Public Summary Document

Product:	Fentanyl, transdermal patch, releasing approximately 12, 25, 50, 75 or 100 micrograms per hour, Durogesic® 12/25/50/75/100
Sponsor:	Janssen-Cilag Pty Ltd
Date of PBAC Consideration:	March 2006

1. Purpose of Application

The submission sought to extend the current restricted benefit of fentanyl on the Pharmaceutical Benefits Scheme (PBS) availability to 'chronic severe disabling pain which is not responding to non-narcotic analgesics'.

2. Background

Fentanyl patches were listed on the PBS on 1 August 1999 as a restricted benefit for chronic severe disabling pain which is associated with proven malignant neoplasia and is unresponsive to non-narcotic analgesics in patients requiring parenteral opioid treatment. The listing was amended on 1 February 2001 with the removal of the words "in patients requiring parenteral opioid treatment" following successful pricing negotiations which allowed a 15% premium over oral slow release morphine (OSRM). The PBAC considered that the equivalent doses in cancer pain appeared to be in the ratio of 1.5 mg transdermal fentanyl daily and 200 mg morphine daily (ie 1:133).

3. Registration Status

Fentanyl transdermal patches were registered on 24 October 1997 for the management of chronic cancer pain requiring opioid analgesia. On 21 December 1999 the indication was amended to the management of chronic pain requiring opioid analgesia.

4. Listing Requested and PBAC's View

CAUTION:
The risk of drug dependence is high
Restricted benefit
Chronic severe disabling pain not responding to non-narcotic analgesics
NOTE: as for current narcotic analgesics

See Recommendations and Reasons for PBAC's view.

5. Clinical Place for the Proposed Therapy

Chronic pain of non-cancer origin is a significant issue in the Australian population. The use of opioids is an appropriate option in the management of chronic non-cancer pain due to the strong body of evidence supporting their role in pain control.

6. Comparator

The submission nominated oral slow release morphine (OSRM) as the appropriate comparator as previously agreed by PBAC.

7. Clinical Trials

The submission presented three trials comparing transdermal fentanyl (TDF) with OSRM in chronic non-cancer pain.

All three trials have been published as follows:

Trial/First author	Protocol/Publication title	Publication citation
Allan L et al (2001) Niemann T (2001)	Evaluation of subject preference for Durogesic (TTS fentanyl) or sustained release morphine, and comparison of their efficacy and safety in the treatment of chronic, non-malignant pain.	British Medical Journal, 2001; 322: 1154-1158. Evidence-based Healthcare, 2001; 5: 131-132.
Allan L et al (2005)	A study to compare the safety and efficacy of Durogesic (TTS fentanyl) with sustained release morphine in strong opioid naïve subjects requiring treatment for chronic low back pain.	Spine, 2005; 30(22):2484-2490
Johnson M (2000)	A study to compare subject acceptability of Durogesic with sustained release morphine in subjects requiring strong opioids for chronic non-malignant pain.	Abstract at 3rd Congress of the European Federation of IASP Chapters (2000): Pain in Europe III – Advances in Pain Research and Therapy, Nice France, p289, September 26-29.

8. Results of Trials

In Allan et al (2001), significantly more patients preferred transdermal fentanyl treatment to OSRM. However, it was difficult to interpret this outcome because of the open-label design and the subjective outcome used. In the other two trials the sole significant difference was evident in constipation assessment in Allan et al (2005), where patients on transdermal fentanyl reported less constipation. Across the three trials, there were no statistically significant differences identified in chronic non-cancer pain control.

9. Clinical Claim

The submission claimed that transdermal fentanyl is no worse than OSRM in terms of effectiveness and toxicity. The PBAC accepted this claim.

10. Economic Analysis

The submission presented a preliminary economic evaluation using a cost-minimisation approach. This approach was considered appropriate by the PBAC.

11. Estimated PBS Usage and Financial Implications

The submission estimated that the number of patients would be <10,000 for cancer/non-cancer pain in Year 4 with the requested PBS listing.

The submission estimated that the net costs would be <$10 million by Year 4. The PBAC considered these estimates to be reasonably documented, although the underlying assumptions could not be verified.

12. Recommendation and Reasons

The PBAC recommended listing on a cost-minimisation basis for patients with non-cancer related pain, concluding that transdermal fentanyl is no worse than oral sustained-release morphine (OSRM) in terms of effectiveness and toxicity for this patient group. The equi-

effective doses are 1 mg fentanyl being equivalent to 98.8 mg morphine across the two indications of cancer and non-cancer pain.

The PBAC considered it appropriate that a NOTE be included in the PBS listing, indicating that there is a high risk of side effects and that initiation in such patients, if needed, should be at the lowest dose. The PBAC requested that the National Prescribing Service considers developing a RADAR article on this product to highlight this issue. The PBAC also requested that the DUSC monitor use and provide a report in 12 months time on the dose relativities of OSRM and transdermal fentanyl.

Recommendation

Amend the current restriction to read:

Restriction:

CAUTION:
The risk of drug dependence is high

NOTE:
Durogesic is not recommended in opioid naive patients with non-cancer pain, because of a high incidence of adverse events in these patients. Patients with cancer pain may be initiated on the lowest strength patch (12 microgram per hour).

Restricted benefit
Chronic severe disabling pain not responding to non-narcotic analgesics.

NOTE:
Authorities for increased maximum quantities and/or repeats will be granted only for:
(i) chronic severe disabling pain associated with proven malignant neoplasia; or
(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
(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
(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.

Maximum Quantity: 5 (all strengths)
Repeats: Nil

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

Janssen-Cilag welcomes the decision by the PBAC to provide access to an additional treatment option for people experiencing chronic severe disabling pain from all causes.