

**6.21 TILDRAKIZUMAB,
Injection 100 mg in 1 mL single dose pre-filled
syringe,
Ilumya[®],
Sun Pharma ANZ Pty Ltd**

1 Purpose of Submission

- 1.1 The Category 3 submission requested adding a grandfathering restriction to the existing Pharmaceutical Benefits Scheme (PBS) listing for tildrakizumab injection 100 mg in 1 mL single dose pre-filled syringe (herein referred to as tildrakizumab) (Ilumya[®]) for the treatment of severe chronic plaque psoriasis (CPP) to allow PBS access to patients enrolled in two new clinical trials.

2 Background

- 2.1 Tildrakizumab is currently listed on the PBS as an Authority Required (Written) listing for severe CPP.

Registration status

- 2.2 Tildrakizumab was Therapeutic Goods Administration (TGA) registered on 10 September 2018 for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy.

Previous PBAC consideration

- 2.3 At its July 2018 meeting, the PBAC recommended tildrakizumab for the treatment of severe CPP. It was subsequently listed on the PBS on 1 February 2019.
- 2.4 In the July 2018 submission, it was 'proposed that a grandfather clause be incorporated in the listing, to allow approximately 250-350 patients in a TIL (tildrakizumab) Patient Familiarisation Program (PFP) to transition to PBS subsidised TIL. Furthermore, the submission stated that 58 patients currently enrolled in clinical trials would need to be grandfathered across to PBS supply' (paragraph 2.3, tildrakizumab, Public Summary Document (PSD), July 2018 PBAC Meeting).
- 2.5 In July 2018, the PBAC considered that it would be appropriate to provide grandfathered PBS supply to patients receiving tildrakizumab who had met initial treatment criteria at the time of entering the clinical trials or the PFP, and that the grandfather provision should be removed from the listing after 12 months (paragraph 7.4, tildrakizumab PSD, July 2018 PBAC Meeting).
- 2.6 The current submission stated that the sponsor previously agreed that the grandfather restrictions were no longer required, however the sponsor did not realise

that removal of the grandfathering restriction may prevent access to subsidised treatment for patients participating in new and ongoing clinical trials.

2.7 The submission noted the PBAC recommended at its March 2022 meeting the extension of a grandfathered listing for risankizumab (RIS) beyond 12 months for severe CPP to allow patients to transition to PBS-subsidised treatment from a clinical trial that finished after the standard grandfathering period elapsed.

- In July 2019 the PBAC recommended PBS-listing of RIS for severe CPP, ‘including the requested grandfather restriction.... The PBAC advised that grandfathered patients will be required to meet the PBS eligibility criteria and that the grandfather restriction be removed from the listing after 12 months in line with standard procedure. The PBAC noted a number of clinical trial patients are expected to transition to PBS-subsidised RIS in January 2022. The PBAC were supportive of allowing the clinical trial patients to transition to PBS-subsidised treatment but advised that an additional submission would be required closer to the date of trial completion to extend the grandfathering clause’ (paragraph 7.8, risankizumab, PSD, July 2019 PBAC Meeting).
- At its March 2022 meeting, the PBAC recommended the extension of the listing of RIS for severe CPP to allow access for patients enrolled in the RIS open label extension trial to be grandfathered on to PBS-subsidised RIS (paragraph 5.1, risankizumab, PSD, March 2022 PBAC Meeting).

3 Requested listing

3.1 The submission requested the following new grandfather restrictions be added to the existing listing:

Add new restriction as follows:

3.2 Suggested additions are in italics and deletions are in strikethrough.

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
TILDRAKIZUMAB					
<i>tildrakizumab 100 mg/mL injection, 1 mL syringe</i>	<i>NEW</i>	<i>1</i>	<i>1</i>	<i>1</i>	<i>Ilumya</i>
Restriction Summary [new] / Treatment of Concept: [new]					
Concept ID (for internal Dept. use)	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required (in writing only via post/HPOS upload)				
PR level	Administrative Advice: TREATMENT OF ADULT PATIENTS WITH SEVERE CHRONIC PLAQUE PSORIASIS The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of the biological medicines adalimumab, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab and ustekinumab for adult patients with severe chronic plaque psoriasis. Therefore, where the term 'biological medicines' appears in notes and restrictions, it refers to				

