PUBLIC SUMMARY DOCUMENT

Product: Imiquimod, cream, 12.5 mg per 250 mg single use sachets (5%), 12, Aldara®

Sponsor: 3M Pharmaceuticals Pty Ltd

Date of PBAC Consideration: July 2006

1. Purpose of Application

The submission requested an authority required listing for imiquimod cream sachet to treat primary (previously untreated) superficial basal cell carcinoma (sBCC) where surgery is inappropriate.

2. Background

Imiquimod cream was considered by the PBAC at its November 2005 for the treatment of superficial basal cell carcinoma. The Committee rejected imiquimod for listing because the restriction was considered inappropriate, trials were not representative of those for whom PBS listing was sought, and cost-effectiveness was both uncertain and inadequately demonstrated.

3. Registration Status:

Imiquimod was approved for registration on 22 July 2004 for the 'primary treatment of confirmed superficial basal cell carcinoma where surgery is considered inappropriate'.

4. Listing Requested and PBAC's View

Authority Required
Treatment of biopsy confirmed primary (previously untreated) superficial basal cell carcinoma (sBCC) in immunocompetent patients who cannot have surgical excision, cryotherapy, nor curettage with diathermy and require drug therapy for at least one of the following:

(i) Keloid or hypertrophic scar from prior surgery;
(ii) Two or more lesions occurring at the same time;
(iii) Lesion size 2cm or more in at least one dimension;
(iv) Lesion below knee;
(v) Lesion on face but not within 1 cm of the hairline, eyes, mouth, ears AND not within 2cm of the nose AND imiquimod is prescribed by a dermatologist or plastic surgeon.

The following information must be provided at the time of application:

(i) The date of the pathology report and name of the Approved Pathology Authority. The report from an accredited laboratory must be available for audit by Medicare Australia;
(ii) A description of the clinical presentation that meets one or more of the criteria;
(ii) Confirmation the patient or carer is able to understand and administer the imiquimod dosing regimen.

Note:

The maximum quantity authorised provides sufficient supply for a treatment course with allowance for rest periods;

Treatment of recurrent (previously treated) lesions will not be authorised.

The PBAC's view was that the re-submission had addressed its concerns from the November 2005 meeting that the then requested restriction would allow for the possibility of usage beyond the intent of the restriction. However, it considered the requested restriction at this current meeting would be unworkable also. The PBAC considered there would be a place for imiquimod in the treatment of patients with frequent multiple primary lesions where access to surgery is difficult.

5. Clinical place for the proposed therapy

Superficial BCC presents as slow-growing, local invasive malignant epidermal skin tumours, and is a common form of non-melanoma skin cancer in Australia and worldwide. Imiquimod cream provides an alternative therapy for patients for whom surgical excision is not appropriate.

6. Comparator

The submission nominated non-intervention monitoring and photodynamic therapy with methyl aminolevulinate (MAL-PDT).

7. Clinical Trials

The same trials as in the previous submission formed the scientific basis of the re-submission (see Public Summary Document from November 2005 PBAC). However, for the five imiquimod studies (two key and three supportive studies), additional data were provided that listed the proportion of patients in each trial that match each eligibility criterion for PBS listing.

The comparison of imiquimod with MAL-PDT was based on the same published trials; however, the Basset et al 2003 abstract was updated in 2005. Studies are re-presented in greater detail compared with the previous submission.

8. Results of Trials

No new trials were presented for either imiquimod or MAL-PDT. The submission's claim of non-inferiority in comparison with MAL-PDT was based on an indirect analysis. There appeared to be a trade-off between a lower recurrence rate (9.5% vs 18%) and the initial cure rate for which imiquimod was almost significantly worse (82.2% vs 91.7%; RR = 0.9 (0.81-1.02)). The imiquimod initial cure rate was based on biopsy evidence of tumour clearance. The MAL-PDT initial cure rate was determined by clinical observation for complete disappearance of the tumour. The recurrence rate estimate for both imiquimod and MAL-PDT was based on clinical observation.

