

Medication Shortages

Submission: Therapeutic Goods Administration (TGA) Consultation - Medicine shortages in Australia

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Online survey link: [Medicine shortages in Australia – Challenges and opportunities - Therapeutic Goods Administration - Citizen Space \(tga.gov.au\)](https://www.tga.gov.au/citizen-space/medication-shortages)

Queensland Aboriginal and Islander Health Council (QAIHC) is a leadership and policy organisation. QAIHC was established in 1990 and is the peak organisation representing all Aboriginal Community Controlled Health Organisations (ACCHOs) in Queensland at both a state and national level.

Context

Australia imports over 90% of its pharmaceutical products¹ leaving the country particularly vulnerable to international drug shortages, with medication shortages in Australia increasing by 300% since the COVID-19 pandemic.²

There is a current international shortage of Pfizer's benzathine benzylpenicillin (Bicillin LA) prefilled syringes due to a disruption at the point of manufacturing, as well as increased global demand for the product.³ This medication is a compelling example of an essential medicine, particularly for Aboriginal and Torres Strait Islander people.

Shortages and supply instabilities of these types of essential medications generate confusion, distrust in health services and may cause adverse health outcomes for individuals.

Benzathine benzylpenicillin shortage

As at time of writing, there is limited or completely depleted stock of Bicillin LA with an estimated recovery date of the second quarter of 2024.⁴ The specific products affected are:

- BICILLIN L-A - benzathine benzylpenicillin tetrahydrate 1,200,000 Units / 2.3 mL suspension for injection pre-filled syringe with needle
- BICILLIN L-A - benzathine benzylpenicillin tetrahydrate 600,000 units/1.17 mL suspension for injection syringe with needle

Intramuscular benzathine benzylpenicillin is indicated in the treatment of infections caused by penicillin-sensitive micro-organisms including^{5,6}:

¹ Therapeutic Goods Administration. Management and communication of medicine shortages and discontinuations in Australia. Version 1.1. Canberra, May 2019. Accessed Nov 20, 2023. <https://www.tga.gov.au/sites/default/files/2023-02/management-and-communication-medicine-shortages-and-discontinuations-australia.pdf>

² Cameron EE, Bushell M-JA, Analysis of drug shortages across two countries during pre-pandemic and pandemic times. Res Social Adm Pharm Sept 2021;17(9):1570-1573. doi: 10.1016/j.sapharm.2020.12.001

³ Martyn K (Pfizer Inc.). Letter to: Customers. Jun 12, 2023. Accessed Nov 20, 2023. <https://www.fda.gov/media/169427/download>

⁴ Pfizer Hospital. Pfizer injectables product availability report. Nov 2023. Accessed Mar 4, 2024. https://www.pfizerhospitalus.com/injectables_availability_report

⁵ Therapeutic guidelines Limited. Therapeutic guidelines. Accessed Nov 20, 2023. <https://tgldcdp.tg.org.au/>

⁶ Western Australia Country Health Service. Public health management of acute post-streptococcal glomerulonephritis guideline. Jun 2019. Accessed Nov 20, 2023. <https://www.wacountry.health.wa.gov.au/~media/WACHS/Documents/About-us/Policies/Public-Health-Management-of-Acute-Post-Streptococcal-Glomerulonephritis-Guideline.pdf>

- Treatment of **acute rheumatic fever** and prevention of **rheumatic heart disease**
- Treatment and prevention of **syphilis, including congenital syphilis**
- Treatment of **streptococcal pharyngitis and tonsillitis**
- Treatment of **impetigo** in endemic settings
- Prevention of **invasive Group A streptococcal infection**
- Treatment and prevention of **acute post-streptococcal glomerulonephritis (APSGN)**

In light of the shortage, the Queensland Statewide Antimicrobial Stewardship Program has made recommendations for clinicians to⁷:

1. Review the need for antibiotic therapy for individual patients
2. Consider alternative agents to benzathine benzylpenicillin
3. Conserve benzathine benzylpenicillin for the following indications:
 - a. Acute rheumatic fever and secondary prophylaxis
 - b. Syphilis
 - c. Acute post-streptococcal glomerulonephritis

