

**7.08 FENTANYL CITRATE**

**100 microgram tablet: buccal, 4**

**100 microgram tablet: buccal, 28**

**200 microgram tablet: buccal, 4**

**200 microgram tablet: buccal, 28**

**400 microgram tablet: buccal, 4**

**400 microgram tablet: buccal, 28**

**600 microgram tablet: buccal, 4**

**600 microgram tablet: buccal, 28**

**800 microgram tablet: buccal, 4**

**800 microgram tablet: buccal, 28**

**Fentora®, Teva Pharmaceuticals Australia Pty Ltd**

**1 Purpose of Application**

- 1.1 The minor resubmission requested an Authority Required (Palliative Care Schedule) listing for the treatment of breakthrough cancer pain.

**2 Requested listing**

- 2.1 The submission requested the following new listing. This remained unchanged from the July 2015 submission. Suggestions and additions proposed by the Secretariat to the requested listing are added in italics:

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Manufacturer	Name and
FENTANYL fentanyl tablet (buccal) 100 micrograms (as citrate), 4 200 micrograms (as citrate), 4 400 micrograms (as citrate), 4 600 micrograms (as citrate), 4 800 micrograms (as citrate), 4	2	0	\$ [REDACTED]	Fentora	Teva

<b>Category / Program</b>	GENERAL – General Schedule Palliative Care (Code PL)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Episodicity:</b>	-
<b>Severity:</b>	-
<b>Condition:</b>	<i>Breakthrough pain</i>
<b>PBS Indication:</b>	<i>Breakthrough pain</i>
<b>Treatment phase:</b>	Initial treatment for dose titration
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input checked="" type="checkbox"/> Authority Required – Emergency <input checked="" type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
<b>Treatment criteria:</b>	<i>Patient must be undergoing palliative care</i>
<b>Clinical criteria:</b>	Patient must have cancer, AND Patient must be receiving opioids for their persistent pain, AND Patient must be unable to tolerate further escalation in the dose of short acting opioids (which may include morphine) for breakthrough pain due to adverse effects
<b>Administrative Advice</b>	<u>Shared Care Model:</u> 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.  <b>Note</b> No increase in the maximum number of repeats may be authorised.  <b>Note</b> <i>Special Pricing Arrangements apply</i>
<b>Cautions</b>	The risk of drug dependence is high.

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Manufacturer	Name and
FENTANYL fentanyl tablet (buccal) 100 micrograms (as citrate), 28 200 micrograms (as citrate), 28 400 micrograms (as citrate), 28 600 micrograms (as citrate), 28 800 micrograms (as citrate), 28	2	0	\$ [REDACTED] (published price)	Fentora	Teva

<b>Category / Program</b>	GENERAL – General Schedule Palliative Care (Code PL)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Episodicity:</b>	-
<b>Severity:</b>	-
<b>Condition:</b>	<i>Breakthrough pain</i>
<b>PBS Indication:</b>	<i>Breakthrough pain</i>
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input checked="" type="checkbox"/> Authority Required – Emergency <input checked="" type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
<b>Treatment phase:</b>	Continuing treatment
<b>Clinical criteria:</b>	Patient must have cancer, AND Patient must be receiving opioids for their persistent pain, AND Patient must be unable to tolerate further escalation in the dose of short acting opioids (which may include morphine) for breakthrough pain due to adverse effects.
<b>Treatment criteria:</b>	Patient must be undergoing palliative care.
<b>Administrative Advice</b>	<p><b>Note:</b> <b>Shared Care Model:</b> 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><b>Note</b> For first continuing supply, applications for increased repeats for up to 3 months' supply may be authorised.</p> <p><b>Note</b> Where consultation with a palliative care specialist or service has occurred, applications for increased repeats for up to 3 months' supply may be authorised.</p> <p><b>Note</b> Telephone approvals are limited to 1 months' therapy.</p> <p><b>Note</b> <i>Special Pricing Arrangements apply</i></p>

<b>Cautions</b>	The risk of drug dependence is high.
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- 2.2 The submission proposed a [REDACTED] % reduction in price from the price proposed in the July 2015 submission, with an effective ex-manufacturer price of \$ [REDACTED] per tablet, and requesting a Special Pricing Arrangement.

