

4.02 OXYCODONE HYDROCHLORIDE + NALOXONE HYDROCHLORIDE, modified release tablet, 2.5 mg/1.25 mg, 15 mg/7.5 mg , and 30 mg/15 mg, Targin®, Mundipharma Pty Ltd.

1 Purpose of Application

1.1 The minor submission sought to list three additional strengths of oxycodone + naloxone under the same conditions as the currently listed strengths.

2 Requested listing

2.1 The submission requested listing the additional strengths of oxycodone + naloxone with the same General Schedule listing as the existing strengths: 5 mg/2.5 mg, 10 mg/5 mg, 20 mg/10 mg, and 40 mg/20 mg.

2.2 The submission sought advice under section 101 (4AC) of the *National Health Act 1953* for the requested strengths.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed for Max. Qty	Price	Proprietary Name and Manufacturer
Oxycodone hydrochloride 2.5 mg + naloxone hydrochloride 1.25 mg: modified release, tablet	28	0	\$ [REDACTED]		Targin® Mundipharma Pty Ltd
Oxycodone hydrochloride 15 mg + naloxone hydrochloride 7.5 mg: modified release, tablet	28	0	\$ [REDACTED]		
Oxycodone hydrochloride 30 mg + naloxone hydrochloride 15 mg: modified release, tablet	28	0	\$ [REDACTED]		

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Condition:	Chronic severe disabling pain
PBS Indication:	Chronic severe disabling pain
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
Clinical criteria:	The condition must be unresponsive to non-narcotic analgesics.

<p>Administrative Advice</p>	<p><u>Note</u> Authorities for increased maximum quantities and/or repeats will be granted only for:</p> <p>(i) chronic severe disabling pain associated with proven malignant neoplasia; or</p> <p>(ii) chronic severe disabling pain not responding to non-narcotic analgesics where the total duration of narcotic 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-narcotic 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 narcotic 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-narcotic analgesics where a PBS authority prescription for treatment beyond 12 months has previously been issued for this patient.</p> <p><u>Note</u> Shared care model: For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</p>
<p>Cautions</p>	<p>The risk of drug dependence is high.</p>

2.3 Expert clinicians have advised that “narcotic” is an outdated term that has been replaced with “opioid” in clinical practice.

For more detail on PBAC’s view, see section 5 “PBAC outcome”

3 Background

3.1 At the March 2015 PBAC meeting, the PBAC deferred making a recommendation regarding the proposed general schedule listing of additional strengths of oxycodone + naloxone and considered that further advice would need to be sought regarding their clinical place and appropriateness. The PBAC recommended that the Department consult with organisations representing physicians experienced in pain management.

3.2 The Department sought advice from the following organisations:

- Faculty of Pain Medicine
- Australian College of Rural and Remote Medicine
- Australian Pain Society
- National Drug and Alcohol Research Centre
- Royal Australasian College of Physicians (Australasian Chapter of Addiction Medicine)

3.3 Responses were received from the Faculty of Pain Medicine, Australian Pain Society, National Drug and Alcohol Research Centre and the Royal Australasian College of Physicians.

3.4 There were varying positions regarding the clinical need for additional strengths of oxycodone + naloxone, especially the lower 2.5 mg/1.25 mg strength.

- 3.5 The Royal Australasian College of Physicians (RACP) considered that there was an unclear clinical need for lower doses of oxycodone + naloxone, stating that combination products have limitations and their benefits are not well established. The RACP did state, however, that the higher dose combination may have some usefulness in palliative, oncological and/or pain medicine settings, given the limitations of the current maximum dose.
- 3.6 The Australian Pain Society (APS), on the other hand, considered that there was a clinical need for additional strengths of oxycodone + naloxone at both the low and higher doses. The APS argued that the varied oxycodone + naloxone strengths would provide for greater flexibility in up- and down-titration, with potential for lessened dose-related side effects. The APS highlighted that older patients with musculoskeletal pain who demonstrate sensitivity to opioid benefits and adverse effects (including skin intolerance to buprenorphine patches) would particularly benefit from the higher strengths of oxycodone + naloxone, especially in terms of analgesic compliance.
- 3.7 The National Drug and Alcohol Research Centre (NDARC) considered that there were some clinical situations, such as using lower doses and dose titrations in the elderly, where having a small dose option may be beneficial.
- 3.8 In July 2015, the PBAC reconsidered the submission in light of expert opinion received. The PBAC noted that while the responses were in general agreement that there was a clinical place for additional strengths of oxycodone + naloxone, it was not clear which additional strengths would be the most appropriate. The PBAC deferred making a recommendation to list additional strengths at this time.

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

4 Clinical place for the proposed therapy

- 4.1 The submission stated that the introduction of three additional strengths was to allow for improved individual dose titration of oxycodone + naloxone, which would avoid unnecessary side effects whilst allowing patients to obtain maximum analgesic benefits. The submission also contended that it would simplify therapy in terms of safety and compliance.

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

5 PBAC Outcome

- 5.1 The PBAC recommended the general schedule listing of oxycodone 2.5mg + naloxone 1.25mg, oxycodone 15mg + naloxone 7.5mg, and oxycodone 30mg + naloxone 15mg under the same conditions as the currently listed strengths, noting that oxycodone (oral) was subject to a 16% statutory price reduction on 1 December 2014.
- 5.2 The PBAC reaffirmed its advice under section 101 (4AC) of the *National Health Act 1953* for the additional strengths of oxycodone + naloxone.
- 5.3 The PBAC noted the advice from the organisations representing physicians experienced in pain management.

- 5.4 The PBAC considered there may be a moderate benefit associated with listing additional strengths of oxycodone + naloxone including flexibility of dose titration.
- 5.5 In accordance with subsection 101 (3BA) of the *National Health Act* 1953, the PBAC advised that it is of the opinion that oxycodone + naloxone should not be treated as interchangeable on an individual patient basis with any other drug.
- 5.6 The PBAC advised that as for existing strengths, new strengths of oxycodone + naloxone are suitable for prescribing by nurse practitioners under a shared care model.
- 5.7 The PBAC recommended that the Safety Net 20 Day rule should not apply, as it currently does not apply to the existing strengths.

Outcome:

Recommended

6 Recommended listing

6.1 Add new items:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
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<p>Cautions</p>	<p>The risk of drug dependence is high.</p>

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 welcomes the PBAC's decision and will be working towards ensuring that patients have access to a broader choice of treatments to control chronic severe disabling pain.