 ml of suspension (i.e. amoxicillin/clavulanic acid 156.25 mg/ 5 ml)[1] • Amoxicillin 250 mg plus clavulanic acid 62.5 mg per 5 ml of suspension (i.e. amoxicillin/clavulanic acid 312.5 mg/ 5 ml)[1] • Off-white powder • Reconstituted suspension is white/cream in colour
Route	• IV, bolus over 3-4 minutes [5] • Oral
Dose	**IV**: 30 mg/kg/dose[1,4,6,7] **Oral:** 15-30 mg/kg[7] ***Note: doses are expressed as a combination of amoxicillin and clavulanic acid i.e. 30 mg = 25 mg amoxicillin and 5 mg clavulanic acid*** **<u>Frequency of administration</u>:** **IV**: administer every 12 hours[1,2,3,4,6,7] If 7+ days postnatal age[4] or >4kg[1] can administer every 8 hours. **Oral**: every 8 – 12 hours[3,6,7] Note: Extend frequency of administration if **renal impairment** (but keep dose

	the same) i.e. administer every 12 hours if eGFR is 10-30ml/min and every 24 hours if eGFR <10ml/min every 24 hours
Contraindications	• Known hypersensitivity to beta-lactam antibiotics e.g. penicillins and cephalosporins or clavulanic acid, or any constituent of the preparation
Precautions	• Reduced urine output – risk of crystalluria. Maintain adequate fluid intake and urinary output to reduce possibility. • Renal impairment – reduce dose • Hepatic impairment • Infectious mononucleosis
Compatibilities & Incompatibilities	• If dilution is required: compatible with sodium chloride 0.9%, Compound Sodium Lactate (Hartmann's)[5] • Limited data is available regarding medication compatibilities – consult a Pharmacist for more information on individual medications • Amoxicillin/clavulanic acid administration should be separated from aminoglycoside antibiotics (e.g. gentamicin, amikacin, tobramycin)[1,3] • Do not mix with blood products, proteinaceous fluids or lipid emulsions[1,3,5]
Adverse effects	• Hypersensitivity reactions • Gastrointestinal disturbances (nausea, diarrhoea, vomiting) • Skin rash, urticarial, pruritis • Superinfection e.g. Mucocutaneous candidiasis, C.difficile-associated diarrhoea • Rarely: antibiotic associated colitis, convulsions, agitation, interstitial nephritis, hematologic disorders, coagulation disorders, hepatitis, cholestatic jaundice

3. Administration

Competency for administration	This procedure is carried out by, or under, the direct supervision of a registered nurse / registered midwife who holds generic IV certification **and** Neonatal specific certifications NCV/NAC if administering via CVAD.
Preparation & Administration	**IV** • Dilute 600 mg vial with 9.5ml of water for injection[5]. The resulting solution is 60 mg/ml • Shake vial vigorously to dissolve powder and check for absence of particulate matter before drawing up final dose. Note: Flush before and after with sodium chloride 0.9%. **Oral** If ordering from Pharmacy it will already be reconstituted, but if not follow the directions below: • Shake the bottle to loosen the powder. • Check instructions on bottle for volume of water to make up to 100ml e.g. Augmentin® brand: add 90ml of water if using "250" strength (or 92ml if using the "125" strength) • Shake well • When first reconstituted allow to stand for 5 minutes to ensure full dispersion.
Observations and management	• Consider if specimen for culture and sensitivity testing is required before first dose • Assess for signs of anaphylaxis and adverse reactions • Observe infusion site for thrombophlebitis • Monitor temperature and other parameters appropriate to the condition • Observe for change in bowel frequency • Monitor renal, hepatic and hematologic function periodically

Storage	• Store vials and unreconstituted suspension at room temperature (below 25°C) • Protect from moisture • Prepare IV solution immediately before use - must be administered within 20 minutes of reconstitution. Discard unused reconstituted solution. • Store reconstituted oral suspension in a refrigerator (2°C to 8°C) and use within 7 days
Special considerations	• Confusion often arises over dosing as previously prescribers just wrote the quantity of amoxicillin present for oral preparations. The current New Zealand recommendation is to prescribe the combined content of both amoxicillin and clavulanic acid for both IV and oral preparations (as per note in dosing section).
Rescue medication	For management of penicillin hypersensitivity: • Discontinue amoxicillin/clavulanic acid • Administer adrenaline, steroids, antihistamines as required • Supportive therapy (i.e. ventilation) as required

4. References

1 The New Zealand Medicines and Medical Devices Safety Authority (Medsafe): Augmentin Data sheet, GlaxoSmithKline NZ Ltd. Version 5.0, April 2013. Last accessed 20th April 2016. Available from http://www.medsafe.govt.nz/profs/datasheet/a/Augmentininj.pdf

2 Pediatric & Neonatal Handbook. 20th edition. American Pharmacists Association. 2013.

3 UpToDate®: amoxicillin and clavulanate Paediatric drug information accessed on 20th April 2016 http://www.uptodate.com/contents/amoxicillin-and-clavulanate-pediatric-drug-information?source=search_result&search=augmentin+children&selectedTitle=1%7E138#F1045071

4 Auckland NICU Drug Protocols – Augmentin, January 2011. Available from: http://www.adhb.govt.nz/newborn/DrugProtocols/Default.htm Last accessed 20th April 2016.

5 New Zealand Hospital Pharmacists Association: Notes on Injectable Drugs, 7th Edition. Published 2015, Wellington NZ.

6 British National Formulary for Children. 2011-2012. Pharmaceutical Press, London, 2011.

7 The New Zealand Formulary Editorial Team. New Zealand Formulary for Children. Amoxicillin+clavulanic acid. New Zealand Formulary, NZ. Last accessed 20th April 2016. Available from http://nzfchildren.org.nz/nzf_3032