**MONOGRAPH**

**Benzylpenicillin Monograph - Paediatric**

<table>
<thead>
<tr>
<th>Scope (Staff):</th>
<th>Medical, Nursing, Pharmacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scope (Area):</td>
<td>PCH</td>
</tr>
</tbody>
</table>

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

**DESCRIPTION**

- Benzylpenicillin (also known as penicillin G) is a narrow spectrum, bactericidal penicillin antibiotic.
- It binds to penicillin binding proteins, thereby interfering with bacterial cell wall peptidoglycan synthesis and resulting in cell lysis.\(^{(1)}\)
- Benzylpenicillin is active against many Gram positive bacteria including *Streptococcus pyogenes*, *Streptococcus agalactiae* (Group B Streptococcus) and *Streptococcus pneumoniae*.
- It has activity against some Gram negative bacteria including *Treponema pallidum* (syphilis) and *Neisseria meningitidis*.
- Resistance is most commonly secondary to the inactivation of benzylpenicillin by bacterially derived beta-lactamases.\(^{(2)}\)

**INDICATIONS AND RESTRICTIONS**

**Oral and IV: Green (unrestricted) antibiotic**

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

**CONTRAINDICATIONS**

- Benzylpenicillin is contraindicated in patients with a history of severe &/or immediate allergic reaction to penicillin, carbapenem &/or cephalosporin antibiotics.
- Cross reactivity may occur between penicillins, cephalosporins and carbapenems.\(^{(1,5,6)}\)

**PRECAUTIONS**

- Administration at a rate greater than 300mg/minute has been associated with an increased risk of CNS toxicity.\(^{(6,7)}\)

**FORMULATIONS**

**Available at PCH:**

- 600mg and 1.2gram powder for injection vial (BenPen®)

**Other formulations available:**

- 3gram powder for injection vial (BenPen®)

**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 (<1 month of age):**
Please refer to neonatal clinical care drug protocols

**IV:**
- **Usual dose:** 30mg/kg/dose (to a maximum of 1.2grams) 6 hourly.\(^{(1, 3)}\)

**Severe infections:**
- 60mg/kg/dose (to a maximum of 2.4grams) 4 - 6 hourly.\(^{(1, 3)}\)

**HiTH dosing:**
- 120-360mg/kg/DAY (to a maximum of 14.4gram per day) via a buffered continuous infusion. **Note:** this infusion MUST be prepared by Baxter.

<table>
<thead>
<tr>
<th>DOSAGE ADJUSTMENT</th>
<th>Dosage adjustment required in renal impairment:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Dosage adjustment may be required in cases of impaired renal function (with creatinine clearance of less than 50mL/min).</td>
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<tr>
<td></td>
<td>• To calculate the estimated glomerular filtration rate (eGFR) in infants &gt; 1 year and children, use the Schwartz formula.</td>
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<tr>
<td></td>
<td>eGFR (\text{mL/min/1.73m}^2) = (\frac{36.5 \times \text{height (in cm)}}{\text{Serum creatinine (micromol/L)}})</td>
</tr>
<tr>
<td></td>
<td>• CrCl &gt;50mL/minute: normal dosing</td>
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<tr>
<td></td>
<td>• CrCl 10 – 50mL/minute: 75% dose at the normal dosing interval</td>
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<tr>
<td></td>
<td>• CrCl &lt; 10mL/minute: 20-50% dose at the normal dosing interval (maximum total daily dose of 6grams).(^{(2, 4)})</td>
</tr>
<tr>
<td></td>
<td>• Sodium content of the injection may accumulate in patients with renal impairment. Electrolyte levels should be closely monitored.(^{(5)})</td>
</tr>
</tbody>
</table>

**Dosage adjustment required in hepatic impairment:**
- No dosage adjustment is required in patients with hepatic impairment.
- In patients with hepatic impairment in conjunction with renal impairment, the dose adjustments above should be used.\(^{(2)}\)
**RECONSTITUTION**

**IV:**
Reconstitute each vial with the volume of water for injection in the table below. Further dilution with a compatible fluid may be required for infusions.\(^{(6)}\)