Alternative formulation

ORSPEC Pharma Pty Ltd has received approval under Section 19A of the Therapeutic Goods Act 1989 to import supply of benzathine benzylpenicillin 1,200,000 units/2.3 mL suspension for injection from a UK manufacturer (Brancaster Pharma) until 31 March 2024.⁸

The main difference is around the formulation. This alternative product comes as a lyophilised powder that is packaged in vials and requires reconstitution into an aqueous suspension immediately prior to administration and does not require a cold chain.^{9,10} The original product, Bicillin LA, is a viscous liquid in a 2mL pre-filled syringe and is administered directly into the patient and requires refrigeration. Pfizer is the only manufacturer of this formulation of benzathine benzylpenicillin.¹¹ The vast majority of the world uses the powdered form of benzathine benzylpenicillin however, historical use of this form in Australia between 2006 and 2008 has led to concerns about the acceptability of administration with issues around viscosity of injection and pain on administration.⁹ The product used in Australia at this time was from a different manufacturer, Pan Benz, and required the suspension in 4.6ml of water which is double the volume of the original Bicillin LA formulation.⁹ The Brancaster Pharma product requires reconstitution in at least 3.5mL diluent¹². The alternative product also contains soy lecithin and should not be used in patients with peanut or soy allergies.

⁷ Queensland Statewide Antimicrobial Stewardship Program. Clinical care alert: benzathine benzylpenicillin (Bicillin LA) shortage. Oct 2023. Accessed Nov 20, 2023. https://www.childrens.health.qld.gov.au/_data/assets/pdf_file/0018/191205/Benzathine-Benzylpenicillin-shortage-communicue.pdf

⁸ Therapeutic Goods Administration. Benzylpenicillin benzathine 1.2 million I.U powder and solvent for suspension for injection (Brancaster Pharma, UK). Accessed Mar 4, 2024. <https://www.tga.gov.au/resources/section-19a-approvals/benzylpenicillin-benzathine-12-million-iu-powder-and-solvent-suspension-injection-brancaster-pharma-uk>

⁹ RHD Action. Global status of BPG report. 2016. Accessed Nov 20, 2023.

https://rhdaction.org/sites/default/files/RHD%20Action_Global%20Status%20of%20BPG%20Report_Online%20Version.pdf

¹⁰ Wyber R, Johnson TD, Patel B. Supply of benzathine penicillin G: the 20-year experience in Australia. Aust N Z J Public Health. Dec, 2015;39(6):506-8. doi: 10.1111/1753-6405.12415. Epub 2015 Aug 10.

¹¹ Therapeutic Goods Administration. Benzathine benzylpenicillin tetrahydrate – medicine shortage information. Accessed Nov 20, 2023. <https://apps.tga.gov.au/Prod/msi/Search/Details/benzathine%20benzylpenicillin%20tetrahydrate>

¹² Electronic Medicines Compendium. Benzylpenicillin benzathine 2.4 Million I.U. powder and solvent for suspension for injection – summary of product characteristics. Jul 17, 2023. Accessed Nov 20, 2023. <https://www.medicines.org.uk/emc/product/11044/smpc>

The product received Therapeutic Goods Administration (TGA) approval in November 2023 but did not receive approval for inclusion into the Pharmaceutical Benefits Scheme (PBS) until January 2024¹³. While awaiting the PBS approval, each vial required a payment of approximately \$44.60 to be paid by the patient¹⁴.

There are now also reports that even this product is now unavailable for use in Australia, with ORSPEC Pharma Pty Ltd now sourcing another product from Spain, *Benzetacil (benzathine benzylpenicillin)*, under the Special Access Scheme.¹⁵

Concurrent medication shortages

When considering using alternative medications to replace benzathine benzylpenicillin, it is also important to note that there are also other concurrent medication shortages in Australia. This considerably complicates the options for clinicians.

