Issue date
5 March 2024

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

Clinical Excellence Commission
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March 2025

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

What's new in this Safety Notice?

This Safety Notice replaces SN:040/23 and has been updated in light of the evolving stock situation, and extension to the 1,200,000 units/2.3 mL product's supply disruption period. Statements surrounding restricting use of the Bicillin-LA brand for specific patient populations have been removed from the 'Priority indications' section.

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 **28 June 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 March 2024.
- The S19A alternative has been subsidised under the Pharmaceutical Benefits Scheme (PBS) since 1 January 2024.

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
- treatment and prevention of rheumatic fever.

Assessment

Urgent action is required to ensure that the remaining supply of the 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 during disruption to supply

- Products containing benzathine benzylpenicillin should be prioritised for use in the following conditions:
  - treatment of definite, probable and possible acute rheumatic fever

- secondary prophylaxis of acute rheumatic fever and/or rheumatic heart disease
- treatment of syphilis in those with proven or suspected infection and their recent sexual contacts
- patients who require treatment for group-A streptococcal infection of the respiratory tract and skin who are at high risk of acute rheumatic fever, rheumatic heart disease or APSGN, where oral therapy is not acceptable or the likelihood of non-adherence is high.

- Where patients fall outside the above priority conditions and settings, prescribers should refer to the Australian Therapeutic Guidelines, appropriate local guidelines and/or infectious disease experts for advice on alternative agents.

Requirements of NSW Health facilities during the disruption to supply

- All supply of benzathine benzylpenicillin held by NSW Health regardless of current location is to be prioritised according to the indications outlined above.
- Where available and clinically acceptable, the S19A alternative should be used to reserve supply of the Australian registered brand of benzathine benzylpenicillin (Bicillin L-A) for those whom the S19A alternative is not appropriate, for example neonatal and paediatric patients.
- Place orders for the S19A alternative 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.
- Where possible, benzathine benzylpenicillin (Bicillin L-A) should be continued for patients on long-term secondary prophylaxis for acute rheumatic fever and/or rheumatic heart disease.
- 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).

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 **48 hours** to CEC-MedicationSafety@health.nsw.gov.au.

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** Reconstitution with single ingredient lidocaine 1% in place of water for injection, can be considered to reduce pain at the injection site.
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) • May be stored below 30°C for a single period of up to 2 months, prior to expiry. 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. After storage outside of refrigeration, the product should be discarded and cannot be returned to refrigerated storage.	• 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

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 **should not** be used to administer smaller doses of 600,000 units unless there is an absence of the ARTG product.