

5.15 HYDROMORPHONE HYDROCHLORIDE

Oral liquid, 1 mg/mL, Dilaudid[®], Mundipharma

1 Purpose of Application

- 1.1 The minor submission requested PBS listing of a 200 mL polyethylene terephthalate (PET) bottle replacement for the currently listed 473 mL glass bottle Dilaudid[®] Oral Liquid presentation.

2 Requested listing

- 2.1 The submission requested the following restriction.
- 2.2 Suggestions and additions proposed by the Secretariat to the requested listing are added in italics and suggested deletions are crossed out with strikethrough.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
HYDROMORPHONE HYDROCHLORIDE 1 mg/mL oral liquid, 200 mL	1	..	\$ [REDACTED]	Dilaudid Mundipharma

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input checked="" type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	-
Severity:	-
Condition:	Chronic sSevere disabling pain
PBS Indication:	Chronic sSevere disabling pain
Treatment phase:	-
Restriction Level / Method:	<input checked="" type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	-
Clinical criteria:	The condition must be unresponsive to non-opioid analgesics.

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Population criteria:	-
Prescriber Instructions	-
Administrative Advice	Authorities for increased maximum quantities and/or repeats will be granted only for: (i) severe disabling pain associated with proven malignant neoplasia; or (ii) chronic severe disabling pain not responding to non-opioid analgesics where the total duration of opioid analgesic treatment is less than 12 months; or (iii) first application for treatment beyond 12 months of chronic severe disabling pain not responding to non-opioid analgesics where the patient's pain management has been reviewed through consultation by the patient with another medical practitioner, and the clinical need for continuing opioid analgesic treatment has been confirmed. The date of the consultation must be no more than 3 months prior to the application for a PBS authority. The full name of the medical practitioner consulted and the date of consultation are to be provided at the time of application; or (iv) subsequent application for treatment of chronic severe disabling pain not responding to non-opioid analgesics where a PBS authority prescription for treatment beyond 12 months has previously been issued for this patient.
Cautions	The risk of drug dependence is high.

3 Background

- 3.1 Hydromorphone hydrochloride is an opioid analgesic available on the PBS in several dosage forms including ampoules (for injection), immediate release and modified release tablets as well as an oral liquid formulation. The oral liquid formulation (Dilaudid®) is TGA registered for the relief of moderate to severe pain.
- 3.2 An oral liquid formulation provides an option for patients with difficulty swallowing. It can also be used to titrate a patients' dose in small increments in order to achieve effective pain control, for breakthrough pain, or to allow a more gradual tapering off when opioid treatment is no longer required.
- 3.3 In 2017, the manufacturer of Dilaudid® Oral Liquid experienced problems in sourcing the glass bottles currently used for PBS supply of the 473 mL presentation (PBS items: 5132D and 8424J). As a result, listing of a new PET bottle of 200 mL on the Australian Register of Therapeutic Goods was sought with approval granted in August 2017.
- 3.4 The submission proposed that the 200 mL Dilaudid® Oral Liquid presentation will replace the currently listed 473 mL presentation once stock supplies of the 473 mL bottle are exhausted. If the 200 mL bottle is PBS listed on 1 August 2018 the

submission proposed that the 473 mL bottle will be delisted from the PBS on 1 January 2019, providing a transition period of 5 months.

- 3.5 The current 473 mL presentation provides 23 days of therapy at the Australian DDD of 20 mg per day¹. Due to the reduced volume, the 200 mL presentation in this submission will provide 10 days of therapy. The proposed change will align with the current hydromorphone hydrochloride tablet presentations which provide 10 days of therapy.
- 3.6 The submission proposed that the change will address the difficulties associated with procuring the glass container registered for use in Australia (i.e. the 473 mL bottle) as evidenced by the low stock levels in 2017. It will improve safety (less likely to break), and reduce weight (by replacing the glass with a much lighter and stronger PET container). In addition, the submission suggested that providing a smaller volume of Dilaudid® Oral Liquid will assist in reducing the potential for abuse by having a smaller volume of opioid in the community at any time.
- 3.7 The submission had not been considered by the PBAC previously.

For more detail on PBAC's view, see section 5 PBAC outcome.

4 Consideration of the evidence

Sponsor hearing

- 4.1 There was no hearing for this item as it was a minor submission.

Consumer comments

- 4.2 The PBAC noted that no consumer comments were received for this item.

Clinical trials

- 4.3 As a minor submission, no clinical trials were presented in the submission.

Proposed pricing, estimated PBS usage & financial implications

- 4.4 The submission proposed that pricing of the 200 mL Dilaudid® Oral Liquid presentation be based on the previous Pricing Manual standard methodology for pricing half strengths at two thirds of the full-strength presentation. A further linear

¹ http://www.whocc.no/atc_ddd_alterations_cumulative/ddd_alterations/ &

<http://www.pbs.gov.au/info/statistics/asm/asm-2014> (See Excel Table 1; accessed 14 April 2017)

adjustment to the price was then applied as the 200 mL presentation is less than half of the currently PBS listed 473 mL. The resulting proposed AEMP for the 200 mL Dilaudid® Oral Liquid presentation is \$ [REDACTED] ([REDACTED] cents per mg).

