



MONOGRAPH

Benzathine Benzylpenicillin (Benzathine Penicillin G) Monograph - Paediatric

Scope (Staff):	Medical, Pharmacy, Nursing
Scope (Area):	Perth Children's Hospital (PCH)

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
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DRUG CLASS

Narrow spectrum penicillin.⁽¹⁾

INDICATIONS AND RESTRICTIONS

- Benzathine benzylpenicillin is used for:
 - Treatment and secondary prevention of acute rheumatic fever/rheumatic heart disease.^(1, 2)
 - Treatment of infections susceptible to prolonged, low concentrations of benzylpenicillin (e.g. early or latent syphilis).^(1, 2)
 - Treatment of impetigo and Group A Streptococcal Tonsillitis/Pharyngitis.^(1, 3)
 - Second line agent for invasive Group A Streptococcal (iGAS) contacts unable to tolerate oral antibiotics.⁽⁴⁾

IM: Unrestricted (green) antibiotic

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

CONTRAINDICATIONS

- Benzathine benzylpenicillin is contraindicated in patients with a history of [high risk allergy](#) to penicillins.^(2, 5-7)
- Allergy to soy products. Benzathine benzylpenicillin products contain lecithin derived from soy bean.⁽⁸⁾

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⁾
- In patients with a previous [low risk allergy](#) to benzathine benzylpenicillin or another penicillin (delayed rash [>1 hr after initial exposure] without mucosal or systemic involvement) the risk of subsequent reaction is low. Re-challenge may be acceptable in discussion with immunology.
- Benzathine benzylpenicillin is for deep intramuscular (IM) injection only. Care must be taken 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 and central nervous system effects. Cardiopulmonary arrest and death have occurred following inadvertent intravenous administration.^(1, 2, 6, 7)
- 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⁾
- Nicolau syndrome has occurred post IM injection of benzathine penicillin. It may present as severe pain, oedema, lesions, pallor, mottling or cyanosis of the extremities, in severe cases significant necrosis and gangrene with permanent neurovascular and neurological damage have been reported. Nicolau syndrome is most likely associated with injection into or near vasculature.⁽⁷⁾

FORMULATIONS

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

- Benzathine benzylpenicillin tetrahydrate 1,200,000 units/2.3 mL in aqueous suspension (Bicillin L-A[®]), pre-filled syringe for IM injection.
- Benzathine benzylpenicillin 1,200,000-unit powder for suspension (Brancaster Pharma[®]).
- Benzathine benzylpenicillin 1,200,000-unit powder for suspension (Extencilline[®]).

Note:

- In 2019 the manufacturer updated the labelling and packaging of benzathine benzylpenicillin to include the tetrahydrate salt and describe the active ingredient in 'units' rather than 'mg'. There was no change to the contents of the product.
- Imprest location: [Formulary One](#)

DOSAGE & DOSAGE ADJUSTMENTS

Doses of benzathine benzylpenicillin should be expressed as units only.

Bicillin L-A® is long term out of stock, Brancaster Pharma® or Extenicilin® brands are available alternative preparations. They have different concentrations and require reconstitution. Refer to the [Reconstitution and Administration](#) section of the monograph or the [Fact Sheet – Safety Considerations during benzathine benzylpenicillin \(Bicillin L-A\) supply disruption](#) for further information.

Neonates:

- Not routinely used in neonates except in cases of congenital syphilis, refer to [Neonatal Medication Protocols](#) or contact Infectious Disease or Clinical Microbiology consultants for advice.

Congenital Syphilis (less than 30 days of age):

- Low-risk infants < 3 kg: contact Infectious Diseases for advice, benzylpenicillin may be appropriate.
- Low-risk infants ≥ 3 kg: 50,000 units/kg IM as a single dose.⁽⁷⁾
- High-risk: treatment with IV benzylpenicillin required.⁽⁷⁾
- Contact Infectious Diseases for all neonates considered to be at-risk of Congenital Syphilis. For further information, refer to: [Syphilis: Investigation and management of the neonate born to a mother with syphilis.](#)

Children:

Impetigo or Presumed *Streptococcus pyogenes* tonsillitis or pharyngitis, scarlet fever (> 4 weeks to 18 years):^(3, 9)

- < 10 kg: 450,000 units IM as a single dose
- 10 to <20 kg: 600,000 units IM as a single dose
- ≥20 kg: 1,200,000 units IM as a single dose

Rheumatic fever (> 4 weeks to 18 years):^(9, 10)

Acute episode:

- < 20 kg: 600,000 units IM as a single dose
- ≥ 20 kg: 1,200,000 units IM as a single dose.

