Issue date
1 December 2023

Distributed to:
Chief Executives
Directors of Clinical Governance
Director, Regulation and Compliance Unit

Action required by:
Chief Executives
Directors of Clinical Governance

We recommend you also inform:
Directors, Managers and Staff of:
- Nursing/Midwifery
- Medical Services
- Pharmacy
- Infectious Diseases /Microbiology
- Cardiology
- Rheumatology
- Sexual Health
- Public Health Units

Drug and Therapeutics Committees
Other relevant clinicians, departments and committees.

Content reviewed by:
Antimicrobial Stewardship Expert Advisory Committee
Centre for Population Health
Health Protection NSW
Medication Safety Expert Advisory Committee
Medication Shortage Assessment and Management Team

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Disruption to supply – Benzathine benzylpenicillin (Bicillin L-A) suspension for injection pre-filled syringe

Situation

There is a current global disruption to the supply of:

- Benzathine benzylpenicillin (Bicillin L-A) 600,000 units/1.17 mL suspension for injection pre-filled syringe until **15 November 2024.**
- Benzathine benzylpenicillin (Bicillin L-A) 1,200,000 units/2.3 mL suspension for injection pre-filled syringe until **29 February 2024.**

This disruption to supply is a result of manufacturing issues (600,000 units) and increases in consumer demand (1,200,000 units). Limited supply of the 1,200,000 units/2.3 mL product may continue to be available.

At the time of publication:

- An alternative 1,200,000-unit product available from ORSPEC Pharma from the United Kingdom (UK) has been approved for supply under Section 19A (S19A) of the Therapeutic Goods Act until 30 May 2024.
- The S19A alternative is not currently subsidised under the Pharmaceutical Benefits Scheme (PBS).

Background

Benzathine benzylpenicillin is an antimicrobial indicated in the treatment of infections caused by penicillin-sensitive micro-organisms that are susceptible to low and prolonged serum levels. Indications include:

- treatment of streptococcal infections (group A without bacteraemia): mild-moderate infections of the upper respiratory tract.
- sexually transmitted infections including syphilis
- prophylaxis against rheumatic fever.

Assessment

Urgent action is required to ensure that the remaining supply of the Australian registered benzathine benzylpenicillin product is preserved for priority indications where alternatives are not available or suitable. **NOTE** – most patients requiring benzathine benzylpenicillin for priority indications access this medicine in the community setting.

The S19A alternative available for the 1,200,000-unit strength from ORSPEC Pharma has safety considerations due to differences in presentation and storage from the Australian registered product (see **Table 1** on page 3 for comparison).

The manufacturer of the S19A alternative has indicated that the powder displacement volume is approximately 1 mL. As this volume is an estimate, the S19A alternative **cannot** be utilised to administer smaller doses due to inability to accurately measure a dose other than 1,200,000-units.

Priority indications in NSW Health facilities during disruption to supply

- Reserve supply of the Australian registered benzathine benzylpenicillin product (Bicillin-LA) for the following priority indications:
  - treatment of definite, probable and possible acute rheumatic fever (ARF)
  - secondary prophylaxis for acute rheumatic fever (ARF) and/or rheumatic heart disease (RHD)
  - in specific circumstances where syphilis prophylaxis may be indicated for high-risk uninfected neonates (600,000 units/1.17 mL product).
- Use the S19A alternative for the treatment of syphilis.
- Alternative antimicrobials should be used for **all other indications**.

Requirements of NSW Health facilities during the disruption to supply

Restrict orders for the Australian registered brand of benzathine benzylpenicillin (Bicillin L-A) to the priority indications outlined above until further notice, so that the limited remaining supply is available for use in the community setting. The S19A alternative should be ordered for the treatment of syphilis noting there is a lead time of 7-10 business days and a difference in cost.

Clinical Recommendations

- Develop a local plan to manage the disruption to the supply of benzathine benzylpenicillin that includes (but is not limited to):
  - assessing the current status and availability of the medicine in each facility, ensuring all locations of stock are identified
  - reviewing historical stock usage
  - determining ongoing clinical needs and ability to obtain alternative supply.
- Seek advice from Infectious Diseases/Microbiology/Sexual Health and/or the Therapeutic Guidelines: Antibiotic (including the Antibiotic prescribing in primary care: Therapeutic Guidelines summary table 2023) for alternative antimicrobials in indications not identified as a priority indication.
- Consider the appropriateness of the S19A alternative for each patient with reference to the information provided in Table 1. Particular attention is drawn to:
  - The volume required to administer a 1,200,000-unit dose (approximately 4.5 mL) and the acceptability of this volume in paediatric patients.
  - The presence of **soy lecithin (like the ARTG product)** making it inappropriate in patients with a soy or peanut allergy.
- Continue to dose benzathine benzylpenicillin according to the Product Information for the Australian registered product and evidence-based resources such as Therapeutic Guidelines: Antibiotic.
- A license to supply by wholesale has been issued to specified public health organisations which allows benzathine benzylpenicillin (Bicillin L-A) 1,200,000 units/2.3 mL suspension for injection pre-filled syringe to be supplied to a community pharmacy on a written order signed by a pharmacist (further detail here including the date at which the license remains in force).

Table 1. Comparison of ARTG listed benzathine benzylpenicillin product and S19A alternative.

	ARTG listed product	**S19A alternative available from ORSPEC Pharma**
Brand	Bicillin L-A (Pfizer)	Brancaster Pharma (image)
Active ingredient	Benzathine benzylpenicillin tetrahydrate 1,200,000 units	Benzathine benzylpenicillin 1,200,000 units
Formulation	White fluid suspension in a pre-filled syringe	Powder (white/off white) and solvent (clear diluent) for suspension for injection
Volume required to administer 1,200,000-unit dose*	1,200,000 units = 2.3 mL	3.5 mL diluent plus powder displacement volume **Total volume** = approximately **4.5 mL**
Consumer Medicines Information leaflet	Access here	Access here
Labelling	English	
Route of administration	**Intramuscular (IM) injection ONLY**	
Storage	2-8 degrees Celsius (Refrigerate, do not freeze)	Room temperature – below 25 degrees Celsius
Doses per pack	10 (individual pre-filled syringes)	1 x vial of powder for suspension 1 x ampoule containing 5 mL water for injection

Table 1 cont.

	ARTG listed product	S19A alternative available from ORSPEC Pharma

Additional excipients	• sodium citrate
	• lecithin#
	• carmellose sodium
	• povidone
	• preservatives:
	  ○ methyl hydroxybenzoate
	  ○ propyl hydroxybenzoate
		• soy lecithin#
		• polysorbate 80
		• sodium citrate
		• carmellose sodium
		• povidone

	#**The presence of lecithin makes these products NOT suitable for patients with an allergy to soy or peanuts.**	

*Please note – the manufacturer of the S19A alternative has indicated that the powder displacement volume is approximately 1 mL. As this volume is an estimate, the S19A alternative **cannot** be utilised to administer smaller doses of 600,000 units.

Required actions for the Local Health Districts/Networks

1. Distribute updated Safety Notice to all relevant clinicians and clinical departments where benzathine benzylpenicillin is held, prescribed, and administered, and include this Safety Notice in relevant handovers and safety huddles.
2. Undertake a local risk assessment and incorporate the requirements and recommendations within this Safety Notice to manage the disruption to supply.
3. Ensure a system is in place to document actions taken in response to this Safety Notice.
4. Report any incidents associated with this disruption to supply into the incident management system (ims+).
5. Confirm receipt and distribution of this Safety Notice within **96 hours** to CEC-MedicationSafety@health.nsw.gov.au