NSW Health

UPDATED: Disruption to supply – Gentamicin (Pfizer®) 80 mg/2 mL (as sulfate) injection BP ampoule

SAFETY NOTICE 003/25

Issue date:	06 February 2025
Content reviewed by:	Medication Safety Expert Advisory Committee (MSEAC) Antimicrobial Stewardship Expert Advisory Committee (AMSEAC) Medication Shortage Assessment and Management team (MSAM) Infection Prevention and Control (IPAC) and Healthcare Associated Infections (HAI) Program
Distributed to:	Chief Executives; Directors of Clinical Governance; Director, Regulation and Compliance Unit
KEY MESSAGE:	NSW Health facilities are informed of the ongoing disruptions to the supply of gentamicin (Pfizer®) 80 mg/2 mL (as sulfate) injection BP ampoule and safety considerations associated with available alternatives.
ACTION REQUIRED BY:	Chief Executives, Directors of Clinical Governance
REQUIRED ACTION:	1. Distribute this Safety Notice to all relevant clinicians and clinical departments where gentamicin 80 mg/2 mL injection ampoules are held, prescribed, and administered, and include this Safety Notice in relevant handovers and safety huddles. 2. Ensure a system is in place to document actions taken in response to this Safety Notice. 3. Report any incidents associated with this disruption to supply into the local incident management system e.g., ims+.
We recommend you also inform:	Directors, Managers and Staff of: • Infectious Disease and Microbiology Departments • Respiratory, Surgical, Anaesthetics, Paediatric and Emergency Departments • Pharmacy Services • Nursing/Midwifery Services • Medical Services Drug and Therapeutics Committees All other relevant clinicians, departments and committees.
Website:	https://www.health.nsw.gov.au/sabs/Pages/default.aspx http://internal.health.nsw.gov.au/quality/sabs/index.html
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What is updated in the Safety Notice from SN: 027/24?

This Safety Notice replaces SN: 027/24 *UPDATED Disruption to supply – Gentamicin (Pfizer®) 80 mg/2 mL (as sulfate) injection BP ampoule*, which has now been rescinded. This Safety Notice has updated advice surrounding:

- information regarding disruptions to supply of Australian registered products
- the availability of an additional international alternative under Section 19A (S19A) of the *Therapeutic Goods Act 1989.*

Situation

There is an ongoing disruption to the supply of gentamicin (Pfizer®) 80 mg/2 mL (as sulfate) injection BP ampoules (ARTG 11376) until June 2025 due to manufacturing issues. Refer to the Therapeutic Goods Administration (TGA) Medicine shortage reports database for the most up-to-date information about supply impact dates.

The alternative Australian registered product gentamicin (Noridem®) 80 mg/2 mL (as sulfate) solution for injection ampoule (ARTG 391250) is presented in a glass ampoule, and contains an additional excipient, **sodium metabisulfite**. Supply of the Noridem product is currently constrained due to unexpected increases in consumer demand.

ORSPEC Pharma have received approval under Section 19A (S19A) of the *Therapeutic Goods Act 1989* to import supply of:

- gentamicin 80 mg/2 mL (HEXAL) SF ampoules from Germany until 30 April 2025
- gentamicin 40 mg/mL (80 mg in 2 mL) (Amdipharm) solution for injection ampoules from the United Kingdom until 30 June 2025.

The S19A alternatives differ in presentation and excipients to the Australian registered products. Refer to **Table 1** for a comparison of Australian registered gentamicin and international alternatives.

NSW Health staff are advised to check the TGA website for updates regarding further changes to supply dates and the TGA S19A approvals database for updates on S19A alternatives.

Background

Gentamicin is an aminoglycoside antibiotic widely used for:

- Short-term empiric therapy of serious Gram-negative infections; normally limited to less than 48 hours, and then changed to an alternative antibiotic based on culture results.
- Surgical prophylaxis.
- Directed therapy against confirmed sensitive pathogens, resistant to antibiotics more appropriate for longer term use.

Gentamicin is listed on the **NSW Medicines Formulary** with a restriction for use in accordance with the local antimicrobial stewardship policy.

Assessment

When selecting an alternative gentamicin product, the following safety issues should be considered:

1. Safe administration of alternatives presented in glass ampoules

The Institute for Safe Medication Practices (ISMP) recommends the use of a filter needle when withdrawing intravenous medications from a glass ampoule (See ISMP Safe Practice Guidelines for Adult IV Push Medications). Therefore, a filter needle or an in-line filter (if administering via intravenous infusion) should be considered when preparing the Noridem and S19A products for administration. The local Drug and Therapeutics Committee (DTC) should consider this recommendation upon introduction of these alternatives, noting that when administering high doses of gentamicin, the risk for contamination with glass particulate is increased due to the number of ampoules required to prepare a dose (for example, 600 mg dose requires 8 ampoules).

There is a lack of consensus regarding the size of filter required, however literature suggests that filters with a pore size of 5 microns or smaller are effective in removing larger particles. Please refer to '*References*' for further information surrounding filters.

2. Presence of excipients

The Noridem product contains an additional excipient, **sodium metabisulfite** and the Hexal S19A alternative contains **acetylcysteine**. Both excipients are commonly used in pharmaceuticals as antioxidants. However, their presence should be considered prior to administration as:

a. Sodium metabisulfite, though not considered a preservative in the concentration that is present within the Noridem product, can potentially trigger allergic reactions in individuals with sulfite sensitivity. This can cause adverse reactions such as asthma symptoms including wheezing, chest tightness and coughing and allergy like reactions including hay fever and hives. In rare cases, anaphylaxis may occur. For more information on sulfite sensitivity, refer to the Australasian Society of Clinical Immunology and Allergy – Sulfite Sensitivity Frequently Asked Questions (FAQ). Allergy status must be taken into consideration prior to administration. The Noridem product should be used with caution in neonates and paediatric patients where allergy status has not been established.

b. Acetylcysteine containing products should be used with caution in patients with asthma due to the potential risk of bronchospasm.

