Benzathine Benzylpenicillin (Benzathine Penicillin G) - Paediatric

**Scope (Staff):** Clinical Staff – Medical, Nursing, Pharmacy

**Scope (Area):** Perth Children’s Hospital (PCH)

This document should be read in conjunction with this **DISCLAIMER**

### DESCRIPTION
- Benzathine benzylpenicillin (also known as benzathine penicillin or BPG) is a long-acting penicillin administered via intramuscular injection. It interferes with bacterial cell wall synthesis by binding to penicillin binding proteins resulting in cell lysis.\(^1\,2\)
  - Benzathine benzylpenicillin is mainly active against Gram positive organisms and is inactivated by beta-lactamases.\(^3\)

### INDICATIONS AND RESTRICTIONS
- Benzathine benzylpenicillin is predominantly used in the treatment and secondary prevention of acute rheumatic fever/rheumatic heart disease and in the treatment of infections susceptible to prolonged, low concentrations of benzylpenicillin (e.g. early or latent syphilis).\(^1\)
  - It may also be used in the treatment of impetigo and Group A Streptococcal Tonsillitis/Pharyngitis.\(^2,4\)
  - May be used as a second line agent for invasive Group A Streptococcal (iGAS) contacts unable to tolerate oral antibiotics.

**IM: Unrestricted (green) antibiotic**
- This is not a restricted agent. Follow standard ChAMP guidelines where appropriate.

### CONTRAINDICATIONS
- Benzathine benzylpenicillin is generally contraindicated in patients with a history of high risk allergy to penicillins.\(^1,2\)

### PRECAUTIONS
- Benzathine benzylpenicillin 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.\(^2,5\)
  - In patients with a previous low risk reaction to benzathine benzylpenicillin 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.

- Care must be taken with intramuscular administration of benzathine benzylpenicillin to avoid intravenous or intra-arterial administration or injection in or near major peripheral nerves or blood vessels due to the risk of neurovascular damage.\(^{(1, 5)}\)

### FORMULATIONS

**Available at PCH:**

- Benzathine benzylpenicillin tetrahydrate 1,200,000 units/2.3mL in aqueous suspension (Bicillin L-A\(^{\circledR}\)), pre-filled syringe for IM injection.
- This is equivalent to benzathine benzylpenicillin 900mg/2.3mL and benzathine benzylpenicillin tetrahydrate 1016.6mg/2.3mL.\(^{(1, 2)}\)

**Note:**

- The manufacturer has recently changed the labelling and packaging of benzathine benzylpenicillin to include the tetrahydrate salt and describe the active ingredient in ‘units’ rather than ‘mg’.
- There is no change to the contents of the product (it has always been benzathine benzylpenicillin tetrahydrate). This update occurred in March 2019.

**Other formulations available:**

- Nil

### DOSAGE

- The doses listed below fall within the standard range. Higher doses may be prescribed for certain situations in consultation with an infectious diseases or clinical microbiology consultant.

#### Neonates (less than 30 days of age):

- Not routinely used in neonates except in cases of congenital syphilis, contact Infectious Disease or Clinical Microbiology consultants for advice

#### Congenital Syphilis:

- Low-risk, children <3kg: contact Infectious Diseases for advice, benzyl penicillin may be appropriate.
- Low-risk, children ≥3kg: 260,000 units IM (0.5mL) as a single dose\(^{(6, 7)}\)
- High-risk: treatment with benzylpenicillin required.\(^{(6)}\)
### Children:

**Impetigo (>1 month to 18 years):**
In remote Indigenous communities *S. pyogenes* is usually the pathogen, even if *S. aureus* is isolated. (4)

- <10kg: 450,000 units IM (0.9mL) as a single dose
- 10-20kg: 600,000 units IM (1.2mL) as a single dose
- ≥20kg: 1,200,000 units (2.3mL) as a single dose (4, 8)

**Presumed *Streptococcus pyogenes* (Group A Streptococcus) tonsillitis or pharyngitis, scarlet fever:**

- < 20kg: 600,000 units IM (1.2mL) as a single dose
- ≥ 20kg: 1,200,000 units IM (2.3mL) as a single dose. (2)

**Rheumatic fever (>1 month to 18 years):**

**Acute episode:**

- < 20kg: 600,000 units IM (1.2mL) as a single dose
- ≥ 20kg: 1,200,000 units IM (2.3mL) as a single dose. (2, 3)

**Prevention of recurrence:**

- < 20kg: 600,000 units IM (1.2mL) every 3 to 4 weeks for at least 10 years.
- ≥ 20kg: 1,200,000 units IM (2.3mL) every 3 to 4 weeks for at least 10 years. (2, 3)

Duration of antibiotic prophylaxis for prevention of rheumatic fever recurrence depends on patient factors such as age, likelihood of ongoing exposure to *S. pyogenes* and time since last episode of acute rheumatic fever.

