Safety Notice 004/24

Issue date
4 April 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:
- Intensive Care Units
- Emergency Departments
- Cardiology
- Haematology
- Dialysis Units
- Medical
- Nursing/Midwifery
- Pharmacy Services

Drug & Therapeutics Committees
All other relevant clinicians and clinical departments where these products are prescribed, stored, and administered

Expert Reference Group Content reviewed by:
Medicine Shortage Assessment and Management Team
Medication Safety Expert Advisory Committee

Clinical Excellence Commission
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Review date
September 2024

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

What's new in this Safety Notice?

This Safety Notice replaces SN:009/23 and includes updated information regarding the dates of impact to supply and a new TGA-approved Section 19A (S19A) alternative.

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 2024.

Alternative products from the United Kingdom (UK) have been approved for supply under S19A of the Therapeutic Goods Act until 30 April 2024 (subject to change). The S19A alternative products differ in presentation and contain additional excipients. One of the S19A alternatives **contains preservatives**. 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.

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 Policy Directive *High-Risk Medicines Management* PD2024_006.
- Orspec Pharma has received approval under S19A of the Therapeutic Goods Act to import supply of heparin sodium (Wockhardt) (1,000 I.U./mL) 5,000 units in 5 mL solution for injection or concentrate for infusion (contains preservatives) and heparin sodium (Wockhardt) (1,000 I.U./mL) 5,000 units in 5 mL solution for injection or concentrate for infusion (no preservatives) from the UK until 30 April 2024.

Assessment

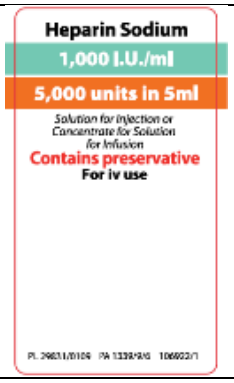
The S19A alternatives from the UK differ from the Australian Registered product in presentation, routes of administration, storage requirements and excipients (see Table 1 for comparison).

Both S19A alternatives are similar in appearance however, one of the S19A products contains the preservatives benzyl alcohol and methyl parahydroxybenzoate, while the other S19A product is preservative free. Clinicians should determine the suitability of the product prior to prescribing, dispensing, or administering it to the patient. The S19A alternative with preservatives **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).

The S19A alternative with preservatives is presented in a multi-dose glass vial. Despite the Product Information stating the product is 'multi-dose', it must be restricted for single use within NSW Health and any remaining product discarded immediately after use (in accordance with the *Medication Handling* Policy Directive PD2022_032 and *Infection Prevention and Control in Health Care Settings* Policy Directive PD2023_025). As the product is presented in a glass vial, it may not be suitable for use in patients receiving at home care (e.g., dialysis patients).

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

Table 1. Comparison between Australian registered and S19A alternative heparin sodium 5,000 units/5 mL products

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 (contains preservative)	Heparin sodium (Wockhardt) 5,000 units in 5 mL solution for injection or concentrate for solution for infusion (preservative free)
Active ingredient	• 5,000 units in 5 mL	• 1,000 I.U./mL (5,000 units in 5 mL)	• 1,000 I.U./mL (5,000 units in 5 mL)
Excipients	• Water for injection	• Benzyl alcohol • Methyl parahydroxybenzoate • Water for injections • Sodium hydroxide solution • Hydrochloric acid	• Water for injections • Sodium hydroxide solution • Hydrochloric acid
Routes of administration	• Intermittent intravenous injection • Intravenous infusion • Deep subcutaneous injection	• Continuous intravenous infusion • Intermittent intravenous injection	• Continuous intravenous infusion • Intermittent intravenous injection
Presentation	• 5 mL steriluer ampoule • Packs of 10 or 50 ampoules	• 5 mL multi-dose neutral glass vial • Packs of 10 vials	• 5 mL glass ampoule • Packs of 10 ampoules
Outer packaging appearance/ artwork			
Single item appearance/ artwork			
Storage requirements	• Store below 25°C • Single use only – discard unused portion	• Do not store above 25°C	• Do not store above 25°C
Additional information	• Single use only	• Multidose vial – must be restricted to single use within NSW Health. • Contains preservatives	• Single use only

Clinical 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 in whom the S19A alternative containing preservatives is not appropriate, or for those receiving at-home care (e.g., dialysis patients). Where the S19A alternatives are available, ensure suitability for use considering the contraindications/precautions outlined above.
- Ensure vials of the S19A alternative containing preservatives are restricted to single use.
- 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 (e.g., aPTT levels) should be continued as per local protocols and evidence-based references.
- In accordance with NSW Health Policy Directive *High-Risk Medicines Management* PD2024_006 and the NSW Health Policy Directive *Medication Handling* PD2022_032, clinicians are reminded that a second person check should be undertaken prior to the preparation and administration of heparin.

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

Required actions for the Local Health Districts/Networks

1. Distribute this updated Safety Notice to all relevant clinicians and clinical departments where heparin 5,000 unit/5 mL 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 above recommendations 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.