NSW Health

UPDATED: Disruption to supply: Heparin sodium (Pfizer®) 5,000 units/5 mL injection ampoule

SAFETY NOTICE 026/24

Issue date:	2 October 2024
Replaces:	SN:004/24
Content reviewed by:	Medication Safety Expert Advisory Committee Medicine Shortage Assessment and Management Team
Distributed to:	Chief Executives; Directors of Clinical Governance; Director, Regulation and Compliance Unit
KEY MESSAGE:	NSW Health facilities are informed of the disruption to the supply of heparin sodium (Pfizer) 5,000 units/5 mL injection ampoule, availability of international alternatives and associated safety considerations.
ACTION REQUIRED BY:	Clinicians
REQUIRED ACTION:	1. Distribute this **updated** Safety Notice to all relevant clinicians and clinical departments where heparin sodium (Pfizer) 5,000 units/5 mL injection 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 below recommendation 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 local incident management system e.g., ims⁺. 5. Confirm receipt and distribution of this Safety Notice within **72 hours** to: CEC-MedicationSafety@health.nsw.gov.au.
DEADLINE:	COB 8 October 2024
We recommend you also inform:	Directors, Managers and Staff of: • Intensive Care Units • Emergency Departments • Cardiology • Haematology • Dialysis Units • Pharmacy Services • Nursing/Midwifery • Medical Services • Digital Health/ICT 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
Review date:	March 2025

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What is updated in this Safety notice from SN:004/24?

This Safety Notice replaces SN:004/24 *Disruption to supply: Heparin sodium (Pfizer) 5,000 units/5 mL injection ampoule* which has now been rescinded. The Safety Notice has been updated to include information on the availability of an additional international alternative **heparin sodium (1,000 I.U./mL) 10,000 units in 10 mL** multi-dose product under Section 19A (S19A) of the *Therapeutic Goods Act 1989* and associated safety considerations. Comparative information is now all included within Table 1 in the *Assessment* section.

Situation

The Australian registered medicine heparin sodium (Pfizer) 5,000 units/5 mL injection (AUST R: 49232) is currently in short supply due to manufacturing issues until June 2025.

Alternative international products from the United Kingdom (UK) and United States of America (USA) have been approved for supply under S19A of the *Therapeutic Goods Act 1989*. The S19A alternatives differ from the Australian registered product in overall volume, presentation, route of administration and storage requirements. Two of the S19A alternatives **contain preservatives**.

At the time of publication, Pfizer have confirmed that supply of heparin 5,000 units/0.2 mL and 5,000 units/1 mL continue to be available.

Background

- Heparin is a parenteral anticoagulant used for several indications including treatment and prevention of venous and arterial thromboembolic disease, treatment of acute coronary syndromes, atrial fibrillation, and prosthetic heart valves.
- Heparin (Pfizer) 5,000 units/5 mL is the recommended product for administration of intravenous bolus doses as per the CEC Intravenous Unfractionated Heparin Recommended Standard.
- Heparin has a narrow therapeutic index, and over- or under- anticoagulation can result in significant adverse patient outcomes.
- As heparin is classed a high-risk medicine, an Anticoagulant Standard exists as part of the NSW Health *High-Risk Medicines Management* Policy Directive (PD2024_006).

Assessment

Table 1 outlines the differences of the international alternatives that have been approved for supply under S19A of the *Therapeutic Goods Act 1989* compared to the Australian registered product, and includes important safety considerations to note. All 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.

Clinicians should determine the suitability of the S19A alternatives prior to prescribing, dispensing, or administration to a patient.

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Table 1. Comparison between Australian registered and S19A alternative heparin sodium products.

	Australian registered product	S19A alternatives		
Product	**Heparin sodium (Pfizer) 5,000 units/5 mL (porcine mucous) injection ampoule**	**Heparin sodium (Wockhardt) 5,000 units in 5 mL solution for injection or concentrate for solution for infusion**	**Heparin sodium (Wockhardt) 5,000 units in 5 mL solution for injection or concentrate for solution for infusion**	**Heparin sodium (Hospira) 10,000 units in 10 mL solution for intravenous and subcutaneous use**
Supplier	Pfizer	Orspec – S19A approval expiry 30 November 2024	Orspec – S19A approval expiry 30 June 2025	Pfizer – S19A approval expiry 30 November 2024
Strength and volume	5,000 units in 5 mL	5,000 units in 5 mL	5,000 units in 5 mL	**10,000 units in 10 mL**
	Important safety consideration: The Hospira S19A product is the same concentration (1,000 units/1 mL) however **differs** in total volume (10 mL) which must be taken into consideration when administering the product.			
Excipients	• Water for injection	• **Benzyl alcohol (preservative)** • **Methyl parahydroxybenzoate (preservative)** • Water for injections • Sodium hydroxide solution • Hydrochloric acid	• Water for injections • Sodium hydroxide solution • Hydrochloric acid	• Sodium chloride • **Benzyl alcohol (preservative)** • Sodium hydroxide • Hydrochloric acid • Water for injections
	Important safety consideration: Products containing preservatives such as benzyl alcohol and methyl parahydroxybenzoate must not be administered in pregnancy[1], to premature babies or neonates and may require a review based on duration of use in other patient groups (see European Medicines Agency leaflet for further information).			

