Public Summary Document

Product:	Fentanyl citrate, lozenge with integral applicator, 200 microgram, 400 microgram, 600 microgram, 800 microgram, 1200 microgram and 1600 microgram, Actiq®
Sponsor:	Orphan Australia Pty Ltd
Date of PBAC Consideration:	March 2006

1. Purpose of Application

The submission requested an authority required 'palliative care' listing for all registered strengths of fentanyl lozenges for the management of breakthrough pain in palliative care patients who were receiving opioids and were unable to take morphine due to renal impairment or had an adverse reaction to other opioids which required cessation or change of that therapy.

2. Background

A submission for a Section 100 (Highly Specialised Drugs Program) listing of Actiq was considered at the June 2003 meeting of the Pharmaceutical Benefits Advisory Committee (PBAC). The PBAC rejected the submission because of a lack of evidence in the proposed patient group with resulting uncertain clinical benefit and uncertain cost-effectiveness. Highly Specialised Drugs are medicines for the treatment of chronic conditions, which, because of their clinical use or other special features, are restricted to supply to public and private hospitals having access to appropriate specialist facilities.

At the July 2004 meeting, the PBAC considered an application for an authority required listing as a Palliative Care Benefit for the management of breakthrough cancer pain by specialists in cancer pain management in palliative care patients who are receiving opioids for their underlying persistent cancer pain and where morphine and one other opioid are each precluded from use due to certain circumstances. The PBAC rejected the application because of uncertain extent of clinical benefit and the resulting uncertain and unfavourable cost effectiveness.

3. Registration Status

Actiq lozenges were registered on 15 November 2002 for the management of breakthrough cancer pain in patients with malignancies who are already receiving and are tolerant to opioid therapy for their underlying persistent cancer pain.

4. Listing Requested and PBAC's View

Section 85 under the Palliative Care Scheme

Authority required

Management of breakthrough cancer pain in palliative care patients who are receiving opioids for their underlying persistent cancer pain where morphine is contraindicated due to:

- Renal impairment defined as estimated glomerular filtration rate (eGFR) of less than 50 mL/min; or
- Documented adverse reaction to other S8 opioids which require cessation or change of that therapy.

For PBAC's view, see Recommendation and Reasons.

5. Clinical Place for the Proposed Therapy

Fentanyl has a number of advantages in patients with renal impairment in that it is metabolised in the liver to inactive metabolites and has a short half-life. For patients with renal impairment, accumulation of active metabolites of other opioids may contribute to the adverse effects of opioids.

6. Comparator

The submission nominated placebo as the main comparator. The July 2004 submission also nominated nominated placebo as the most appropriate comparator. This was accepted by the PBAC in its review of the first submission at the June 2003 meeting.

7. Clinical Trials

The pivotal trial, AC 200/013, used in support of this minor submission was the same as that in the June 2003 and July 2004 submissions.

8. Results of Trials

The PBAC noted that, as the sponsor had submitted this as a minor submission, the data and arguments presented had not undergone evaluation by the Pharmaceutical Evaluation Section or consideration by the Economics Subcommittee. Without these evaluations, the Committee was unable to draw any conclusions about the cost-effectiveness of the product as required by the Guidelines.

9. Clinical Claim

The submission claimed that fentanyl lozenge was statistically significantly superior to placebo for all measures of pain relief in cancer breakthrough pain. The Committee was unable to assess the validity of this claim on the basis of this submission.

10. Economic Analysis

No new economic evaluation was provided. The submission presented a series of arguments addressing the economic reasons for rejection of the last submission. As before, the Committee had insufficient information to assess the validity of these arguments.

11. Estimated PBS Usage and Financial Implications

The submission estimated the expected market penetration to be < 10,000 patients in year 4 of listing with a cost to the PBS of < $10 million per year in year 4 of listing. As before, the Committee had insufficient information to assess the accuracy of these estimates.

12. Recommendation and Reasons

The PBAC was sympathetic to the need of palliative care patients for an alternative to morphine for use in breakthrough pain and acknowledged that the overall patient population was likely to be small. However the Committee considered that the current minor submission did not provide sufficient information to enable it to reach a decision on the cost-effectiveness of fentanyl. As required by the Guidelines, a major submission would need to be submitted for evaluation for consideration by the PBAC.

The submission was therefore rejected.

13. 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.

14. Sponsor's Comment

The sponsor does not agree that the current minor submission did not provide sufficient information to enable the PBAC to reach a decision on the cost effectiveness of fentanyl. There is no new data to submit. All available data had previously been evaluated and presented to the PBAC. Estimated PBS usage had been based on an audit on patient data of representative palliative care facilities, presented in this submission. Orphan Australia had made this resubmission upon request of the Palliative Care Medications Working Group, for the proposed PBS population of a small number of deserving individuals with short life expectancy in palliative care with cancer pain and not tolerating morphine, 1 in 3 of whom only survive for < 1 month.