Examples of the proposed alternative agents and their availability is shown in the table below as per the Therapeutic Guidelines⁵ and the TGA Medicine shortage reports database¹⁶:

Alternative agent	Current availability	Notes
<i>Treatment of acute rheumatic fever</i>		
Oral phenoxymethylpenicillin for 10 days	Available (but recent shortage of oral liquid formulation)	Intramuscular benzathine benzylpenicillin is a single dose, long acting, and preferred due to poor adherence with long course of oral therapy and is the most efficacious for ongoing secondary prophylaxis to prevent recurrent acute rheumatic fever.
Oral cefalexin for 10 days	Limited availability of liquid formulations	Penicillin is the drug class of choice to treat residual Group A strep infection and to eliminate carriage.
Oral azithromycin for 5 days	Available (but recent shortage of 500mg tablets)	Penicillin is the drug class of choice to treat residual Group A strep infection and to eliminate carriage.
<i>Treatment of early syphilis</i>		
Intramuscular procaine benzylpenicillin for 10 days	Discontinued	Intramuscular benzathine benzylpenicillin is single dose, long acting, and the drug of choice for early syphilis.
Oral doxycycline for 14 days	Limited availability of 100mg tablets	Doxycycline cannot be used in pregnant patients, and benzathine benzylpenicillin is the drug of choice for early syphilis.

¹³ Pharmaceutical Benefits Scheme. Benzathine benzylpenicillin. Accessed Mar 4, 2024. <https://www.pbs.gov.au/medicine/item/13790T-13801J-13816E>

¹⁴ ORSPEC Pharma team, internal communication, Nov 6, 2023.

¹⁵ National Aboriginal Community Controlled Health Organisation (NACCHO), internal communication, Mar 1, 2024.

¹⁶ Therapeutic Goods Administration. Medicine shortage reports database. Canberra. Accessed Mar 4, 2024.

<https://apps.tga.gov.au/Prod/msi/search>

<i>Treatment of streptococcal pharyngitis and tonsillitis</i>		
Oral phenoxymethylpenicillin for 10 days	Available (but recent shortage of oral liquid formulation)	Intramuscular benzathine benzylpenicillin is preferred when oral therapy is not tolerated, or single-dose treatment is preferred due to concerns about adherence.
Oral amoxicillin for 10 days	Limited availability of both tablet and liquid formulations.	Not recommended first-line treatment.

Impact of this shortage on Queensland Aboriginal community-controlled health organisations

Nationally, Aboriginal and Torres Strait Islander people account for 92% of the diagnoses of **acute rheumatic fever** between 2017 and 2021¹⁷. In northern Australia, Aboriginal and Torres Strait Islander people experience **invasive Group A streptococcal infections** at 6-10 times the rate of non-Indigenous Australians¹⁸. Notification rates for **non-congenital syphilis** in Aboriginal and Torres Strait Islander people were 5.8 times the rate for non-Indigenous Australians nationally but goes up to 27 times in remote and very remote areas¹⁹. **Acute post-streptococcal glomerulonephritis** has only recently become notifiable in Queensland, and there are already reports of clusters of APSGN in North Queensland²⁰.

Benzathine benzylpenicillin is a powerful example of an essential medicine, particularly for Aboriginal and Torres Strait Islander people. Shortages and supply instability of this medication generates confusion and may cause adverse health outcomes for individuals. QAIHC also has ongoing concerns about the reliance on a formulation produced by a single manufacturer.

Current strategies to address medication shortages

Alternative supply options

In addition to *section 19A of the Therapeutic Goods Act 1989*, prescribers can use the *Special Access Scheme (SAS) Category A pathway* and the *Authorised Prescriber (AP) scheme* to access ‘unapproved’ medicines from overseas²¹. However, accessing an unapproved product requires consideration of the patient’s informed consent, adherence to relevant standards of good medical practice, and poses risks of treatment with an alternative product. The product must also be available and affordable to the patient, as they are generally not subsidised by the Pharmaceutical Benefits Scheme (PBS)²².