Prevention of recurrence:

- < 20 kg: 600,000 units IM every 3 to 4 weeks
- ≥ 20 kg: 1,200,000 units IM every 3 to 4 weeks
- Duration of antibiotic prophylaxis for prevention of rheumatic fever recurrence depends on patient factors including age, likelihood of ongoing exposure to *S. pyogenes*, time since last episode of acute rheumatic fever and assessment of any existing valve lesions refer to: [The 2020 Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease \(3.2 edition\).](#)

Syphilis (> 4 weeks to 18 years):

- 50,000 units/kg IM (to a maximum of 2,400,000 units).⁽⁵⁻⁷⁾
- Early syphilis requires a single dose.
- Late latent syphilis requires 3 doses given at one-week intervals.
- Contact Infectious Diseases for advice.

Dosing in Overweight and Obese Children: Dose based on measured body weight.⁽¹¹⁾

Renal impairment:

- [eGFR calculator](#)
- Excretion of benzathine benzylpenicillin is delayed in renal impairment and it should be used with caution in patients requiring repeat dosing. There are no recommendations regarding dose reduction in renal impairment.^(5, 7)

Hepatic impairment:

- No dosage adjustment is necessary in hepatic impairment.^(5, 7)

RECONSTITUTION & ADMINISTRATION**IM Reconstitution:**

Reconstitute each vial with the volume of water or lidocaine 1% in the table below.

IM Administration:

Benzathine benzylpenicillin brand	Bicillin L-A ^{®(8)}	Brancaster Pharma ^{®(8)}	Extencilline ^{®(8)}
Reconstitution volume	Reconstitution not required	3.5 mL	4 mL

Dose of benzathine benzylpenicillin	Volume required: Bicillin L-A ^{®(8)}	Volume required: Brancaster Pharma ^{®(8)}	Volume required: Extencilline ^{®(8)}
1,200,000 units	2.3 mL	Entire contents of vial (approximately 4.5 mL)	Entire contents of vial (approximately 5 mL)
600,000 units	1.2 mL	2.4 mL	2.4 mL
450,000 units	0.9 mL	1.8 mL	1.8 mL

- 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, 5)
- It should be administered at a slow, steady rate, preferably over 2-3 minutes to avoid blockage of the needle and to minimise pain. The injection site should be rotated for subsequent doses.^(2, 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.⁽⁸⁾
- Stop injection immediately if there is severe pain at the injection site.⁽⁸⁾

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, 10)

Administering Benzathine Benzylpenicillin (Bicillin L-A®) with Lidocaine 1%⁽¹⁰⁾:

- Benzathine benzylpenicillin may be administered with lidocaine. It is reported to significantly reduce pain during injection and in the first 24 hours after injection.⁽¹⁰⁾

Equipment:

- Pre-filled benzathine benzylpenicillin syringe
- 3 mL syringe
- 2 drawing-up needles
- 21G needle

Preparation:

1. Attach a drawing-up needle to a 3 mL syringe.
 2. Draw the required contents of benzathine benzylpenicillin from the pre-filled syringe into the 3mL syringe.
 3. Using a new needle, draw up 0.5 mL of lidocaine 1% into the tip of the 3mL syringe.
 4. Avoid mixing to keep the lidocaine in the tip of the syringe.
 5. Push plunger up carefully to remove any air in the syringe.
 6. Remove the drawing-up needle.
 7. Attach IM needle (e.g. 21 gauge) to the syringe to administer injection.
- Note: Lidocaine is contraindicated in people with a known hypersensitivity to local anaesthetics of the amide type; second or third degree heart block.⁽¹⁰⁾

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

Caution: Inadvertent intravascular administration may result in neuromuscular damage, seizures, cardiac arrest and/or severe, and potentially permanent, neurovascular damage. CNS effects include anxiety, agitation, fear of death and hallucinations.⁽¹⁾

Common: pain and inflammation at the injection site, rash, urticaria, skin eruptions (most commonly maculopapular), nausea, diarrhoea, 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).^(1, 5)

Infrequent: vomiting, *Clostridioides difficile*-associated disease, arthralgia, leucopenia, nephropathy^(1, 5)

Rare: Anaphylaxis or other immediate hypersensitivity reactions, black tongue, neurotoxicity with high doses (including drowsiness, hallucinations, coma and seizures), blood dyscrasias, bleeding, hepatic disorders, tubulointerstitial nephritis, severe cutaneous adverse reactions (SCARs).^(1, 5)

STORAGE

- Bicillin L-A[®] brand:
 - Store between 2-8°C. Refrigerate, do not freeze.^(2, 8)
 - Bicillin L-A[®] brand of benzathine benzylpenicillin may be stored below 30°C for a single period of up to 2 months prior to expiry.⁽²⁾
 - The product should be discarded if not used – do not return to the fridge. The date the product is placed outside of refrigerated storage and stored below 30°C should be written in the space provided on the carton.⁽²⁾
- Brancaster[®] Pharma and Extencilline[®] brands:
 - Store the powder for suspension below 25°C and use immediately follow reconstitution.⁽⁸⁾

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 benzathine benzylpenicillin. Any variations to the doses recommended should be clarified with the prescriber prior to administration

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