

**6.10 APREMILAST,
Tablet 30 mg,
Pack containing 4 tablets of 10 mg, 4 tablets of 20 mg
and 19 tablets of 30 mg,
Otezla[®],
Amgen Australia Pty Ltd**

1 Purpose of Application

- 1.1 The Category 3 submission requested changing the treatment criteria of apremilast (Otezla[®]) to allow accredited dermatology registrars to initiate treatment in consultation with a dermatologist; and to allow general practitioners to prescribe maintenance treatment of severe chronic plaque psoriasis in patients who have failed treatment with, or who are contraindicated or intolerant to, methotrexate.

2 Background

Registration status

- 2.1 Apremilast was registered in the Australian Register of Therapeutic Goods on 19 March 2015 for the treatment of signs and symptoms of active psoriatic arthritis in adult patients; and the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

Previous PBAC consideration

- 2.2 Apremilast is on the PBS as a General Schedule, Authority Required (STREAMLINED) listing for the treatment of severe chronic plaque psoriasis in patients who have failed treatment with, or who are contraindicated or intolerant to, methotrexate.
- 2.3 At its July 2020 PBAC meeting, the PBAC noted that apremilast could be prescribed by either a dermatologist or a general physician with expertise in the management of plaque psoriasis, while the ciclosporin listing for severe psoriasis was limited to dermatologists only. The PBAC advised that the treatment criteria for apremilast should match that of ciclosporin hence be limited to 'dermatologists only' (paragraph 3.4 - apremilast Public Summary Documents (PSD) - July 2020 PBAC Meeting).

For more detail on PBAC's view, see section 5 PBAC outcome.

3 Requested listing

3.1 The submission proposed the following changes to existing treatment criteria for apremilast. The restriction has been produced in full in section 3.5.

PBS item 12218C (titration pack)

| | |
|--------|---|
| [8052] | Treatment criteria: |
| New | Must be treated by a dermatologist or by an accredited dermatology registrar in consultation with a dermatologist |

PBS item 12223H (maintenance pack)

| | |
|--------|--|
| [8052] | Treatment criteria: |
| New | Must be treated by a dermatologist or by an accredited dermatology registrar in consultation with a dermatologist for the first prescription under this item code. |

- 3.2 The submission also proposed not to transfer prescribing responsibility until the second script for a maintenance pack i.e. after 6 months of therapy.
- 3.3 The submission considered it appropriate for a dermatologist (or registrar) to prescribe the first maintenance pack and then to manage any emergent side effects and assess response to treatment over the first 6 months of therapy.
- 3.4 The Secretariat proposed the following changes to the existing restriction to simplify the treatment criteria for both PBS items (titration pack and maintenance pack).
- 3.5 Suggested additions are in *italics* and deletions are in strikethrough

| Name, Restriction, Manner of administration and form | PBS item code | Max. qty packs | Max. qty units | №.of Rpts | Proprietary Name and Manufacturer | |
|---|---------------|----------------|----------------|-----------|-----------------------------------|----------------------------|
| APREMILAST | | | | | | |
| apremilast 10 mg tablet [4] (& apremilast 20 mg tablet [4] (& apremilast 30 mg tablet [19], 27 | 12218C | 1 | 27 | 0 | Otezla Titration Pack | Amgen Australia Pty Ltd |
| apremilast 30 mg tablet, 56 | 12223H | 1 | 56 | 5 | Otezla | Otezla |
| Restriction Summary 11098 / ToC: 11115: Authority Required: Streamlined | | | | | | |
| Category / Program: GENERAL – General Schedule (Code GE) | | | | | | |
| Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners | | | | | | |
| Restriction type: <input checked="" type="checkbox"/> Authority Required – Streamlined (11115) | | | | | | |
| Administrative Advice: No increase in the maximum quantity or number of units may be authorised. | | | | | | |
| Administrative Advice: No increase in the maximum number of repeats may be authorised. | | | | | | |
| Administrative Advice: Special pricing arrangements apply. | | | | | | |
| Indication: Severe <i>chronic</i> plaque psoriasis | | | | | | |
| Clinical criteria: | | | | | | |

| | |
|--|---|
| | Patient must have failed to achieve an adequate response after at least 6 weeks of treatment with methotrexate prior to initiating treatment with this drug; or |
| | Patient must have a contraindication to methotrexate according to the Therapeutic Goods Administration (TGA) approved Product Information; or |
| | Patient must have demonstrated severe intolerance of, or toxicity due to, methotrexate |
| | AND |
| | Clinical criteria: |
| | The condition must have caused significant interference with quality of life |
| | AND |
| | Clinical criteria: |
| | Patient must not be undergoing concurrent PBS-subsidised treatment for psoriasis with each of: (i) a biological medicine, (ii) ciclosporin |
| | AND |
| | Treatment criteria: |
| | Must be treated by a dermatologist; OR |
| | <i>Must be treated by a medical practitioner (other than a specialist specified above) who has consulted a specialist as specified above where treatment is being initiated, OR</i> |
| | <i>Must be treated by a medical practitioner (other than a specialist specified above) where treatment is being continued.</i> |
| | AND |
| | Population criteria: |
| | Patient must be aged 18 years or older |

4 Consideration of the evidence

Sponsor hearing

4.1 There was no hearing for this item as it was a Category 3 submission.

Consumer comments

4.2 The PBAC noted and welcomed the input from an organisation (1) via the Consumer Comments facility on the PBS website. Creaky Joints Australia (Part of Global Healthy Living Foundation Australia Pty Ltd) supported the proposed change to the treatment criteria for apremilast, and noted it would significantly help patients living in rural and remote areas gain greater access to care.

