BRIEF ADMINISTRATION GUIDE

(For more detailed guideline information please see the following pages)

Indications: Bacterial infections sensitive to benzylpenicillin

Route:
- Intravenous: IV Infusion (preferred), or Direct IV Injection
- Intramuscular Injection

Dose:
- 15 - 30 mg/kg/dose,[5] can increase to 50 mg/kg/dose[6,7]
- 45 - 60 mg/kg/dose for meningitis[5]

Frequency of administration:
- Neonate under 7 days: administer every 12 hours
- Neonate 7 - 28 days: administer every 8 hours[6,7]

Supplied as: Benzylpenicillin sodium 600 mg vial, powder for reconstitution.

Preparation and administration:

- Dilute each vial with 1.6 ml of compatible diluent to make 2 ml of benzylpenicillin 300 mg/ml (Note: 600 mg of benzylpenicillin displaces 0.4 ml of diluent).
- Rotate the vial while adding water for injection slowly, directing the stream against the wall of the vial.
- Shake vial vigorously to dissolve powder.

IV infusion (recommended)
Dilute further to 60 mg/ml or weaker with compatible IV fluid and infuse over at least 30 minutes. Maximum concentration if necessary: 300 mg/ml via a **central line only**.[9]

Direct IV injection
Give slowly over 3 - 10 minutes. Can give at maximum rate of 300 mg/min.

IM injection
Administer by deep injection in the anterior aspect of the quadriceps muscle in the thigh. Injection may be painful, apply ice to the injections site to alleviate pain and discomfort.[4]

Monitoring:

- Observe infusion site for thrombophlebitis or extravasation.[5]
- Assess for signs of anaphylaxis and adverse reactions.
- Observe for change in bowel frequency.
- Monitor renal, hepatic, cardiac and hematologic function during prolonged therapy.[3]

1. Purpose and scope

To facilitate the safe administration of benzylpenicillin to neonates within the Neonatal Intensive Care Unit (NICU) and ward E2.

2. Drug

Drug	**Benzylpenicillin sodium, penicillin G sodium, penicillin**
Drug action	Benzylpenicillin has bacteriostatic/bactericidal activity against most gram positive bacteria and gram negative cocci. It works by inhibiting the biosynthesis of cell wall mucopeptides[1] Benzylpenicillin is acid labile and is therefore only given parenterally. It is distributed widely throughout the body tissues and fluids, with little passing the blood brain barrier unless the meninges are inflamed. 55% of benzylpenicillin is bound to plasma proteins in the circulation and largely eliminated by renal pathways. [2] The elimination half-life of benzylpenicillin is 3.1 hours in neonates < 6 days of age and 1.4 hrs ≥14 days of age.[3]
Indications	• Bacterial infections sensitive to benzylpenicillin
Presentation	• Benzylpenicillin sodium 600 mg vial, powder for reconstitution. • White powder; reconstituted solutions are clear.
Route	• Intravenous: IV Infusion (preferred), or Direct IV Injection • Intramuscular Injection
Dose	• 15 – 30 mg/kg/dose,[5] can increase to 50 mg/kg/dose[6,7] • 45 – 60 mg/kg/dose for meningitis[5] <u>Frequency of administration:</u> • Neonate under 7 days: administer every 12 hours • Neonate 7 - 28 days: administer every 8 hours[6,7]
Contraindications	• Known hypersensitivity to beta-lactam antibiotics e.g. penicillins and cephalosporins[2,3,6,8]
Precautions	• Avoid intra-arterial administration or injection into or near major peripheral nerves or blood vessels as can cause permanent neurovascular damage. • Use with caution if history of seizures, may increase risk of seizures.[3] • Caution in preterm infants, especially extreme immaturity. • Caution in infants with liver or gastrointestinal disease.[1] • Dose adjustment recommended in renal impairment.[3]
Compatibilities & Incompatibilities	• Compatible with water for injection and glucose 5%. • Avoid sodium chloride 0.9%, Hartmann's and Ringer's solutions due to their additional electrolyte content.[4] • Incompatible with amphotericin B, aminophylline, phenytoin and tobramycin[5], dopamine, heparin and vancomycin. • Benzylpenicllin sodium is readily destroyed by oxidising agents, reducing agents, alkaline or acidic solutions and salts of easily reducible metals. Consult a Pharmacist for information on other medications .[4]