### **3 Background**

- 3.1 Fentanyl buccal tablets were registered by the TGA in February 2015 for the treatment of breakthrough pain in adults with cancer who are already receiving maintenance opioid therapy for chronic cancer pain.
- 3.2 The PBAC previously rejected a submission for fentanyl buccal tablets in July 2015. At the July 2015 meeting, the PBAC considered that the submission had not adequately addressed immediate-release opioids as an appropriate comparator. Further, the PBAC did not consider that the submission's utilisation estimates were reliable, and was concerned that no strategy was proposed by the sponsor to mitigate this risk.

**Table 1: Summary of key issues from the previous submission and current resubmission**

	July 2015	Current re-submission
Comparator	<p>Fentanyl lozenges</p> <p><b>PBAC Comment:</b></p> <p>The PBAC considered that the submission had not adequately addressed immediate-release opioids as an appropriate comparator. (para 7.1, July 2015 minutes)</p> <p>The PBAC considered both other immediate-release oral opioids and fentanyl lozenges to be appropriate comparators. In addition, for the small group of patients who are unable to swallow oral opioids, the PBAC considered that subcutaneous morphine may be an appropriate comparator. (para 7.4, July 2015 minutes)</p>	<p>Fentanyl lozenges as main comparator. Considered immediate release opioids may be displaced in calculating price discount.</p>
Patient population	<p>Market share approach</p> <p><b>PBAC Comment:</b></p> <p>The PBAC agreed that the market share approach based on the use of fentanyl lozenges is likely to substantially underestimate the utilisation for fentanyl buccal tablets. The PBAC recalled its previous advice (March 2014 – fentanyl sublingual Public Summary Document) and agreed that an epidemiological approach would have been a more appropriate estimation basis. (para 7.5, July 2015 minutes)</p>	<p>Epidemiological approach, where the same Section E excel file (utilising a market share approach from the July 2015 submission) has been used, setting an “Expected market growth due to listing of another fentanyl formulation” parameter to █%, which the re-submission describes as achieving “concordance between the epidemiological and market share approaches”.</p>
Duration of treatment and uptake of use	<p><b>PBAC Comment:</b></p> <p>The PBAC recommended that a RSA is required to address the following uncertainties:</p> <ul style="list-style-type: none"> <li>Uncertain size of patient population, duration of treatment and uptake of use. (para 6.39, July 2015 minutes)</li> </ul>	<p>Proposed duration of use based on previous fentanyl lozenge submissions.</p> <p>Proposed uptake of use based on rapidly achieving market potential, which the re-submission considered the “most conservative assumption”.</p>
Risk sharing arrangement	<p>None.</p> <p><b>PBAC Comment:</b></p> <p>The PBAC considered that the size of the eligible population remains uncertain given the wide ranges in the published literature. The PBAC considered that a risk share arrangement would be needed to address this uncertainty as well as manage the financial implications for any use beyond the restriction including into the first-line treatment of breakthrough pain in cancer patients. (para 7.6, July 2015 minutes)</p>	<p>Proposed expenditure caps and Special Pricing Arrangement.</p>

#### **4 Clinical place for the proposed therapy**

- 4.1 The PBAC previously considered that the likely clinical place in therapy for fentanyl buccal would be a second-line listing in a palliative care setting. The Committee considered that withholding fentanyl buccal to third- and subsequent lines for breakthrough pain may not be practical or reasonable. Furthermore, the Committee considered that, in rare circumstances, fentanyl buccal may be used in first-line setting for patients unable to swallow oral immediate-release opioids.

#### **5 Comparator**

- 5.1 The re-submission nominated fentanyl lozenges as the main comparator. In July 2015 this was considered an appropriate comparator; however the PBAC noted that other immediate-release opioids were also appropriate alternate comparators.
- 5.2 The re-submission considered the displacement of both fentanyl lozenges and immediate release opioids in calculating a price discount for fentanyl buccal tablets.

#### **6 PBAC consideration of the evidence**

##### **Sponsor hearing**

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

##### **Consumer comments**

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

##### **Clinical trials**

- 6.3 As a minor submission, no new clinical trials were presented in the re-submission.

##### **Economic analysis**

- 6.4 In the previous major submission considered by PBAC in July 2015, the submission presented a cost-minimisation analysis against fentanyl lozenges.

##### **Estimated PBS usage & financial implications**

- 6.5 In July 2015 the PBAC considered that the size of the eligible population remains uncertain given the wide ranges in the published literature. The PBAC considered that a Risk Share Arrangement would be needed to address this uncertainty as well as manage the financial implications for any use beyond the restriction including into the first-line treatment of breakthrough pain in cancer patients.
- 6.6 The submission provided revised estimates of patient numbers eligible for fentanyl buccal tablets (or fentanyl lozenges) – ██████ to ██████ compared to ██████ to ██████ in the July 2015 submission. In July 2015, the PBAC agreed that the market share approach based on the use of fentanyl lozenges is likely to substantially underestimate the utilisation for fentanyl buccal tablets. The re-submission estimated population numbers using an epidemiological approach.