Clinical study

4.3 The submission provided the following safety reports. As a Category 3 submission, no evaluation of the safety reports was undertaken.

Table 1: Trials and associated reports presented in the submission

| Trial ID/First Author | Protocol title/ Publication title | Publication citation |
|------------------------------|--|--|
| Jeffrey Crowley et al | Long-term safety and tolerability of apremilast in patients with psoriasis: Pooled safety analysis for ≥156 weeks from 2 phase 3, randomized, controlled trials (ESTEEM 1 and 2) | J AM ACAD DERMATOL Volume 77, Number 2, p 310-317, August 2017 |
| Kristina Callis-Duffin et al | Long-term Safety of Apremilast Treatment in Patients With Psoriasis or Psoriatic Arthritis: Pooled Analysis of Phase 3 Studies Over 5 Years | American Academy of Dermatology Annual Meeting March 20–24, 2020; Denver (Poster presentation) |
| Amgen Inc. | Periodic Benefit-Risk Evaluation Report/Periodic Safety Update Report Period Covered By this Report: 21 March 2020 to 20 March 2021 | Date of Report 17 May 2021 |

Source: submission documents

- 4.4 The submission stated that apremilast is well tolerated with minimal risk of severe or serious side effects. Common or very common mild to moderate side effects, include diarrhoea, nausea, upper respiratory tract infections, nasopharyngitis, headache and tension headache which, occur primarily within the first two weeks of treatment and are generally self-resolving. Only a small percentage of patients with these side-effects require dose adjustment or discontinuation of therapy.
- 4.5 The submission considered the proposed treatment criteria allowing initiation treatment of apremilast by a dermatology registrar is similar to the treatment criteria for PBS-listed medicines dexamethasone and aflibercept. Dexamethasone and aflibercept are ophthalmologicals listed on the PBS with the treatment criterion ‘Must be treated by an ophthalmologist or by an accredited ophthalmology registrar in consultation with an ophthalmologist’.
- 4.6 The submission stated GP continuation of apremilast is permitted in many countries including the US, Canada, the UK and Austria.
- 4.7 The submission stated that apremilast is well suited for GP continuation for the following reasons:
- Being an oral therapy, administration of apremilast is not complicated;
 - Mild-moderate adverse events occur early in the treatment course and tend to self-resolve; and
 - Unlike other psoriasis treatments, there are no monitoring requirements for apremilast.
- 4.8 The submission did not include any financial estimates to support the requested change.
- 4.9 The submission stated no change in utilisation of apremilast is anticipated as result of changing the treatment criteria. No evidence was provided in the submission to support this statement.

For more detail on PBAC's view, see section 5 PBAC outcome.

5 PBAC Outcome

- 5.1 The PBAC recommended amendments to the treatment criteria for apremilast to allow accredited dermatology registrars to initiate treatment in consultation with a dermatologist and to allow general practitioners to prescribe maintenance treatment in consultation with a dermatologist or accredited dermatology registrar.
- 5.2 The PBAC noted the Sponsor's claim that apremilast is well tolerated with minimal risk of severe or serious side effects.
- 5.3 The PBAC noted the Sponsor's claim that apremilast is well suited for GP continuation for the following reasons:
 - Being an oral therapy, administration of apremilast is not complicated;
 - Mild-moderate adverse events occur early in the treatment course and tend to self-resolve; and
 - Unlike other psoriasis treatments, there are no monitoring requirements for apremilast.
- 5.4 The PBAC noted that no change in utilisation of apremilast is anticipated as result of changing the treatment criteria.
- 5.5 The PBAC advised that the changes to the initial treatment criteria of apremilast to include dermatology registrar prescribing should flow-on to ciclosporin for the treatment of severe psoriasis.
- 5.6 The PBAC noted that, given the treatment criteria changes to Otezla are not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met.
- 5.7 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

6 Recommended listing

- 6.1 Amend existing treatment criteria as follows:

Public Summary Document – March 2022 PBAC Meeting with May 2022 Corrigendum

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| Indication: Severe <i>chronic</i> plaque psoriasis |
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| Patient must have a contraindication to methotrexate according to the Therapeutic Goods Administration (TGA) approved Product Information; or |
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| AND |
| Clinical criteria: |
| The condition must have caused significant interference with quality of life |
| AND |
| Clinical criteria: |
| Patient must not be undergoing concurrent PBS-subsidised treatment for psoriasis with each of: (i) a biological medicine, (ii) ciclosporin |
| AND |
| Treatment criteria: |
| Must be treated by a dermatologist <i>or by an accredited dermatology registrar in consultation with a dermatologist; OR</i> |
| <i>Must be treated by a general practitioner in consultation with a dermatologist or accredited dermatology registrar where treatment is being continued.</i> |
| AND |
| Population criteria: |
| Patient must be aged 18 years or older |

- 6.2 Flow-on changes to ciclosporin's existing treatment criteria for the treatment of severe psoriasis to allow dermatology registrars to prescribe (PBS item codes: 5633L, 6125J, 5632K, 6232B, 5635N, 6353J, 5634M, 6352H, 5636P and 6354K).

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| Treatment criteria: |
| Must be treated by a dermatologist <i>or by an accredited dermatology registrar in consultation with a dermatologist</i> |

This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.

7 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

8 Sponsor's Comment

The sponsor had no comment.