NSW Health

# Disruption to supply: midazolam 5 mg/1 mL injection ampoules (multiple brands)

## SAFETY NOTICE 008/25

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| Issue date: | 15 April 2025 |
| Content reviewed by: | Medication Safety Expert Advisory Committee (MSEAC)<br>Medication Shortage Assessment and Management Team (MSAM) |
| 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 multiple brands of midazolam 5 mg/1 mL injection ampoules, availability of alternative Australian registered products (different strengths and/or concentrations), an international alternative, and associated safety considerations. |
| ACTION REQUIRED BY: | Chief Executives, Directors of Clinical Governance |
| REQUIRED ACTION: | 1. Distribute this Safety Notice to all relevant clinicians and clinical departments where midazolam 5 mg/1 mL injection is held, prescribed, and administered, and include this Safety Notice in relevant handovers and safety huddles.<br>2. Undertake a local risk assessment and incorporate the below recommendations to manage the disruption to supply.<br>3. Ensure a system is in place to document actions taken in response to this Safety Notice.<br>4. 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:<br>• Intensive Care Units<br>• Emergency Departments<br>• Cardiology<br>• Paediatrics<br>• Palliative care<br>• Pharmacy Services<br>• Nursing/Midwifery<br>• Medical Services<br>Drug and Therapeutics Committees<br>All other relevant clinicians, departments and committee |
| Website: | https://www.health.nsw.gov.au/sabs/Pages/default.aspx<br>http://internal.health.nsw.gov.au/quality/sabs/index.html |
| Review date: | November 2025 |

Contact: Clinical Excellence Commission
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# Disruption to supply: midazolam 5 mg/1 mL injection ampoules (multiple brands)

**SN:008/25**

## Situation

There are ongoing disruptions to the supply of all brands of Australian registered midazolam 5 mg/1 mL injection ampoules due to manufacturing issues and unexpected increases in consumer demand. The disruption to supply is expected to resolve in late May/early June 2025.

At the time of publication, supply of midazolam 5 mg/5 mL and 15 mg/3 mL injection ampoules remain available; however, supply may be intermittent due to increases in consumer demand.

Aborns Pharmaceuticals have received approval under Section 19A (S19A) of the *Therapeutic Goods Act 1989* to import supply of midazolam (Aguettant) 5 mg/mL injection ampoules from France until 30 June 2025. Supply is expected to arrive in late April/early May 2025. NSW Health staff are advised to check the Therapeutic Goods Administration (TGA) website for updates regarding further changes to supply and the TGA S19A approvals database for updates on potential S19A alternatives. Further alternatives may also be available via the TGA Special Access Scheme (SAS).

## Background

Midazolam is a short-acting benzodiazepine which is used for a number of indications including but not limited to:

- Use in anaesthetics including procedural sedation, induction of anaesthesia, sedation during ventilation and as a premedication.
- Adjunctive treatment for epilepsy refractory to other antiepileptic drugs, in particular absence and myoclonic seizures, and infantile spasms.
- Acute treatment of seizures, including status epilepticus.

Midazolam 5 mg/1 mL injection is typically administered via intravenous (IV) or intramuscularly (IM) routes and is listed on the NSW Medicines Formulary without restriction. It also has accepted uses via subcutaneous (subcut) route of administration for palliative care, and buccal and intranasal route for epilepsy management in paediatric patients.

## Assessment

There is potential for a complete disruption to the supply of midazolam 5 mg/1 mL injection ampoule products during late April 2025, prior to the S19A alternative arriving in Australia. The S19A alternative is identical in ingredient, active strength, and storage requirements, and is labelled in French and English (see table 1 for overview).

In the absence of the Australian registered products, or where the S19A or SAS alternatives are unavailable, clinicians can utilise alternative concentrations of midazolam injection ampoules including 5 mg/5 mL and 15 mg/3 mL formulations.

Clinicians are to determine the suitability of the alternative midazolam injection ampoule products prior to prescribing, dispensing or administration to a patient.

