AUSTRALIAN COMMISSION
ON SAFETY AND QUALITY IN HEALTH CARE

FACT SHEET
for health service organisations and clinicians

Safety considerations during benzathine benzylpenicillin (Bicillin L-A) supply disruption

Background

At the request of the Department of Health and Aged Care, this fact sheet has been developed by the Australian Commission on Safety and Quality in Health Care (the Commission). It aims to assist health service organisations (HSOs) and clinicians understand and manage the safety issues related to the disrupted supply of benzathine benzylpenicillin (Bicillin L-A) in Australia.

Benzathine benzylpenicillin is a long-acting antibiotic formulation that is typically used in uncomplicated syphilis and rheumatic heart disease (RHD) prevention. Refer to the **Therapeutic Guidelines: Antibiotic** for additional information.

Situation

The Therapeutic Goods Administration (TGA) has advised of a worldwide disruption to the supply of:

- Benzathine benzylpenicillin tetrahydrate (Bicillin L-A) 600,000 units/1.17 mL suspension for injection pre-filled syringe
- Benzathine benzylpenicillin tetrahydrate (Bicillin L-A) 1,200,000 units/2.3 mL suspension for injection pre-filled syringe.

Updates and information about the shortage, and return to supply dates, are available on the TGA **Medicine Shortage Reports Database**.

At the time of publication

To alleviate the impact, the TGA has approved the importation and supply of registered alternatives under Section 19A (S19A) of the Therapeutic Goods Act:

- Benzylpenicillin benzathine 1,200,000 units powder and solvent for suspension for injection (Brancaster Pharma, from the United Kingdom (UK)) until 30 March 2024
- Benzathine benzylpenicillin (EXTENCILLINE) 1,200,000 units powder and solvent for IM injectable suspension (from France) until 30 September 2024.

The **S19A alternatives**, available locally via **ORSPEC Pharma**, differ from the Australian registered product (Bicillin L-A) in presentation, storage and excipients.

Table 1 (at the end of this fact sheet) provides a comparison of the products/formulations.

The dose specifications (including for special populations), warnings and precautions and side effect information may vary across the labelling (Product Information or Summary of Product Characteristics) according to the country where the product is registered. This information is appropriate at the time of initial or renewed product registration. For the recommended dosing information for the approved indications, prescribers are referred to the Australian Product Information for Bicillin L-A benzylpenicillin tetrahydrate 1,200,000 Units / 2.3 mL suspension for injection pre-filled syringe with needle. Clinicians are expected to use their clinical judgement supported by the most recent evidence-based information to ensure safe and quality use of the products.

Safety and suitability considerations

There are safety considerations due to differences between Bicillin L-A and the **S19A alternatives**.

The **S19A alternatives** requires reconstitution with a diluent, which must then be administered immediately. This may make them less suitable for use in some

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patient cohorts and settings, than the pre-filled syringes.

The need to reconstitute the **S19A alternatives** prior to administration, and larger volume for administration, should be considered as part of conserving ongoing supply of available benzathine benzylpenicillin (Bicillin L-A) prefilled syringes for rural and remote settings as well as paediatric patients.

The **same safety and suitability considerations** should be applied to any alternative brands of benzathine benzylpenicillin that might be sourced via the Special Access Scheme (SAS) but may be unavailable under S19A.

Practice points

The following practice points are recommended to support clinical decision-making around the use of benzathine benzylpenicillin:

1. **CONFIRM THE NEED** to use an antibiotic.
2. **CONSIDER if prescribing for a priority indication of benzathine benzylpenicillin**.
   Benzathine benzylpenicillin should be prioritised for use in the following conditions:
   - treatment of definite, probable and possible acute rheumatic fever (ARF)
   - secondary prophylaxis of ARF and secondary prophylaxis of RHD
   - 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 ARF, RHD or post-streptococcal glomerulonephritis, where oral therapy is not acceptable or the likelihood of non-adherence is high.
3. **SEEK ADVICE** from local Infectious Diseases experts and/or the Therapeutic Guidelines: Antibiotic (including the **Antibiotic prescribing in primary care: Therapeutic Guidelines summary table 2023)** for **ALTERNATIVE AGENTS** for indications not identified as a priority indication.
4. **CONSERVE** benzathine benzylpenicillin (Bicillin L-A) **prefilled syringes** where the medicine is administered in rural and remote settings (for example, Aboriginal Medical Services or Aboriginal Community Controlled Health Organisations); and for certain patient cohorts where the **S19A alternatives** may not be suitable (for example, in paediatric patients, including neonates, where the larger volume should be determined is appropriate for administration).

