Issue date
21 May 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:

- Palliative Care
- Pain Services
- Aged Care
- Oncology/Cancer Care
- Neonatal/Paediatric Departments
- Maternity Services
- Alcohol and Other Drugs Services
- Intensive Care Units
- Emergency Departments
- Nursing/Midwifery Services
- Pharmacy Services
- Medical Services
- Drug & Therapeutics Committees

All other relevant clinicians and clinical departments where morphine oral liquid is prescribed, stored, and administered.

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

Clinical Excellence Commission
Tel: 02 9269 5500
Email
Internet
Intranet

Review date
21 May 2025

UPDATED: Changes to supply of morphine oral liquid in Australia

What's new in this Safety Notice?

This Safety Notice replaces SN:028/23 and has been updated to include information about:

- Sponsorship of Ordine (no longer discontinued).
- Availability of additional Section 19A (S19A) alternatives from LumaCina.

Situation

- In 2023, Mundipharma announced the discontinuation of all strengths of immediate-release morphine hydrochloride trihydrate (Ordine) oral solution from the Australian market.
- Since then, sponsorship of all strengths of Ordine has been transferred to Arrotex Pharmaceuticals, with supply expected to resume from August 2024. The brand name and outer packaging will remain identical except for the logo which will change from Mundipharma to Arrotex Pharmaceuticals.
- In the interim, additional S19A alternatives (RA-MORPH 1 mg/mL, 5 mg/mL, and 10 mg/mL oral solution) from LumaCina will be available until 30 September 2024. The formulation and presentation of these alternatives are identical to Ordine.
- Other forms of morphine (including controlled-release tablets and capsules, and ampoules for injection) continue to be available.

Background

Immediate-release morphine oral solution is indicated for the short-term management of moderate to severe pain for which other treatment options have failed, are contraindicated, not tolerated or are otherwise inappropriate to provide sufficient management of pain. It also has accepted, off-label indications for:

- neonatal pain and sedation, including during assisted ventilation
- neonatal abstinence syndrome (NAS) secondary to maternal opioid dependency
- iatrogenic opioid withdrawal secondary to infant opioid infusions
- pain and dyspnoea in patients receiving palliative/end-of-life care.

Assessment

Alternatives to immediate-release morphine hydrochloride trihydrate (Ordine) oral solution are available and can be utilised after consideration of the precautions and safety issues. These include:

S19A immediate-release morphine oral solution alternatives

The Therapeutic Goods Administration (TGA) have released a web statement regarding the supply of immediate-release morphine hydrochloride trihydrate oral solution and of the availability of S19A alternatives. Table 1 provides a comparison of S19A alternatives approved at the time of publication. For updates on the S19A alternatives, refer to the TGA Section 19A approvals database.

Other immediate-release opioid oral solution alternatives

- Oxycodone hydrochloride (OxyNorm®) oral liquid 1 mg/mL, 250 mL bottle – ARTG 77464.
- Hydromorphone hydrochloride 1 mg/mL oral solution bottle – Multiple brands available under S19A of the Therapeutic Goods Act 1989. **Note:** hydromorphone hydrochloride 1 mg/mL oral solution is not currently listed on the NSW Medicines Formulary and may not be stocked at all facilities.

Opioid conversion tools (e.g., ANZCA Opioid Calculator, eviQ Conversion Calculator) should be used to guide switching opioids and to determine a suitable starting dose. Specialist advice should be sought if there is limited experience with opioid conversions. Careful monitoring is required until the patient is stabilised on a dose of an alternative opioid.

Safety considerations of S19A alternatives

There are differences between the Ordine oral solution and the S19A immediate-release morphine oral solution alternatives that clinicians need to be aware of, including (see **Table 1** for a detailed comparison):

- Morphine salt – two of the S19A alternatives contain morphine sulfate pentahydrate, while Ordine oral solution contains morphine hydrochloride trihydrate, however there is no difference in efficacy.
- Excipients – there are important differences in excipients in the S19A alternatives that may not be appropriate in some patient groups, including sucrose and alcohol. The amount of alcohol in the alternate product is an important consideration if the patient is pregnant or breast-feeding, has a history of alcohol use, has long term (chronic) liver problems or epilepsy, or if the patient is a child. Two of the S19A alternative products also contain parahydroxybenzoates (E216, E217, E218 and E219) as excipients, which may cause allergic reactions in some patients.
- Packaging – there are differences in the form, packaging, and appearance of the products.
- Storage – there are differences in storage requirements and expiration dates once the bottle is opened.

