Safety Notice 009/23

Issue date
27 April 2023

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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Email
Internet
Intranet

Review date
September 2023

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:008/23 and includes information surrounding a TGA-approved Section 19A 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.

An alternative product from the United Kingdom (UK) has been approved for supply under Section 19A (S19A) of the Therapeutic Goods Act until 31 August 2023. The S19A alternative product differs in presentation and contains several clinically significant excipients, including preservatives.

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* PD2020_045.
- 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, an alternative agent from the UK until 31 August 2023.

Assessment

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

The S19A product contains the preservatives benzyl alcohol and methyl parahydroxybenzoate. Clinicians should determine the suitability of the product prior to prescribing, dispensing, or administering the product to the patient. It **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 product 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 Policy Directive PD2017_013). 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.

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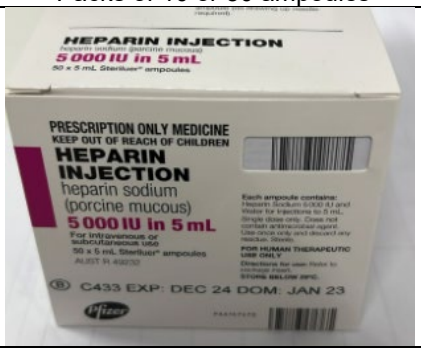
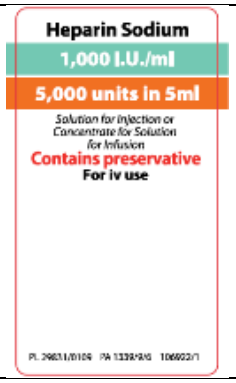
Table 1. Comparison between Australian registered and S19A alternative heparin sodium 5,000 units/5 mL

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 solution for infusion
Active ingredient	• 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
Routes of administration	• Intermittent intravenous injection • Intravenous infusion • Deep subcutaneous 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
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
Additional information	• Single use only	• Multidose vial – **must be restricted to single use within NSW Health**. • Contains preservatives

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 S19A alternative and proactively place orders.
- Reserve remaining supply of Australian registered heparin 5,000 units/5 mL for patients in whom the S19A alternative is not appropriate or those receiving at-home care (e.g., dialysis patients).

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- Where the S19A alternative is available, ensure suitability for use considering the contraindications/precautions outlined above.
- Ensure vials of the S19A alternative are restricted to single use.
- In the absence of the Australian registered product or where the S19A alternative is 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* PD2020_045 and the Medication Handling Policy Directive 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.