<table>
<thead>
<tr>
<th>Vial</th>
<th>Volume of water required</th>
<th>Resulting concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>600mg</td>
<td>9.6mL</td>
<td>60mg/mL</td>
</tr>
<tr>
<td>1.2gram</td>
<td>19.2mL</td>
<td>60mg/mL</td>
</tr>
</tbody>
</table>

**IM:**
Reconstitute each vial with the volume of water for injection in the table below.\(^{(6)}\)

<table>
<thead>
<tr>
<th>Vial strength</th>
<th>Volume of water required</th>
<th>Resulting concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>600mg</td>
<td>1.6mL</td>
<td>300mg/mL</td>
</tr>
<tr>
<td>1.2 gram</td>
<td>3.2mL</td>
<td>300mg/mL</td>
</tr>
</tbody>
</table>

**ADMINISTRATION**

**IV push:**
- Give doses of \(<50\text{mg/kg}\) via slow IV push over 5 to 10 minutes at a rate no greater than 300mg/min (final concentration should not exceed 300mg/mL).
- For doses greater than 50mg/kg IV, infusion is recommended to avoid CNS toxicity (e.g. seizures) and electrolyte imbalance.
- Infusions over at least 30 minutes are preferred in infants and children.\(^{(6)}\)

**IV infusion:**
- Further dilute reconstituted vial with compatible fluid to a suitable volume and infuse over 30 to 60 minutes.\(^{(6)}\)

**HiTH administration:**
- Give via continuous Baxter® infusion. This solution must be buffered to ensure stability.\(^{(6)}\)

**IM Injection:**
- If IV access is not available this medication may be given by IM injection.
- Reconstitute as directed above with water for injection to a concentration of 300mg/mL and inject as per PCH guideline [Intramuscular Injections](internal link).

**MONITORING**
- Renal & hepatic function and full blood count should be monitored weekly with prolonged high-dose therapy (i.e. longer than 10 days).\(^{(1)}\)
### ADVERSE EFFECTS

- **Common (>1%):** diarrhoea, nausea, pain and inflammation at injection site, hypersensitivity reactions (including maculopapular or urticarial rash, pruritus, erythema, fever, anaphylactic shock, angioedema, bronchospasm, interstitial nephritis, haemolytic anaemia, eosinophilia, serum sickness-like syndrome, exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis).

- **Infrequent (0.1-1%):** *Clostridium difficile*-associated disease, vomitng.

- **Rare (<0.1%):** black tongue, electrolyte disturbances, neurotoxicity (including: drowsiness, hallucinations, coma, seizures), bleeding, blood dyscrasias (including neutropaenia & thrombocytopaenia)\(^{(1, 5)}\).

### COMPATIBLE FLUIDS

- Glucose 5%
- Sodium chloride 0.9\(^{(5, 6)}\)

### STORAGE

- Store unreconstituted vials at <25°C and protect from light.\(^{(6)}\)

### INTERACTIONS

Benzylpenicillin has a number of drug interactions; please consult PCH approved references, your ward pharmacist or **Pharmacy on 6456 0190 (option 1)** for more information.

- IV aminoglycoside antibiotics are inactivated by IV penicillins and cephalosporins. Aminoglycoside antibiotics are rapidly bactericidal and should be administered first. The line should then be flushed well with a compatible fluid before benzylpenicillin is administered.\(^{(1)}\)

- Probenecid inhibits excretion of penicillins; this may increase benzylpenicillin levels and increase the risk of seizures in certain patients.\(^{(1)}\)

- Benzylpenicillin inhibits methotrexate excretion and may result in excessive methotrexate levels.\(^{(5)}\)

- High doses of penicillins may affect platelet aggregation and prolong bleeding time. Care should be taken when used in conjunction with other medications that may affect the clotting process.\(^{(1, 5)}\)

### COMMENTS

- Each 600mg of benzylpenicillin sodium salt contains 41.4mg of sodium.\(^{(6)}\)

- 600mg of benzylpenicillin is equivalent to 1million units.\(^{(1, 6)}\)

### MANUFACTURER SAFETY DATA SHEET (SDS)

To access to the Manufacturer SDS for this product, use the following link to **ChemAlert**.

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

Antimicrobial Stewardship Policy (Medication Management Manual)

ChAMP Empiric Guidelines (ChAMP Manual)

References