- 4.5 The Secretariat noted that the alternative method for pricing the 200 mL Dilaudid Oral Liquid would be to apply the same per mg price ([REDACTED] cents) to the 200 mL quantity as is currently agreed for the 473 mL quantity. This would result in an AEMP of \$ [REDACTED]. This may be the more appropriate method as the strength and dose of the product is unchanged. It is only the volume in which it is supplied that is changing. In the pre-PBAC response the sponsor argued that there are fixed overhead costs associated with production and packaging which result in a higher cost of goods per mL in the production of the 200 mL bottle as compared to the 473 mL bottle. As such, the sponsor states in the pre-PBAC response that the proposed AEMP price of \$ [REDACTED] is commercially unsustainable.
- 4.6 The submission proposed that the 473 mL presentation is larger than the majority of patients require for a course of treatment. As a result, the submission estimated that a second bottle of the 200 mL presentation will be required in less than [REDACTED]% of cases. The [REDACTED]% estimate is based on expert opinion and is unable to be verified via the documentation provided.
- 4.7 The submission used a market share approach to estimating the likely financial impact of the proposed listing. The projected 200 mL PBS/RPBS services were calculated based on a linear forward projection of the 473 mL services over 2014–16, adjusted upwards by [REDACTED]% to accommodate the lower quantity of medication contained in the bottle. It was assumed that utilisation of the 200 mL and 473 mL bottle would be approximately [REDACTED] during 2018 and that the 473 mL bottle will be delisted from the PBS on 1 January 2019.
- 4.8 The minor submission estimated a net save to the PBS of less than \$10 million in Year 5 of listing, with a total net save to the PBS of less than \$10 million over the first 5 years of listing. This save may not be realised if more patients require a second prescription.
- 4.9 As a minor submission, the financial implications have not been independently verified. The PBAC noted that the financial implications need to be recalculated to take into account the outcome of its considerations.

For more detail on PBAC's view, see section 5 PBAC outcome.

5 PBAC Outcome

- 5.1 The PBAC recommended the listing of a 200 mL PET bottle replacement, containing hydromorphone hydrochloride, for the currently listed 473 mL glass bottle Dilaudid® Oral Liquid presentation indicated for use in severe disabling pain.

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- 5.2 The PBAC considered the listing of a 200 mL presentation of Dilaudid® Oral Liquid to be appropriate. The PBAC noted that a reduction in the volume of opioid available in the community at any one time may be a positive outcome from a quality use of medicines perspective.
- 5.3 The PBAC considered that pricing based on the same cost per mg of hydromorphone hydrochloride was appropriate. The PBAC noted the pre-PBAC response claim that an AEMP based on the same per mg price would not be financially viable and considered the addition of a small premium may be appropriate.
- 5.4 The PBAC considered the financial implications of the proposed change in availability of hydromorphone oral liquid to be unclear, noting that the realisation of a save is highly dependent on the assumption that a second bottle of the 200 mL presentation will be required in less than █% of cases, and this assumption is uncertain.
- 5.5 The PBAC advised that hydromorphone hydrochloride 1 mg/mL oral liquid is suitable for prescribing by nurse practitioners.
- 5.6 The PBAC recommended that the Early Supply Rule should not apply.
- 5.7 The PBAC noted that this submission was not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

6 Recommended listing

6.1 Add new item:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
HYDROMORPHONE HYDROCHLORIDE 1 mg/mL oral liquid, 200 mL	1	..	Dilaudid Mundipharma

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input checked="" type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	-
Severity:	-
Condition:	Severe disabling pain
PBS Indication:	Severe disabling pain
Treatment phase:	-

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Restriction Level / Method:	<input checked="" type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	-
Clinical criteria:	The condition must be unresponsive to non-opioid analgesics.
Population criteria:	-
Prescriber Instructions	-
Administrative Advice	<p>Authorities for increased maximum quantities and/or repeats will be granted only for:</p> <p>(i) severe disabling pain associated with proven malignant neoplasia; or</p> <p>(ii) chronic severe disabling pain not responding to non-opioid analgesics where the total duration of opioid analgesic treatment is less than 12 months; or</p> <p>(iii) first application for treatment beyond 12 months of chronic severe disabling pain not responding to non-opioid analgesics where the patient's pain management has been reviewed through consultation by the patient with another medical practitioner, and the clinical need for continuing opioid analgesic treatment has been confirmed. The date of the consultation must be no more than 3 months prior to the application for a PBS authority. The full name of the medical practitioner consulted and the date of consultation are to be provided at the time of application; or</p> <p>(iv) subsequent application for treatment of chronic severe disabling pain not responding to non-opioid analgesics where a PBS authority prescription for treatment beyond 12 months has previously been issued for this patient.</p>
Cautions	The risk of drug dependence is high.

7 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

8 Sponsor's Comment

The sponsor is pleased to make available on the PBS 200 mL hydromorphone hydrochloride oral liquid bottle providing benefits to the PBS, the patient and the community.