¹⁷ Australian Institute of Health and Welfare. Acute rheumatic fever and rheumatic heart disease in Australia, 2017–2021. May 2023. Accessed Nov 20, 2023. <https://www.aihw.gov.au/reports/indigenous-australians/arf-rhd/summary>

¹⁸ Hla TK, Cannon JW, Bowen AC, Wyber R. Getting to grips with invasive group A streptococcal infection surveillance in Australia: are we experiencing an epidemic? *Med J Aust.* Aug 21, 2023. doi: 10.5694/mja2.52056

¹⁹ Australian Institute of Health and Welfare. Aboriginal and Torres Strait Islander Health Performance Framework. 1.12 HIV/AIDS, hepatitis and sexually transmissible infections. Feb 15, 2023. Accessed Nov 20, 2023. <https://www.indigenoushpf.gov.au/measures/1-12-hiv-aids-hepatitis-sex-transmissible-infect>

²⁰ Townsville Public Health Unit. Public health alerts: APSGN, measles, pertussis, shortage of Bicillin LA. Nov 13, 2023. Accessed Nov 20, 2023. <https://nqphn.com.au/index.php/news/public-health-alerts-apsgn-measles-pertussis-shortage-bicillin-lar>

²¹ National Aboriginal Community Controlled Health Organisation. Shortages of medicines in Australia. Aug 12, 2021. Accessed Nov 20, 2023. <https://www.naccho.org.au/shortages-of-medicines-in-australia/>

²² Therapeutic Goods Administration. Prescribe an unapproved therapeutic good (health practitioners). Canberra. Accessed Nov 20, 2023. <https://www.tga.gov.au/products/prescribe-unapproved-therapeutic-good-health-practitioners>

Serious Scarcity Substitution Instruments (SSSIs)

In the event of serious medication shortages, community pharmacists can substitute specific medicines with another dosage form or strength of the same medicine, without prior approval from the prescriber. This relies on the availability of an alternate formulation of the same product. This legislative instrument remains in effect until a specific date, or when the 'scarce medicine' is no longer scarce²³. During the shortage of the antibiotic phenoxymethylpenicillin in 2023, the TGA made a SSSI declaring phenoxymethylpenicillin oral liquid and suspension products as scarce medicines, and allowed pharmacists to offer patients²⁴:

- an alternative phenoxymethylpenicillin oral liquid or suspension product when the prescribed one is unavailable
- phenoxymethylpenicillin 250mg capsules or 250mg tablets where the prescribed dose is divisible by 250 mg.

In certain circumstances, a PBS subsidy can be allocated to the substitution medicine. This subsidy is determined by the Minister for Health for each SSSI that is issued by the TGA²⁵.

National Medical Stockpile

The National Medical Stockpile is a strategic reserve of supplies, including medicines, vaccines, personal protective equipment (PPE), for national health emergencies and supplements the stock held by state and territory health authorities²⁶. The supply of products is only when commercial supply is unavailable and there is a demonstrated need for its use. For security reasons, details about the content of the stockpile are not released publicly²⁶.

Minimum Stockholding Requirements

From 1 July 2023, the amendments to the National Health Act 1953 took effect and imposed requirements for 'Responsible Persons' to keep four or six months of 'usual demand' stock in Australia for 'designated brands'. These medications must meet certain criteria but are generally the mainstay of treatment for some of the most prevalent health conditions in Australia²⁷. While these measures cannot prevent shortages at a manufacturing level, they can support Australian manufacturers to continue supply of essential medications when global shortages occur for a sufficient time until stock is available again.

Pfizer's benzathine benzylpenicillin (Bicillin LA) was not listed on the 'designated brands list' on 1st October 2023 but is projected to be added and will be subject to a 6-month supply stockholding requirement from 1st April 2025²⁸. This means Pfizer will be required to hold a 6-month supply of Bicillin LA, physically located onshore in Australia. This

²³ Therapeutic Goods Administration. Serious Scarcity Substitution Instruments (SSSIs). Canberra. Sept 29, 2023. Accessed Nov 20, 2023.