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## 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) for the affected strength.
    - Identification of the most suitable alternative option(s) based on local usage, clinical needs and accounts for the lead time/availability of the S19A alternative.
    - Ensuring back orders are placed for the 5 mg/1 mL injection ampoule product(s) with regular wholesalers enabling stock to be received as it becomes available.
- Reserve remaining supply of Australian registered midazolam 5 mg/1 mL injection products for:
    - Clinical scenarios or indications where smaller volumes (such as subcut administration for palliative care) or IM administration is required.
    - Reserve remaining supply of Pfizer branded **steriluer (plastic) ampoules** for paediatric populations requiring take-home packs for the management of paediatric epilepsy.
        - Please note, clinicians are to ensure formulations provided to at home care patients are not presented in glass ampoules/vials (unless absolutely necessary).
- If utilising an alternative midazolam concentration/volume where the 5 mg/1 mL injection ampoule product is usually used, consider the clinical indication(s), local protocols, and procedural steps associated with the use of midazolam.
- When using a 15 mg/3 mL midazolam injection ampoule product in the absence of the 5 mg/1 mL injection product:
    - Ensure clinicians are aware of the difference in total overall **volume** (3 mL vs. 1 mL) and the higher **total drug amount** (15 mg vs. 5 mg).
    - Withdraw only the required dose (for example, 1 mL for 5 mg) and discard the remaining volume.
- When using a 5 mg/5 mL midazolam injection ampoule product in the absence of the 5 mg/mL injection product:
    - Ensure clinicians are aware of the differences in **concentration** (1 mg/mL vs. 5 mg/mL).
    - Withdraw only the required dose and discard the remaining volume.
- Ensure clinicians adhere to local policy regarding safe and accurate medication administration, including the 6 Rights (right patient, right drug, right dose, right time, right route and right documentation) and independent second person checks where applicable. These checks should include (but are not limited to) carefully reading the medication label to verify the name, strength, form and route of administration against the medication order, rather than relying on packaging or label recognition. Refer to Sections 6.6 to 6.8 of NSW Health *Medication Handling* Policy Directive (PD2022_032) for more information.

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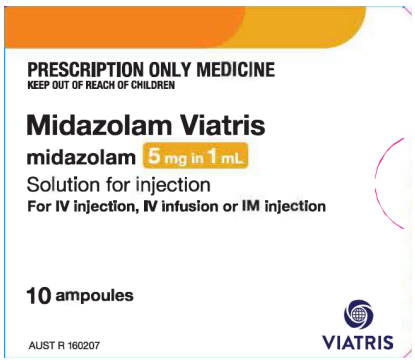
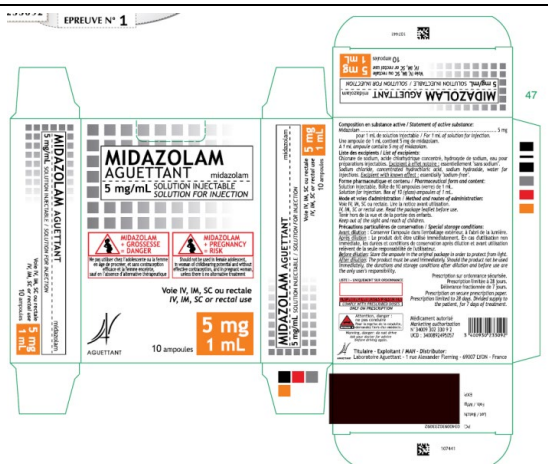
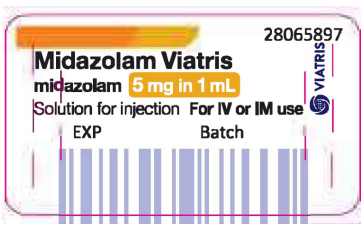
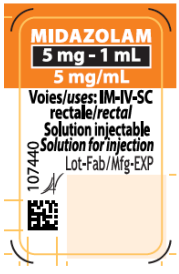
**Table 1**: Comparison of Australian registered midazolam 5 mg/1 mL injection ampoule and the international alternative available via S19A.

| | *Australian registered product*<br>**Midazolam (Viatris) 5 mg/1 mL** | *S19A alternative*<br>**Midazolam (Aguettant) 5 mg/mL** |
|---|---|---|
| ***Country of registration*** | Australia (ARTG 160207) | France |
| ***Active ingredient and strength*** | Midazolam 5 mg/1 mL | Midazolam 5 mg/1 mL |
| ***Presentation*** | Glass ampoule | Glass ampoule |
| ***Pack size*** | 10 x glass ampoule | 10 x glass ampoule |
| ***Excipients*** | Sodium chloride<br>Hydrochloric acid<br>Sodium hydroxide<br>Water for injection | Sodium chloride<br>Hydrochloric acid<br>Sodium hydroxide<br>Water for injection |
| ***Approved routes of administration*** | IV, IM | IV, IM, rectal (PR), subcut |
| ***Storage*** | Below 25°C<br>Protect from light | Room temperature<br>Protect from light |
| ***Labelled language*** | English | French – Active strength and ingredient clearly distinguishable in English |
| ***Product images***<br>***Carton artwork*** |  |  |
| ***ampoule artwork*** |  |  |

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