PUBLIC SUMMARY DOCUMENT
Product: Imiquimod, cream 50 mg per g (5%), 250 mg single use sachets, 12, Aldara®
Sponsor: iNova Pharmaceuticals (Aust) Pty Ltd
Date of PBAC Consideration: March 2009

1. Purpose of Application
To consider the findings of the Independent Review Report on imiquimod.

2. Background
Imiquimod has been listed on the Pharmaceutical Benefits Scheme (PBS) from 1 December 2006 for the treatment of superficial basal cell carcinoma (sBCC).

At its July 2008 meeting, the PBAC rejected a request to extend the PBS listing of imiquimod to include field therapy of multiple clinically evident solar keratosis because of uncertain evidence of effectiveness and safety over the comparator, 5-flurouracil gel, and the resulting uncertain cost-effectiveness.

Following the July 2008 rejection by the PBAC, the sponsor sought an Independent Review.

3. Registration Status
Imiquimod 5% cream is registered for the treatment of solar (actinic) keratosis in the face and the scalp, and primary treatment of confirmed superficial basal cell carcinoma where surgery is considered inappropriate, and the treatment of external genital and peri-anal warts (Condyloma acuminata) in adults.

4. Listing Requested
The submission to the July 2008 PBAC meeting sought the following listing:
Authority Required
Solar keratosis on the face or scalp in a patient with normal immune function who has multiple clinically evident solar keratosis lesions and requires topical drug treatment as field therapy.

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.

5. Matters for Independent Review
The sponsor nominated the following issues on which the Review was sought:
a whether there is value in treating solar keratosis.
b whether there is certainty in the comparative effectiveness of imiquimod.
c whether there is a safety issue with imiquimod as a true field therapy.
d whether imiquimod is a cost-effective therapy for solar keratosis.

6. Findings of the Review
a *Value in treating solar keratosis*
The Review considered that there would be value in treating solar keratosis if it prevented squamous cell carcinoma-related adverse health outcomes, improved the quality of life for

people with solar keratoses and demonstrated long-term beneficial effects. The Review found that it was not possible to assess imiquimod as a therapy to prevent adverse health outcomes related to squamous cell carcinoma due to the absence of supporting data. There have been no studies that have examined quality-adjusted life years (QALYs) in relation to solar keratosis. There was no reliable data on the duration of the treatment effect after 16 months. It was concluded that it was not possible to demonstrate that there was value in treating solar keratosis.

The PBAC noted that the Review's finding that there is a lack of data to support the claims that treating solar keratosis with imiquimod would reduce the malignancy potential or improve the quality of life for people with solar keratosis.

b. *Comparative effectiveness of imiquimod*

The Review considered that imiquimod was superior to placebo in reducing solar keratoses of the face and scalp. It was considered that the sponsor's claim of unequivocal superiority of imiquimod over 5-flurouracil was not supportable due to the limitations of the randomised controlled trial (Krawtchenko et al., 2007) and the contradictory results from two Randomised Clinical Trials (RCTs).

The PBAC noted that the Review's finding that there is no reliable evidence to support a claim that imiquimod is superior to its comparators, 5-flurouracil and cryotherapy.

c. *Safety issues*

The Review found that there was a lack of safety data for treatment surface areas exceeding 25 cm^2, which is consistent with the opinion of the Therapeutic Goods Administration (TGA) and the allowed treatment area in the TGA-approved prescriber information. For treatment areas up to 25cm^2 imiquimod has both local and systemic side effects but these are usually within a clinically acceptable range.

The PBAC noted the Review's finding on this matter and that patients could potentially apply the drug to a greater surface area due to the amount of drug supplied (250 mg sachets) which could treat a field up to 386cm^2.

d. *Cost-effectiveness of treating solar keratosis with imiquimod*

In the submitted economic evaluation, a cost effective analysis using cost per patient-year in remission (either disease-free or recurrence-free) over a three year timeframe was presented, in the form of an incremental cost effectiveness ratio (ICER). The Review concluded the cost effectiveness analysis used in the submission is inadequate to demonstrate that imiquimod offers more of a given health outcome than the main comparators largely due to a lack of reliable data on relevant health outcomes, a lack of demonstrated superiority over comparator therapies and inadequate study of the durability of the treatment response.

SUMMARY OPINION

The Review concluded the appropriate economic analysis is a cost-minimisation analysis. A cost-minimisation analysis conducted during the Review found that imiquimod was significantly more expensive than its comparators, 5-flurouracil and cryotherapy.

The PBAC noted the Review's recommendation that the most appropriate pharmaco-economic analysis is cost minimisation analysis as imiquimod has not been demonstrated to

be superior to its comparators. The PBAC also noted that the Review found that imiquimod is inferior to its comparators in terms of cost.

7. Recommendation and Reasons

The PBAC noted the findings of the Independent Review.

The PBAC noted the comment in the sponsor's Pre-PBAC Response that the PBAC should seek further advice from dermatologists in making its decisions. The PBAC considered that further consultation was inappropriate as it should base its decisions on evidence presented at the time of the July 2008 submission.

The PBAC considered that the Review provided no new basis for the Committee to reconsider its recommendation made at the July 2008 meeting.

8. 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.

9. Sponsor's Comment

The Sponsor has no comments.