Recommendations

To effectively manage the discontinuation of Ordine oral solution:

- Facilities should select an appropriate alternative(s) considering individual product specifications (such as alcohol content) and requirements in relation to the intended patient populations and clinical indications.
- Orders for alternative products should be placed by Pharmacy Departments well in advance to ensure the timely receipt and ongoing supply. Contact suppliers for further information on availability and lead times (noting that lead times are variable and can be lengthy).
- Clinicians should refer to the Australasian Neonatal Medicines Formulary (ANMF) monograph for the most up to date information on the preferred alternative immediate-release morphine oral solution for use in neonates.
- Pharmacist compounded morphine oral solution may be an option, depending on local resourcing/expertise and the availability of an appropriate formula that includes data to support the intended shelf life.
- Actions to prepare for the safe transition to the alternative morphine oral solution product should be implemented with liaison between representatives from the local Pharmacy Departments, Drug and Therapeutic Committees, and relevant clinicians.
- Clinicians should be made aware of the change in product locally and provided with education regarding the alternative products and any specific requirements, such as the product's expiry date after opening. This information should be documented on the dispensing labels and communicated to clinical areas when distributing as ward stock.
- Clinicians should take extra precaution when prescribing, dispensing and administering alternative oral morphine solutions, and when communicating medicine information during transitions of care.
- Patients and caregivers should be provided with appropriate education on the alternative product being prescribed including any specific requirements, and this information should be clearly documented during transitions of care (for example, on discharge).
- Pharmacy departments should take extra precaution when dispensing and storing the morphine hydrochloride trihydrate (Streuli Pharma AG) oral drops. Appropriate cautionary and advisory labels should be applied in English. Where possible, clinicians are encouraged to use an appropriately sized oral syringe (rather than the product's medicine dropper) to draw up and administer this product to ensure accuracy of dosing. Clinicians should refer to the Australian Product Information for Ordine oral solution and other evidence-based reference texts for dosing information.
- Governance committees should liaise with local electronic Medication Management (eMM)/ICT teams to update configurations (for example, order sentences and product catalogues) in eMM systems where required to reflect the change in product. Where eMM systems are in use, mechanisms are to be built to prevent selection errors at the point of prescribing.
- Drug registers and automated dispensing cabinets (ADCs) should be reviewed and updated to include the alternative product and reflect appropriate stock counts.
- Clinical guidelines and protocols that include morphine oral solution should be reviewed and updated to reflect any changes associated with the use of the alternative product(s).
- These recommendations are to be considered and implemented in conjunction with the requirements of the NSW Health Policy Directive Medication Handling PD2022_032 and the CEC High Risk Medicine Standard - Opioid Analgesic.

Table 1. Comparison between the Australian registered product and S19A alternatives of morphine oral solution.

