Issue date
1 December 2022

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:

- Medical
- Pharmacy
- Nursing
- Mental Health
- Emergency
- Aged Care
- Anaesthetics
- Drug and Therapeutics committees

Other relevant staff and committees

Expert Reference Group

Content reviewed by:

- Medication Safety Expert Advisory Committee
- ACI Mental Health Network
- eHealth Clinical Engagement and Patient Safety

Clinical Excellence Commission
Email
Internet Website
Intranet Website

Review date
December 2024

Newly registered Australian product: Risks associated with lorazepam 4 mg/1 mL solution for injection

Situation

Lorazepam SXP® **4 mg/1 mL** was added to the Australian Register of Therapeutic Goods (ARTG) on 31 March 2022. This product contains **double** the concentration of previous lorazepam solution for injection available via the TGA's Special Access Scheme (SAS), and has different dilution requirements. These differences pose a significant potential for error.

Background

Parenteral lorazepam is a highly potent benzodiazepine used for the treatment of acute anxiety states and agitation in adult and older populations, and the control of status epilepticus in adults, adolescents, and children. It is also used in pre-operative settings and as pre-medication for prolonged investigations in adult and older populations. Parenteral lorazepam is listed on the NSW Medicines Formulary with the following restriction for use – "*in accordance with local DTC approved protocols*".

Prior to the ARTG listing of Lorazepam SXP® (Southern Cross Pharmaceuticals) **4 mg/1 mL** solution for injection, parenteral lorazepam was only available via the TGA's Special Access Scheme (SAS). The international SAS product available in Australia is lorazepam **2 mg/1 mL** (West Ward Pharmaceuticals).

Figure 1: SAS lorazepam 2 mg/mL

Figure 2: ARTG listed Lorazepam SXP 4 mg/1 mL

Important considerations

The Product Information for Lorazepam SXP notes that the solution for injection is slightly viscid when cool. **Dilution** of lorazepam injection with sodium chloride 0.9% or sterile water for injection is:

- **required** for intravenous (IV) administration
- **recommended** for intramuscular (IM) administration.

The 1 mL lorazepam solution is presented in a 2 mL ampoule to facilitate this dilution.

Clinicians must be mindful that **once diluted**, the final concentration of the ampoule becomes **2 mg/mL.** Incorrect calculation of dosing and administration can lead to unintentional overdose and the potential for serious adverse effects, including significant sedation and respiratory arrest.

The differences in concentration and dilution requirements between the Australian and SAS lorazepam products may also impact the way parenteral lorazepam is built in eMM systems. Care must be taken to minimise clinician confusion surrounding dilution requirements, and volume of the medicine required to achieve the desired dose.

Table 1: Summary of differences between SAS product and Australian listed SXP product

		SAS product	Australian SXP Product
Presentation		2 mg/1 mL vial Pack of 25 vials	4 mg/1 mL solution in 2 mL ampoule Pack of 5 ampoules
Storage		2-8ºC	2-8ºC
Protect from light		Yes	Yes
IV ADMINISRATION	**Dilution required**	**YES** – must be diluted with an equal volume of a compatible solution	**YES –** must be diluted with an equal volume of 0.9% sodium chloride or sterile water for injection
	Concentration after dilution	**1 mg/1 mL**	**2 mg/1 mL**
	Volume required to administer 1 mg dose	1 mL once diluted	0.5 mL once diluted
IM ADMINSTRATION	**Dilution required**	No	Recommended dilution with 0.9% sodium chloride or sterile water for injection
	Concentration after dilution	Not applicable – remains at 2 mg/1 mL	**2 mg/1 mL**
	Volume required to administer 1 mg dose	0.5 mL	0.5 mL once diluted

Recommendations for local governance committees

- Review stock holdings of the SAS product and develop a plan to changeover to the Australian registered product. **It is not recommended that both formulations are used concurrently.**
- Develop and deliver staff education and training in local areas/units that use parenteral lorazepam. Education should cover the differences between the SAS and ARTG (SXP) product, changeover procedures between these products, need for dilution and how this change impacts dosing, as well as any changes within eMM systems.
- Prior to changeover to the Australian registered product, liaise with local eMM teams to determine changes required in eMM systems to facilitate the safe prescribing and administration of parenteral lorazepam. Strategies may differ based on local configurations and the eMM system in use.
    - Particular attention should be taken to ensure that pre-populated volumes for administration are disabled for parenteral lorazepam due to the system's inability to factor in further dilution requirements. For example, in facilities with Cerner eMM systems this can be achieved by removing strength information for the new ARTG listed product in PharmNet.
    - Use of alerts or pre-populated comments on electronic orders for parenteral lorazepam. For example, in facilities with Cerner eMM systems the following order comment can be applied to parenteral lorazepam order sentences: *"CAUTION – may require dilution prior to administration".*
- Ensure flumazenil is available in clinical areas where parenteral lorazepam is utilised in case of overdose and ensure sufficient patient monitoring is in place. Given lorazepam's long half-life, repeated dosing may be required.
- Ensure the storage of parenteral lorazepam complies with PD2022_032 – Medication Handling (see Section 5.4.4). At the time of publication, no additional studies have been completed by the product sponsor to determine the stability of the product at room temperature. Dispose of any unused lorazepam solution safely in accordance with PD2022_032 – Medication Handling.

Required actions for the Local Health Districts/Networks

1. Distribute this Safety Notice to all relevant clinicians, clinical departments, and governance committees. Include this Safety Notice in relevant handovers and safety huddles.
2. Review current stock of parenteral lorazepam and plan for the transition by determining risk mitigation strategies to reduce under/overdosing of patients which incorporate the recommendations outlined in this Safety Notice.
3. Report any incidents associated with the use of parenteral lorazepam into the local incident management system (e.g., ims+).
4. Acknowledge receipt and distribution of this Safety Notice **within 72 hours** to CEC-MedicationSafety@health.nsw.gov.au.