Key messages

The Therapeutic Goods Administration (TGA) has notified of a **worldwide shortage of benzathine benzylpencillin: Bicillin L-A prefilled syringes**.

To limit supply disruption, the TGA has approved the importation and supply of alternatives under Section 19A (S19A) of the Therapeutic Goods Act.

The **S19A alternatives**, available locally via **ORSPEC Pharma**, **differ from the Australian registered Bicillin L-A** in presentation, storage, and excipients. There are **safety and suitability considerations** due to these differences (see Table 1 for comparison).

During shortage, benzathine benzylpenicillin should be used for priority indications.

Bicillin L-A pre-filled syringes should be **CONSERVED** for settings and patient cohorts, where the **S19A alternatives** may not be suitable.

SEEK ADVICE from Infectious Diseases/Microbiology 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 priority indications.

This factsheet is for use during a period of shortage only. If adequate stock of the Australian registered product of benzathine benzylpenicillin: Bicillin L-A (Pfizer brand) is assured, health services and clinicians should return to using it in line with relevant local and national evidence-based guidelines.

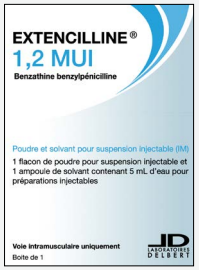
The same safety and suitability considerations should be applied for additional brands of benzathine benzylpenicillin available via SAS, but **not approved by the TGA under S19A**.

Useful resources

- Therapeutic Goods Administration (TGA) publishes medicines shortages, including CRITICAL shortages, on the **Medicine Shortage Reports Database**.
- Therapeutic Guidelines Antibiotic. **Antibiotic prescribing in primary care: Therapeutic Guidelines summary table 2023**.
- Australian Commission on Safety and Quality in Health Care **general information for prescribers and pharmacists** on how to manage shortages in acute and primary healthcare settings.
- National Centre for Antimicrobial Stewardship **Medication Shortage Fact Sheets** provide information about prescribing choices and alternatives for common infections.
- **eTG complete** [online]. Melbourne: Therapeutic Guidelines Limited.
- **Australian Medicines Handbook** [online]. Adelaide: Australian Medicines Handbook Pty Ltd.
- The RHD Australia **Guidelines for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease 3rd Edition**.
- Australasian Society of Infectious Diseases (ASID) guidelines: **Management of perinatal infections 3rd Edition**.
- Australian Commission on Safety and Quality in Health Care **Principles for safe selection and storage of medicines** provides guidance on risk reduction strategies to address safe selection and storage of all medicines, including look-alike, sound-alike (LASA) medicines.
- Australian Commission on Safety and Quality in Health Care **guidance on conserving medicines within a focus on medicines shortages**.
- Australian Commission on Safety and Quality in Health Care **information on antibiotic shortages for Aboriginal and Torres Strait Islander consumers**.
- Australian Commission on Safety and Quality in Health Care **general information for clinicians working in the Aboriginal and Torres Strait Islander health sector**.

Safety considerations during Benzathine benzylpenicillin (Bicillin L-A) supply disruption

Table 1. Comparison of the ARTG listed 1,200,000 unit product and the S19A alternative.

	ARTG-listed product	S19A alternative (UK)	S19A alternative (France)	Safety considerations
Brand and image of outer packaging	Bicillin L-A (Pfizer) 	Brancaster Pharma (available from ORSPEC Pharma) 	Extencilline Delbert Laboratories (available from ORSPEC Pharma) 	The Principles for safe selection and storage of medicines be applied given that the storage location will differ. The **S19A alternatives** are not stored in the fridge and could inadvertently be placed on a shelf adjacent to similar looking outer packaging. Risk reduction strategies may need to be considered to ensure differentiation from other similar looking packaging. For example, storing in a separate location from other injectable medicines.
Active ingredient and strength	Benzathine benzylpenicillin tetrahydrate 1,200,000 units	Benzylpenicillin benzathine 1,200,000 units	Benzathine benzylpenicillin 1,200,000 units (1.2 MIU[1]) French language labelling and packaging; strength expressed as 1,200,000 UI[2] or 1.2 MUI[1] *1. MIU or MUI = million international units* *2. UI or IU = international units*	The active ingredient name on the **UK S19A alternative** is expressed differently. Benzathine benzylpenicillin tetrahydrate and benzylpenicillin benzathine are synonyms. The strength on the **French S19A alternative** is expressed differently. The Principles for safe selection and storage of medicines should be applied – for example, when selecting from a drop down menu within prescribing and dispensing systems.