Product	*ARTG listed product*	*S19A alternatives*			
	Morphine hydrochloride trihydrate (Ordine) oral solution	**Morphine sulfate pentahydrate (Martindale Pharma®) oral solution**	**Morphine sulfate pentahydrate (Hikma®) oral solution**	**Morphine hydrochloride trihydrate (Streuli Pharma AG®) oral drops**	**Morphine hydrochloride trihydrate (RA-MORPH®) oral solution**
Country of origin	Australia	UK	USA	Switzerland	New Zealand
Supplier	Mundipharma	Link Healthcare	Medsurge Healthcare	Medsurge Healthcare	LumaCina
S19A approval expiry	Not applicable	31 July 2025			30 September 2024 **(expected to be available late May 2024**)
PBS status **Note:** current at the time of publication	PBS subsidised	PBS subsidised	PBS subsidised	PBS subsidised	Not PBS subsidised
Active ingredient and strength(s)	Morphine hydrochloride trihydrate 1 mg/mL, 2 mg/mL, 5 mg/mL, 10 mg/mL	Morphine **sulfate** pentahydrate **2 mg/mL**	Morphine **sulfate** pentahydrate **2 mg/mL**	Morphine hydrochloride trihydrate **10 mg/mL**	Morphine hydrochloride trihydrate 1 mg/mL, 5 mg/mL, 10 mg/mL
		Note: Both alternative products available from Medsurge Healthcare are also available in other strengths internationally. Only the strengths mentioned above are approved for supply under Section 19A.			
Form	Oral solution – colourless	Oral solution – colourless	Oral solution – **blue-green colour**	Oral drops – colourless (**Note:** 20 drops is equal to 1 mL)	Oral solution – clear colourless to pale yellow
Excipients	Anhydrous citric acid, sodium citrate, glycerol & disodium edetate with sodium methyl hydroxybenzoate 0.23% w/v as preservative, water for injections.	**Sucrose (2.25 g/ 5 mL), sodium methyl hydroxybenzoate (E219), sodium propyl hydroxybenzoate (E217)**, disodium edetate, raspberry flavour, hydrochloric acid, purified water.	Citric acid monohydrate, edetate disodium, FD&C Green No. 3, glycerin, methylparaben, propylparaben, sodium benzoate, sorbitol, water.	**Methyl hydroxybenzoate (E218) and propyl hydroxybenzoate (E216)**. (**Note**: No added flavours – may be taken with fruit juice to mask bitter taste).	Citric acid, sodium citrate dihydrate, disodium edetate, glycerol, sodium methyl hydroxybenzoate 0.2% w/v as preservative, water for injections.
Alcohol content	Nil	**Alcohol** 0.4 mL/5 mL	Nil	**Alcohol** 0.01 mL/1 mL	Nil
Specific patient considerations (as per the respective Product Information leaflets)	Not recommended for children under 1 year old. May be used in neonates under the direction of a neonatologist.	Not recommended for children under 1 year old.	Not indicated in children under 2 years old.	Use with extreme caution in children under 1 year old.	Not recommended for children under 1 year old.
	Note: Immediate-release morphine oral solution may be used in neonatal and paediatric patients under the supervision of a relevant specialist for accepted, off-label indications such as neonatal abstinence syndrome. See Australasian Neonatal Medicines Formulary (ANMF) monograph for more information.				

Product	Morphine hydrochloride trihydrate (Ordine) oral solution	Morphine sulfate pentahydrate (Martindale Pharma®) oral solution	Morphine sulfate pentahydrate (Hikma®) oral solution	Morphine hydrochloride trihydrate (Streuli Pharma AG®) oral drops	Morphine hydrochloride trihydrate (RA-MORPH®) oral solution
Storage	Store below 30°C. Protect from light.	Store below 25°C.	Store between 20-25°C. Protect from moisture.	Store between 15-25°C in the original packaging. Protect from light.	Store at or below 30°C. Protect from light.
Expiry	Discard 6 months after opening.	Discard **90 days** after opening.	Discard **90 days** after opening. **Note:** Sourced from Hikma Pharmaceuticals	Discard **8 weeks** after opening.	Discard 6 months after opening.
Appearance	200 mL brown polyethylene terephthalate bottle	100 mL, 250 mL, 300 mL or 500 mL **amber glass bottles**	5 mL, 100 mL and 500 mL **amber plastic bottles**	20 mL **amber glass bottle**	200 mL **amber** polyethylene terephthalate bottle
Outer packaging artwork					
Bottle image/ artwork					
Labelling language	English	English	English	**French and German** (**Note:** active ingredient and strength are identifiable in English).	English

Required actions for the Local Health Districts/Networks

1. Distribute this Safety Notice to all relevant clinicians, clinical departments where immediate-release morphine oral solution is stocked, 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 this discontinuation.
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.