<https://www.tga.gov.au/resources/resource/guidance/serious-scarcity-substitution-instruments-sssis>

²⁴ Therapeutic Goods Administration. Substitution allowed to address shortage of phenoxymethylpenicillin. Canberra. Apr 14, 2023. Accessed Nov 20, 2023. <https://www.tga.gov.au/safety/shortages/medicine-shortage-alerts/substitution-allowed-address-shortage-phenoxymethylpenicillin>

²⁵ The Pharmaceutical Benefits Scheme. PBS subsidy for medicines subject to a Serious Scarcity Substitution Instrument FAQs. Canberra. Nov 2, 2023. Accessed Nov 20, 2023. <https://www.pbs.gov.au/files/serious-shortage-medicine-substitution-files/PBS-subsidy-for-medicines-subject-to-a-Serious-Scarcity-Substitution-Instrument-FAQ.pdf>

²⁶ Australian Government Department of Health and Aged Care. National Medical Stockpile. Canberra. Jun 2, 2023. Accessed Nov 20, 2023.

<https://www.health.gov.au/our-work/national-medical-stockpile>

²⁷ The Pharmaceutical Benefits Scheme. Minimum stockholding guidelines. Canberra. Oct 21, 2022. Accessed Nov 20, 2023.

<https://www.pbs.gov.au/industry/pricing/medicines-supply-security-guarantee/Pharmaceutical-Benefits-Scheme-Minimum-Stockholding-Guidelines-published-21-Oct-2022.pdf>

²⁸ The Pharmaceutical Benefits Scheme. Designated brands. Canberra. Oct 1, 2023. Accessed Nov 20, 2023.

<https://www.pbs.gov.au/info/industry/pricing/designated-brands>

would enable continued use of stock within Australia during further international shortages, allowing more time for the supply disruption to resolve or to identify alternative sources of supply.

Access to medications for priority populations during medication shortages

There are currently no mechanisms for prioritising access to medications during a shortage to priority populations, including for Aboriginal and Torres Strait Islander people.

Redistribution of essential medicines and health supplies has been used in other countries to mitigate overstocking, wastage and stockouts by moving unused stock to locations where it is required²⁹. Stakeholders at multiple levels, from primary care to the national level, could collaborate to implement efficient and real-time inventory management surveillance tools to aid in the redistribution of essential medications. A real-time surveillance tool could assist in the effective channelling of excess stock or soon-to-expire medicines to health services with high consumption rates of the product or high prevalence rates of the specific treatable condition.

Conclusion

Medication shortages can have drastic implications on patients with suboptimal treatment and delays to treatment with clinical complications. Rural and remote communities in Queensland face even more challenges with long distances to transport stock, with potential for compromise to cold chain.

While QAIHC welcomes the addition of Bicillin LA to the designated brands list for minimum stockholding requirements, there needs to be strategies to improve stability of supply and procurement of essential medicines in Australia, as well as prioritizing access to medications for priority populations.

Recommendations

1. **QAIHC recommends** the TGA explore secondary suppliers for medications that lack alternatives, are difficult to manufacture, and prevent severe adverse health outcomes particularly for priority populations such as Bicillin LA for Aboriginal and Torres Strait Islander people.
2. **QAIHC recommends** the federal and State health authorities create and formalise the process for redistribution of essential medications to priority populations/areas during medication shortages (e.g. Bicillin LA secured for use, and distributed to Aboriginal community-controlled health organisations)³⁰.
3. **QAIHC recommends** the TGA expands on the national medicine shortage reports database to include investigation into substitutes for medicines in short supply. Investigation of the substitute medication should include ingredients, method of administration, labelling, storage information, transport requirements and comparison to the original product to reduce the need for individual prescribers to carry out this work themselves³¹.

²⁹ Mabizela S, Nakambale HN, Bangalee V. Predictors of medicine redistribution at public healthcare facilities in King Cetshwayo District, KwaZulu-Natal, South Africa. BMC Health Services Research. Oct 17, 2023;23 (1108). doi: 10.1186/s12913-023-10096-4.

³⁰ Shuka S, Zahoor F, Hayat K, Saeed A, Gillani AH, Omer S et al. Drug shortage: causes, impact, and mitigation strategies. Front Pharmacol. 2021;12:693426. doi: 10.3389/fphar.2021.693426.

³¹ Ryan MJ. Medicine shortages: there are solutions! Actions to take to reduce medicine shortages. Aust Health Rev. 2021 Aug;45(4):504-506. doi: 10.1071/AH20306.