Table 1 (cont.): Comparison between Australian registered and S19A alternative heparin sodium products

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Routes of administration	• Intermittent intravenous injection • Intravenous infusion • Deep subcutaneous injection	• Continuous intravenous infusion • Intermittent intravenous injection	• Continuous intravenous infusion • Intermittent intravenous injection	• Continuous intravenous infusion • Intermittent intravenous injection • Deep subcutaneous injection
	Important safety consideration: The Wockhardt S19A alternative products from the UK are not registered for deep subcutaneous injection like the ARTG listed (Pfizer) product.			
Presentation	• 5 mL steriluer ampoule (single use) • Packs of 10 or 50 ampoules	• 5 mL multi-dose neutral glass vial • Packs of 10 vials	• 5 mL glass ampoule (single use) • Packs of 10 ampoules	• 10 mL glass vial • Packs of 25 vials
	Important safety considerations: • Multi-dose presentations must be restricted for single use within NSW Health and any remaining product discarded immediately after use in accordance with the NSW Health *Medication Handling* Policy Directive (PD2022_032) and NSW Health *Infection Prevention and Control in Health Care Settings* Policy Directive (PD2023_025). • As the S19A products are presented in a glass vial/ampoule, they may not be suitable for use in patients receiving at home care (for example, dialysis patients).			
Storage requirements	Store below 25°C	Do not store above 25°C	Do not store above 25°C	Store between 20°C and 25°C

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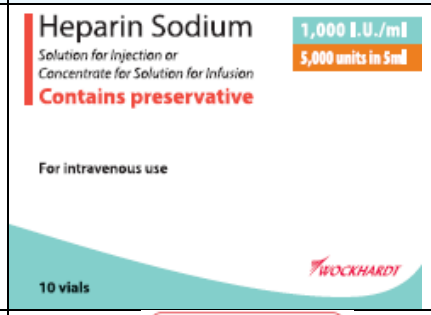
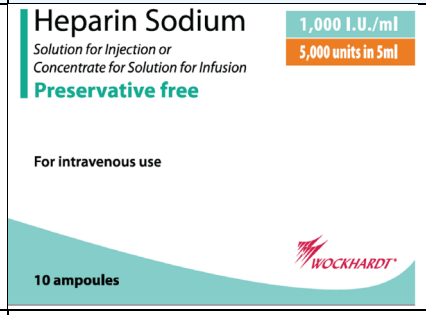
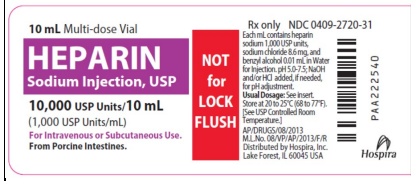
Outer packaging appearance/ artwork				
Single item appearance/ artwork				

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Recommendations

- Assess the current status and availability of heparin 5,000 units/5 mL in each facility, ensuring all locations of stock are identified.
- Develop a local plan to manage the supply shortage that includes (but is not limited to); assessing local stock holdings, historical stock usage, ability to obtain alternative supply, and ongoing clinical needs. Sites should consider the lead time required for processing the S19A alternative and proactively place orders.
- Reserve remaining supply of Australian registered heparin 5,000 units/5 mL and the preservative free S19A alternative for patients whereby the S19A alternatives containing preservatives are not appropriate, or for those receiving at-home care (e.g., dialysis patients). Where the S19A alternatives are available, ensure suitability for use with consideration of the contraindications/precautions outlined above.
- Ensure vials of the S19A alternatives containing preservatives are restricted to single use.
- If using the Hospira S19A 10,000 units/10 mL alternative:
    - Ensure clinicians are aware of the difference in total overall volume (10 mL) compared to the Australian product (5 mL).
    - Only withdraw the required volume for the dose. For example, withdraw 5 mL if 5,000 units is intended to be administered and **discard** the remaining product.
- In the absence of the Australian registered product or where the S19A alternatives are unavailable/contraindicated, clinicians wishing to prepare a heparin 5,000 units/5 mL (1,000 units/1 mL) preparation can do so using alternative products (see **Table 2**).

Table 2. Preparation instructions to achieve required concentration of 5,000 units/5 mL (1,000 units /1 mL)

Alternate Australian registered product	Preparation to achieve required concentration of 5,000 units/5 mL (1,000 units/1mL)
Heparin 5,000 units/0.2 mL	Dilute with 4.8 mL of sodium chloride 0.9% Use solution immediately after dilution
Heparin 5,000 units/1 mL	Dilute with 4 mL of sodium chloride 0.9% Use solution immediately after dilution

- Extra caution should be taken to avoid confusion between the different heparin preparations available as alternative products may differ from local clinical protocols.
- Patients receiving heparin should be closely monitored for signs and symptoms of sub- or supra-therapeutic dosing. Laboratory testing (for example, aPTT levels) should be continued as per local protocols and evidence-based references.
- In accordance with NSW Health *High-Risk Medicines Management* Policy Directive (PD2024_006) and the NSW Health *Medication Handling* Policy Directive (PD2022_032), clinicians are reminded that an independent second person check should be undertaken prior to the preparation and administration of heparin.
- Consider the need to update configurations (for example, order sentences and product catalogues) within Electronic Medication Management (eMM) systems where required to reflect change in products based on local availability.

References

1. Hull RD, Garcia, DA., Burnett, AE., Heparin and LMW heparin: Dosing and adverse effects. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2023.

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