	ARTG-listed product	S19A alternative (UK)	S19A alternative (France)	Safety considerations
Appearance and formulation	White fluid suspension in a pre-filled syringe 	Powder (white/off-white) and solvent (clear/colourless liquid) for suspension for injection  Left: Vial of powder for suspension Right: Glass ampoule containing WFI Reconstitution may be undertaken with 1% injectable lidocaine solution (not supplied)	Powder (white/off-white) and solvent (clear/colourless liquid) for suspension for injection  The image includes a vial of powder for reconstitution and a glass ampoule containing WFI Reconstitution may be undertaken with 0.5% injectable lidocaine solution (not supplied)	The **S19A alternatives**, differ from the Australian registered (ARTG-listed) product in presentation and storage. The **S19A alternatives** also require reconstitution prior to administration by: – drawing up **3.5 mL (UK) or 4 mL (France) of the water for injection** (WFI) diluent and adding to the vial containing the powder – agitating the suspension carefully for at least 20 seconds until a homogeneous suspension is obtained. The **S19A alternatives** must be administered immediately once reconstituted
Volume required to administer 1,200,000 units dose	**2.3 mL**	3.5 mL diluent (WFI) + powder displacement volume (results in a final volume of approximately **4.5 mL**)	4 mL diluent (WFI) + powder displacement volume (results in a final volume of approximately **5 mL**)	The final volume of both **S19A alternatives** is approximately double that of the ARTG-listed product. This has implications particularly in paediatrics. The use of a local anaesthetic, such as lidocaine 1% (UK) or 0.5% (France), **in place of water for injection (WFI)**, will potentially reduce pain at the injection site (see UK SmPC or English translation of the French Summary of Product Characteristics (SmPC) from ORSPEC Pharma)

	ARTG-listed product	S19A alternative (UK)	S19A alternative (France)	Safety considerations
Consumer medicines information (CMI)	Access the Australian CMI **here**	Access the UK leaflet **here**	Access the English translated version of the French product leaflet from **ORSPEC Pharma**)	The medicines information leaflets for the **S19A alternatives** contain similar information but are not TGA approved.
Product Information (PI)	Access the Australian PI **here**	Access the UK Summary of Product Characteristics (SmPC) **here**	Access the English translation of the French Summary of Product Characteristics (SmPC) from **ORSPEC Pharma**)	The product information for the **S19A alternatives** contain similar information but are not TGA approved.
Labelling	English	English	French	The active ingredient is in English. However, the balance of the labelling for the **S19A alternative from France** is in French.
Preparation requirements	The suspension for injection is already in a prefilled for **single use only**.	The suspension for injection **must be reconstituted** with 3.5 mL diluent before administration.	The suspension for injection **must be reconstituted** with 4 mL diluent before administration.	The **S19A alternatives** must be reconstituted using **aseptic technique**.
Route of administration	**For deep intramuscular (IM) injection ONLY**			Refer local clinical practice guidelines on appropriate administration technique for deep IM injection in conjunction with full details on method of administration in the UK SmPC, or English translation of the French SmPC from **ORSPEC Pharma**, including specific instructions for paediatric patients (including neonates).

	ARTG-listed product	S19A alternative (UK)	S19A alternative (France)	Safety considerations
Storage conditions	2 to 8 degrees Celsius* (Refrigerate, do not freeze) *[*Storage at 30°C, is allowed for a single period of 2 months prior to batch expiry.]*	Below 25 degrees Celsius	Below 25 degrees Celsius	The **Principles for safe selection and storage of medicines** should be applied given that the storage location of the **S19A alternatives** will differ.
Additional excipients	Sodium citrate; soy lecithin#; carmellose sodium; povidone; and preservatives: – methyl hydroxybenzoate – propyl hydroxybenzoate	Soy lecithin#; polysorbate 80; sodium citrate; carmellose sodium; and povidone	Soy lecithin^#; anhydrous sodium citrate; carmellose sodium; and povidone. *^The manufacturer describes the product as containing soyabean phospholipids originating from the lecithin.*	The list of excipients within the **S19A alternatives**, differ from the Australian registered product. *#The presence of excipients such as soy lecithin should be considered, especially for consumers with a soy or peanut allergy.*
Doses per pack	10 (individual pre-filled syringes)	1 x vial of powder for suspension 1 x glass ampoule containing 5 mL WFI	1 x vial of powder for suspension 1 x glass ampoule containing 5 mL WFI	

Find out more

For more information, visit TGA **Medicine Shortage Reports Database** or contact the Safety and Quality Advice Centre at **AdviceCentre@safetyandquality.gov.au** or call 1800 304 056.