The initial response and long-term tumour clearance in the MAL-PDT group were similar to those in the cryosurgery group and to rates obtained in single arm supportive studies of Horn et al, 2003 and Vinciullo et al, 2005.

No particular age-related safety & tolerability differences were detected in imiquimod trials in a population aged >70 years compared to younger patients. In the MAL-PDT studies, local skin reactions constituted the majority (70%) of the adverse events (Horn et al, 2003 and Vinciullo et al, 2005; Basset-Seguin et al, not reported). There was only one drug-related serious AE (severe burning and pain).

9. Clinical Claim

Based on presented evidence imiquimod had significant advantages in effectiveness over placebo (non-intervention monitoring) but had more toxicity, and was no worse than MAL-PDT in terms of effectiveness and toxicity. The PBAC had previously accepted (November 2005 meeting) that, based on indirect comparison, imiquimod was no worse than other non-surgical comparators such as cryotherapy or curettage and cautery, but that imiquimod was less effective than surgical excision.

10. Economic Analysis

The trial-based incremental cost per extra initial cure gained at 12 weeks was < $15,000. The modelled economic evaluation was presented to represent the value that imiquimod offers patients over a two year time frame. The base case modelled incremental cost per extra discounted disease free year was < $15,000.

11. Estimated PBS Usage and Financial Implications

The likely number of treatment courses per year for the listing requested was calculated to be up to 22,663 by Year 3 (the resubmission assumed 1.6 treatments per patient per year). This equates to 45,326 imiquimod scripts by Year 3 as a treatment course consists of one imiquimod prescription for twelve sachets with one repeat, allowing for treatment rest periods.

The financial cost per year to the PBS (excluding co-payments) was calculated to be < $10 million in Year 3 for the listing requested. This also applies to the PBAC recommended listing below**.**

12. Recommendation and Reasons

The PBAC recommended listing on the basis of acceptable cost-effectiveness compared to placebo for patients who cannot have surgical excision, cryotherapy or curettage.

As previously, the PBAC acknowledged that imiquimod has a clinical place in the treatment of superficial basal cell carcinoma (sBCC), but considered it should not be available as first line treatment, as surgical excision is more effective than imiquimod.

The Committee noted the re-submission had addressed its concerns at the November 2005 meeting that the then requested restriction would allow for the possibility of usage beyond the intent of the restriction. However, it considered the requested restriction at this current meeting would be unworkable also, and that limiting imiquimod to last line treatment, and noting the willingness of the sponsor to enter into a price volume agreement would reduce the potential for inappropriate use.

The PBAC also noted there were no absolute contraindications to surgical excision, cryotherapy and curettage so it is a clinical judgement about whether surgery is contraindicated and whether patients will benefit more from using a treatment other than surgery, although the recurrence rate after surgery is much lower than it is after imiquimod therapy. The PBAC considered there would be a place for imiquimod in the treatment of patients with frequent multiple primary lesions where access to surgery is difficult.

The PBAC requested that an NPS RADAR be published for this listing highlighting that imiquimod was not the preferred treatment for sBCC.

Recommendation
Imiquimod**,** cream, 12.5 mg per 250 mg single use sachets (5%), 12

Restriction: Authority Required
Treatment of biopsy confirmed primary (previously untreated) superficial basal cell carcinoma (sBCC) in immunocompetent patients who cannot have surgical excision, cryotherapy, or curettage with diathermy.

The date of the pathology report and name of the Approved Pathology Authority must be provided at the time of application.

NOTE:

The patient or carer must be able to understand and administer the imiquimod dosing regimen.

No applications for increased maximum quantities and/or repeats will be authorised. Treatment of recurrent (previously treated) lesions will not be authorised.

Maximum quantity: 1
Repeats: 1

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