3. Approved routes of administration

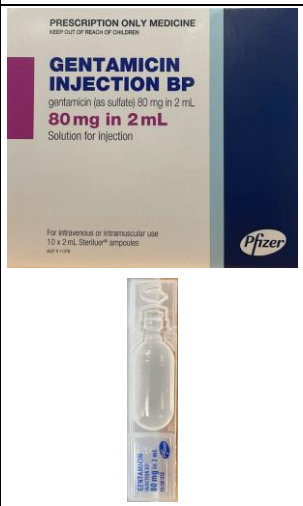
Australian registered gentamicin products have been approved for administration via the intravenous (IV) and intramuscular (IM) routes. Alternative routes of administration are considered **off-label**.

An example of an off-label indication is the administration of gentamicin via inhalation for the treatment of chronic pulmonary infections. The presence of excipients in available alternatives may preclude use via this route due to the risk of airway irritation associated with sodium metabisulfite and acetylcysteine. Tobramycin, an alternate aminoglycoside, is available and certain brands are approved for administration via inhalation. Supply of tobramycin (Sun) 300 mg/5 mL solution for inhalation ampoule remains available.

Recommendations

- Develop a local plan to manage the disruptions to supply that includes (but is not limited to):
  - evaluation of local stock holdings, historical usage, local protocols to determine clinical indication(s)
  - identification of the most suitable alternative option(s) based on local usage, clinical needs and the lead time/availability of the S19A alternatives
  - ensure back orders are in place with regular wholesalers/ORSPEC Pharma to ensure supply is received when it is available.
- Where possible, avoid the use of multiple presentations of gentamicin concurrently to avoid confusion.
- Ensure clinicians are made aware of the differences in presentation between the Pfizer, Noridem and S19A products, including additional excipients, and allergy risk (specific to Noridem product in individuals with sulfite sensitivity). Consider use of alerts or reference information within the electronic Medication Management (eMM) system where appropriate. Note that some eMM systems may list the allergy as 'sul**ph**ite'.
- For those patients where use of the Noridem or S19A products are unsuitable or contraindicated, expert advice should be sought from Infectious Diseases/Microbiology regarding possible alternatives. For example, tobramycin can be substituted for gentamicin at the same doses for most indications. Supply of tobramycin 80 mg/2 mL ampoules remain available.
- A filter needle is recommended when withdrawing gentamicin from a glass ampoule or an in-line filter is recommended if administering via intravenous infusion. The local DTC should consider this recommendation upon introduction of the alternative products and, if deemed necessary, ensure filter needles are readily available in treatment areas where gentamicin is administered.
- Utilise tobramycin products approved for administration via inhalation (for example, tobramycin (Sun) 300 mg/5 mL) in patients where nebulised doses of aminoglycosides are indicated.
- Local DTC approval is required when administering gentamicin via alternative routes of administration that are considered off-label. Important considerations prior to approval include the presence of excipients in available alternatives (such as sodium metabisulfite and acetylcysteine).
- Regularly review prescriptions for gentamicin and assess ongoing need for use, in accordance with local antimicrobial stewardship policy.

Table 1: Comparison of Australian registered gentamicin and international alternatives.

	Gentamicin (Pfizer) (ARTG 11376)	Gentamicin (Noridem) (ARTG 391250)	Gentamicin (HEXAL) Section 19A	Gentamicin (Amdipharm) Section 19A
Country of registration	Australia	Australia	Germany	United Kingdom
Active ingredient	Gentamicin (as sulfate) 80 mg/2 mL	Gentamicin (as sulfate) 80 mg/2 mL	Gentamicin (as sulfate) 80 mg/2 mL	Gentamicin (as sulfate) 40 mg/mL (80 mg/2 mL)
Presentation	Steriluer® (plastic ampoule)	Glass ampoule	Glass ampoule	Glass ampoule
Pack size	10 x steriluer 50 x steriluer	50 x ampoule	5 x ampoule 10 x ampoule 20 x ampoule	10 x ampoule
Excipients	Disodium edetate Water for injections Sodium hydroxide Sulfuric acid	Disodium edetate **Sodium metabisulfite (3.2 mg in a 2 mL vial)** Water for injections Sodium hydroxide Sulfuric acid	**Acetylcysteine (5 mg per mL)** Disodium edetate Sodium hydroxide Water for injections	Water for injection Sulfuric acid
Storage requirements *When diluted*	Below 25°C Use immediately	Below 25°C Use immediately – as per NSW Health Infection Prevention and Control in Healthcare Settings Policy Directive (PD2023_025)	Below 25°C Use immediately – as per NSW Health Infection Prevention and Control in Healthcare Settings Policy Directive (PD2023_025)	Below 25°C Use immediately
Labelling	English	English	German	English
Product image				

References

- Acedemie Nationale de Pharmacie, (2017) '*Particulate contamination associated with the manipulation of drugs in glass ampules: A literature review*' access here.
- *Australian Medical Student Journal*, (2015) 'Glass micro-particulate contamination of intravenous drugs – should we be using filter needles?' access here.
- *International Journal for Quality in Health Care,* (2021), 'Safety concerns with glass particle contamination: improving the standard guidelines for preparing medication injections' access here.
- SpringerPlus 5, (2016) '*The effect of different methods of intravenous injection on glass particle contamination from ampules*' access here.