- The minimum recommended duration is 10 years after the most recent episode of acute rheumatic fever or until age 21 years (whichever is longer). (1, 8)

**Syphilis (>1 month to 18 years):**

- 50,000 units/kg IM (to a maximum of 2.4 million units) as a single dose. (8)
- Early latent syphilis requires a single dose, for late latent syphilis, 3 doses given at one week intervals is required. Contact Infectious Diseases for advice. (9)

### DOSAGE ADJUSTMENT

<table>
<thead>
<tr>
<th><strong>Dosage adjustment required in renal impairment:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>No dosage adjustment is necessary in renal impairment. (1, 10)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Dosage adjustment required in hepatic impairment:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>No dosage adjustment is necessary in hepatic impairment. (1, 10)</td>
</tr>
</tbody>
</table>

### RECONSTITUTION

- Not applicable
### ADMINISTRATION

- Benzathine benzylpenicillin must only be administered via intramuscular injection into the mid-lateral aspect of the thigh (preferred in children) or upper, outer quadrant of the buttock.\(^{(2)}\)
- It should be administered at a slow, steady rate preferably over 2-3 minutes to avoid blockage of the needle and to minimise pain.\(^{(5)}\) The injection site should be rotated for subsequent doses.\(^{(5)}\)
- After insertion of the needle, aspiration is recommended and the barrel should be observed for any blood or discolouration.
- If there is any discolouration, the needle should be withdrawn and the syringe discarded. Stop injection immediately if there is severe pain at the injection site.\(^{(5)}\)

**The pain of administration can be reduced by:**

- Allowing the alcohol from the alcohol swab to dry before injection
- Applying pressure with thumb for 10 seconds before injection
- Warming the syringe to room temperature immediately prior to the injection
- Using a 21 gauge needle.\(^{(8)}\)

### MONITORING

- In patients being treated for syphilis and other spirochete infections monitor for Jarisch-Herxheimer reaction (fever, chills, headache, hypotension and flare-up of lesions lasting for 12-24 hours). Consideration should be given to the use of prednisolone to minimise the likelihood of this in patients where this could be dangerous (i.e. cardiovascular syphilis or neurosyphilis).\(^{(1)}\)

### ADVERSE EFFECTS

- Inadvertent intravascular administration may result in neuromuscular hyperirritability, seizures, cardiac arrest and/or severe, and potentially permanent, neurovascular damage.

**Common:** pain and inflammation at the injection site, rash, urticaria, skin eruptions (most commonly maculopapular), nausea, diarrhoea, fever, fatigue, Jarisch-Herxheimer reaction (fever, chills, headache, hypotension and flare-up of lesions due to the release of pyrogens from the organism at the time of first administration e.g. syphilis).\(^{(1, 2, 11)}\)

**Rare:** *Clostridium difficile*-associated disease, anaphylaxis or other immediate hypersensitivity reactions, black tongue, electrolyte disturbances, neurotoxicity with high doses (including anxiety, agitation, hallucinations), blood dyscrasias, bleeding.\(^{(1, 2)}\)

### COMPATIBLE FLUIDS

Not applicable: Benzathine benzylpenicillin must only be administered via intramuscular injection.\(^{(1, 5)}\)
### STORAGE
- Store between 2-8°C. Refrigerate, do not freeze. \(^{(2)}\)

### INTERACTIONS
Benzathine benzylpenicillin may interact with other medications; please consult PCH approved references (e.g. Clinical Pharmacology), your ward pharmacist or Pharmacy on 63543 for more information.
- Tetracyclines may antagonise the bactericidal effect of penicillin; concurrent use of these drugs should be avoided. \(^{(1, 2)}\)

### COMMENTS

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

### MANUFACTURER SAFETY DATA SHEET (SDS)
To access to the Manufacturer SDS for this product, use the following link to ChemAlert.

### Related CAHS internal policies, procedures and guidelines

- Antimicrobial Stewardship Policy
- ChAMP Empiric Guidelines and Monographs
- KEMH Neonatal Medication Protocols

### References and related external legislation, policies, and guidelines

9. Centres for Disease Control and Prevention. 2015 Sexually Transmitted Disease