Queensland Health

Fact sheet

Constrained supply of morphine oral liquid

Purpose

To provide information to assist clinicians in managing the ongoing constrained supply of morphine oral liquid.

Situation

There has been a delay in the previously announced TGA[1] timeline for supply of replacement products of all morphine oral liquid strengths.

Background

Morphine oral liquid (Ordine) is used to manage severe pain and difficult or laboured breathing in many care settings, including cancer treatment and end-of-life care. Additionally, it has accepted off-label indications in neonates (neonatal abstinence syndrome) and infants (iatrogenic opioid withdrawal secondary to infant opioid infusions).

In 2023, Mundipharma announced the company's plan to discontinue the manufacture of Ordine (morphine oral liquid) products in Australia. A new sponsor (Arrotex) will manufacturer these products however a gap in supply is expected.

In the interim, substitute overseas-registered products have been approved by the TGA under S19A arrangements —the TGA[1] has been providing updates on anticipated availability.

Prioritisation of morphine oral liquid

After consultation with a range of Queensland Health clinical networks it is recommended that during times of constrained supply, preparations of morphine oral liquid should be prioritised for situations where:

1. the intended dose cannot be achieved by dispersing or breaking a scored morphine immediate release tablet[2].
2. the medicine will be administered outside of hospital, and it is inappropriate for the patient/carer to break or disperse a tablet form of morphine.
3. reasonable therapeutic alternatives (see below) are inappropriate (e.g. excipient allergies, impaired organ function) or are clinically contraindicated.
4. there is not sufficient evidence base for alternative therapeutic agents for the proposed indication and patient group being treated.

Principles to enhance safe medication practices

Constrained supply presents an opportunity to reassess a patient's management plan with regard to ongoing need. The following medication safety principles should be considered during an assessment of suitability of alternative therapeutic medicines and non-pharmacological treatments:

1. Equianalgesic dosing – When changing/switching between opioids or different routes of administration, equianalgesic doses must be considered. There are multiple opioid conversion resource tools available to assist in determining a suitable dose (e.g. ANZCA FPM app, palliMEDS app, eTG, AMH). Specialist advice should be sought if there is limited experience with opioid conversions.
2. Monitoring - Careful observation of the patient is required if changed to an alternative medicine or route; continue monitoring as appropriate.
3. Pharmacokinetic profile – consider the pharmacokinetic profile when determining new dosage regimen:
    - Dose adjustments may be required when using alternative medicines for patients with impaired kidney or liver function.
    - Duration of action and appropriate dosing interval for alternative agents may be different.
    - Onset of action and time to peak effect may vary for alternative agents.
4. Formulation – Consider suitability of dose formulation for the intended clinical use, for example modified release preparations are typically more appropriate for chronic dosing. Modified release preparations should generally not be halved or crushed. Patients with swallowing difficulties may be able to crush tablets but should be assessed for suitability; check *Don't rush to crush*[2] or seek advice.
5. Product factors
    - Look-alike, sound-alike (LASA) issues – several examples of LASA medicine names are present in the opioid therapeutic group4 (e.g. HYDROmorphone and morphine).
    - SAS/S19A status - potential for label to contain information in a language other than English.
6. Patient factors - a variety of patient factors can impact on the suitability and safety of alternative agents:
    - Patient dexterity in opening bottles versus blister strips.
    - Many opioids have similar packaging for different strengths which can lead to incorrect administration.
    - Consider the impact of cost on adherence when alternative options are initiated; SAS and some S19A products are not PBS reimbursable.
7. Patient counselling – changes present an opportunity to promote shared decision-making. Some key factors to discuss with the patient include:
    - Reconfirming clinical indication for alternative agent noting what has been replaced.
    - Dosing instructions and the need for any specialised measuring device.
    - Potential new side effects and the appropriate management.
8. Transition of care – ensure any changes are communicated to all healthcare practitioners, and people involved in the care of the patient (e.g. carers). Encourage the use of an up-to-date medicines list. When ceasing a medicine that is no longer available, record this information.

Alternative therapeutic agents

During constrained supply, consider the following therapeutic alternatives when clinically appropriate to help reserve morphine oral liquid products for the compelling situations outlined in the section on *Prioritisation of morphine oral liquid*.

Therapeutic alternatives for analgesia

Table 1: Selected therapeutic alternatives for analgesia with oral liquid presentations

Medicine	Considerations
Non-opioid analgesia	Consider if opioids are the most appropriate choice and whether non-opioid analgesics may be suitable.
Oxycodone 1 mg/mL liquid	Appropriate in kidney impairment with reduced dose initially—i.e. if kidney function is 10-30 mL/min, give three quarters of estimated dose, if less than 10 mL/min give half the estimated dose[4]. Approximate duration of action 3 to 4 hours compared to 2 to 3 hours with morphine[4].
Hydromorphone 1 mg/mL liquid	Easily confused with morphine but is approximately five times as potent[3]. Therapeutic Guidelines recommends that use is limited to prescribers experienced in the use of hydromorphone[3]. Renally excreted metabolite can accumulate and lead to dose dependent neurotoxic effects[4].

Respiratory indications

Review all medicines that could be contributing to laboured breathing.

High quality comparative trials between morphine and oxycodone (also available as a liquid) for respiratory indications are absent. Respiratory indications are one situation where it may be appropriate to prioritise morphine oral liquid (see section on *Prioritisation of morphine oral liquid*, point 4).

Table 2: Selected therapeutic alternatives for distressing breathlessness[3]

According to the Therapeutic Guidelines, a suitable as required anticipatory prescribing starting dose for intermittent symptoms of distressing breathlessness in a palliative care patient who has not been taking benzodiazepines, is as follows[3]:

Medicine	Dosage
Clonazepam - various strengths	0.2-0.5 mg sublingually or subcutaneously, 2 hourly as required. Monitor response and adjust dose as needed. Review therapy after 3 doses or sooner if patient is not responding to treatment.
Midazolam - various strengths	2.5 mg subcutaneously, 1 hourly as required. Monitor response and adjust dose as needed. Review therapy after 3 doses or sooner if patient is not responding to treatment.

References:

1. Therapeutic Goods Administration (2024). Information about major medicine shortages. https://www.tga.gov.au/safety/shortages/information-about-major-medicine-shortages/about-shortage-ordine-morphine-oral-liquid#:~:text=Ordine%20(morphine)%20oral%20liquid%20products,the%20supply%20of%20Ordine%20recommences.
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5. Australian Commission on Safety and Quality in Health Care (year). National mixed-case lettering list. https://www.safetyandquality.gov.au/our-work/medication-safety/safer-naming-and-labelling-medicines/national-mixed-case-lettering-list

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