Adverse effects	• CNS effects: coma, hyperreflexia, myoclonus, seizure at high doses. • Dermatologic: Contact dermatitis, skin rash. • Electrolyte disturbance (high doses). • Anaphylaxis, serum sickness. • Gastrointestinal: Pseudomembranous colitis,[3] clostridium difficile diarrhoea,[6] stomatitis, lingua villosa nigra, nausea and vomiting.[2] • Haematologic: Neutropenia, positive direct Coombs test (rare, high doses), [3] bone marrow depression, granulocytopenia.[5] • Localized phlebitis, local thrombophlebitis. • Renal: Acute interstitial nephritis and renal tubular disease at high doses. [3] • Hepatitis rarely.[5]

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.
Preparation & Administration	**Vial Reconstitution** • Reconstitute each 600 mg vial with 1.6 ml of compatible diluent to make 2 ml of benzylpenicillin 300 mg/ml. • Note: 600 mg of benzylpenicillin displaces 0.4 ml of diluent. • Rotate the vial while adding water for injection slowly, directing the stream against the wall of the vial. • Shake vial vigorously to dissolve powder. **IV infusion (recommended)** • Dilute further to 60 mg/ml or weaker with compatible IV fluid and infuse over at least 30 minutes. • Maximum concentration if necessary: 300 mg/ml via a **central line only**.[9] **Direct IV injection** • Give slowly over 3 - 10 minutes. Can give at maximum rate of 300 mg/min. **IM injection** • Administer by deep injection in the anterior aspect of the quadriceps muscle in the thigh. • Injection may be painful, apply ice to the injections site to alleviate pain and discomfort.[4]
Observations and management	• Consider if specimen for culture and sensitivity testing is required before first dose.[4] • Observe infusion site for thrombophlebitis or extravasation.[5] • Assess for signs of anaphylaxis and adverse reactions. • Observe for change in bowel frequency. • Monitor renal, hepatic, cardiac and hematologic function during prolonged therapy.[3]

Special considerations (audit, funding, storage)	• Sodium content: 1.68 mmol sodium per 600 mg vial.[4] • The pH of benzylpenicillin is 5.5 - 7.5.[4] • Do not confuse with benzathine penicillin which is only used for IM injection.[5] • 1 million units (1 mega unit) = 600 mg.[6] • Prepare immediately before use. • Store unopened vials at room temperature. • Discard reconstituted solution immediately after use.[4]
Rescue medication	Initiate symptomatic treatment, excessive blood levels can be corrected by haemodialysis.[2] For management of penicillin hypersensitivity: • Discontinue benzylpenicillin. • Administer adrenaline, steroids, antihistamines as required. • Supportive therapy (i.e. ventilation) as required.

4. Guardrails Information

Benzylpenicillin is not currently Guardrails profiled for NICU. The profile will be added at the next upload (scheduled for December 2018). See below for likely limits:

Guardrails Drug Name	Benzylpenicillin*
Pump	CC
Concentration (mg/ml)	
Minimum	3.75
Maximum	100
Administration Rate (mg/kg/hr)	
Default	60
Soft minimum	15
Soft maximum	120
Hard maximum	150

5. References

1. Auckland DHB Newborn Services. Benzylpenicillin Drug Protocol. September 1998. Available from: http://www.adhb.govt.nz/newborn/DrugProtocols
2. Novartis NZ Ltd. Penicillin G Sodium Injection Data sheet. 08 March 2017. Available from: http://www.medsafe.govt.nz/profs/Datasheet/p/penicillinginj.pdf
3. UpToDate®. Penicillin G (intravenous and short acting intramuscular): Paediatric drug information. Accessed 13th June 2017. Available from: https://www.uptodate.com
4. New Zealand Hospital Pharmacists Assoc. Inc. Notes on Injectable Drugs 7th ed, 2015.
5. Truven Health Analytics Inc. Micromedex®. 2017. Penicillin G. Accessed 13th June 2017. Available from : http://www.micromedexsolutions.com/
6. New Zealand Formulary for Children (NZFC). 2017. Benzylpenicillin. Accessed 13th June 2017. Available from: http://www.nzfchildren.org.nz/nzf_3001
7. British National Formulary for Children. 2016-2017. Pharmaceutical Press, London, 2016.
8. Phelps SJ, Hagemann TM, Lee KR, Thompson AJ. The Teddy Bear Book: Pediatric Injectable Drugs. 10th edition. American Society of Health-System Pharmacists; 2013.
9. The Royal Children's Hospital Melbourne. Paediatric Injectable Guidelines. Accessed 13th June 2017. Available from: https://pig.rch.org.au