- 6.7 The submission estimated the likely duration of use of fentanyl buccal tablets as second line therapy to be around ■■■ to ■■■ days. This appeared to be based on a Survey of ■■■ practitioners conducted in 2003 for the first fentanyl lozenge submission and the latest fentanyl lozenge PBAC submission (July 2007).
- 6.8 The submission stated that the most conservative assumption to estimate uptake of fentanyl buccal tablet use, is to adjust uptake rate to ■■■% in Year 1 ■■■% in Year 2 and ■■■% by Year 3 following PBS listing.
- 6.9 The submission proposed a Risk Sharing Arrangement with annual caps based on projected expenditure, shown in the table below.

**Table 2: Proposed Risk Share caps and rebates**

	Rebate Beyond Cap	Year 1	Year 2	Year 3	Year 4	Year 5
Special Pricing Arrangement (artificial published price)	■■■%	For all Commonwealth Expenditure for Fentora				
<b>Proposed Annual PBS Contribution Caps</b> = Forecast PBS Government Expenditure on Fentora (in this November 15 re-submission - 50% growth)	■■■%	\$■■■	\$■■■	\$■■■	\$■■■	\$■■■

Source: submission, Table 6 p.22

- 6.10 The sponsor also proposed a Special Pricing Arrangement (SPA) with the sponsor rebating ■■■% of annual Government expenditure on fentanyl buccal tablets.
- 6.11 The PBAC advised that a Risk Sharing Arrangement should include a subsidisation cap where higher than expected use of fentanyl buccal tablets is rebated. The PBAC considered that fentanyl citrate buccal tablets should be included in the same financial cap and subject to the same rebate arrangements as fentanyl citrate sublingual tablets.

*For more detail on PBAC’s view, see section 7 “PBAC outcome”*

## 7 PBAC Outcome

- 7.1 The PBAC recommended listing fentanyl citrate buccal tablets as an Authority Required benefit on the Palliative Care Schedule for the treatment of breakthrough pain in patients undergoing palliative care for cancer.
- 7.2 The recommendation was made on a cost-minimisation basis with fentanyl citrate sublingual tablets, which was recommended at the July 2015 PBAC meeting. The PBAC recalled that fentanyl citrate sublingual tablets were recommended on a cost-minimisation basis with immediate-release opioids and fentanyl lozenges. The equi-effective doses were not estimated. However, an assumption of one dose per episode of breakthrough pain was considered reasonable, and it was noted that the resubmission proposed flat pricing across dose strengths, addressing the issue of

variability during titration.

- 7.3 The PBAC advised that fentanyl citrate buccal tablets should join the existing Risk Sharing Arrangement for fentanyl citrate sublingual tablets and be subject to the same subsidisation caps and rebate arrangements.
- 7.4 The resubmission nominated fentanyl lozenge as the main comparator, but considered the displacement of immediate release opiates in calculating a revised price. The PBAC considered, as previously, both immediate-release oral opioids and fentanyl lozenges to be appropriate comparators.
- 7.5 The PBAC noted that the resubmission had appropriately estimated population numbers using an epidemiological approach rather than a market share approach, as in the previous submission. The PBAC also noted the revised estimate of uptake of ■■■% of the fentanyl lozenge market by Year 3 of listing. The PBAC considered that the size of the eligible population was still uncertain and that a risk sharing arrangement would be required to address this uncertainty and manage the financial implications.
- 7.6 The PBAC noted the restriction should be aligned with fentanyl citrate sublingual tablets, which the Department was currently in the process of finalising.
- 7.7 The PBAC recommended that fentanyl citrate buccal tablets should not be treated as interchangeable on an individual patient basis with any other drugs.
- 7.8 The PBAC advised that fentanyl citrate buccal tablets are suitable for prescribing by nurse practitioners under a Shared Care model.
- 7.9 The PBAC recommended that the Safety Net 20 Day Rule should not apply.
- 7.10 The submission is not eligible for an Independent Review as the PBAC has made a positive recommendation.

**Outcome:**

Recommended

**8 Recommended listing**

- 8.1 Add new item: Restrictions to be finalised.

**9 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.

**10 Sponsor's Comment**

Teva welcomes the PBAC recommendation and will work with the department to progress the listing of Fentora.