	<p>adalimumab, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab only.</p> <p>A patient is eligible for PBS-subsidised treatment with only 1 of the above biological medicines at any 1 time.</p> <p>A patient who received PBS-subsidised adalimumab, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab treatment prior to 1 February 2019 is considered to start their first cycle as of 1 February 2019.</p> <p>A patient receiving PBS-subsidised treatment for chronic plaque psoriasis is able to commence a 'treatment cycle', where they may trial biological medicines without having to experience a disease flare, when swapping to an alternate biological medicine. Under these arrangements, within a single cycle, a patient may receive long-term treatment with a biological medicine as long as they sustain a response to therapy.</p> <p>Within the same treatment cycle, a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised biological medicine more than once. Therefore, once a patient fails to meet the response criteria for a PBS-subsidised biological medicine, they must change to an alternate biological medicine if they wish to continue PBS-subsidised biological treatment.</p> <p>Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment, including serious infusion or injection related reactions, Steven's Johnson Syndrome, development of a demyelinating lesion, progressive multifocal leukoencephalopathy and malignancy related to treatment with the biological medicine, is not considered as a treatment failure.</p> <p>A patient must be assessed for response to each course of treatment according to the criteria included in the relevant continuing treatment restriction.</p> <p>Once a patient has either failed or ceased to sustain a response to treatment 3 times, they are deemed to have completed a treatment cycle and they must have, at a minimum, a 5-year break in PBS-subsidised biological medicine therapy before they are eligible to commence the next cycle.</p> <p>The duration of the break in therapy will be measured from the date the last prescription for PBS-subsidised treatment was approved in the most recent cycle to the date of the first application for initial treatment with a biological medicine under the new cycle.</p> <p>A patient who has failed fewer than 3 biological medicines in a treatment cycle and who has a break in therapy of more than 5 years may commence a new treatment cycle under Initial 3 treatment restriction.</p> <p>A patient who has failed fewer than 3 biological medicines in a treatment cycle and who has a break in therapy of less than 5 years may commence a further course of treatment within the same treatment cycle under Initial 2 treatment restriction.</p> <p>There is no limit to the number of treatment cycles a patient may undertake in their lifetime.</p> <p>How to prescribe PBS-subsidised biological medicine treatment for severe chronic plaque psoriasis.</p> <p>There are separate restrictions for both the initial and continuing treatment for psoriasis affecting the whole body, versus psoriasis affecting the face, hands and feet.</p> <p>(1) Initial treatment.</p> <p>An application for initial treatment should be made where:</p> <ul style="list-style-type: none"> (i) a patient has not received prior PBS-subsidised biological medicine treatment for this condition and wishes to commence such therapy (Initial 1 - New patient); or (ii) a patient who has received prior PBS-subsidised biological medicine therapy for this condition (initial or continuing) and wishes to trial an alternate biological medicine (Initial 2 - Change or Recommencement of treatment after a break in biological medicine of less than 5 years) [further details are under (4) 'Swapping therapy' below]; or (iii) a patient wishes to recommence treatment with a specific biological medicine following a break in PBS-subsidised therapy of less than 5 years with the same medicine (Initial 2 - Change or Recommencement of treatment after a break in biological medicine of less than 5 years). (iv) a patient wishes to recommence treatment with a biological medicine following a break in PBS-subsidised therapy of more than 5 years (Initial 3 - Recommencement of treatment after a break in biological medicine of more than 5 years). <p>An application for initial treatment will be limited to provide for a maximum of 16 weeks of therapy for adalimumab, etanercept, ixekizumab, and secukinumab, 20 weeks of therapy for guselkumab, 22 weeks of therapy for infliximab and 28 weeks of therapy for risankizumab, tildrakizumab and ustekinumab.</p>
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	<p>It is recommended that a patient is reviewed for response following a minimum of 12 weeks of therapy and no later than 4 weeks from the completion of their course of initial treatment to ensure uninterrupted biological medicine supply.</p> <p>Grandfather patients (risankizumab and <i>tildrakizumab</i> only).</p> <p>A patient who commenced treatment with risankizumab for chronic plaque psoriasis prior to 1 August 2022, or <i>tildrakizumab</i> prior to [date of listing], and who continues to receive treatment at the time of application, may qualify for treatment under the Initial treatment Grandfather treatment restriction.</p> <p>(2) Assessment of response to initial treatment.</p> <p>When prescribing initial treatment with a biological medicine, it is recommended that a PASI assessment is conducted after at least 12 weeks of treatment and no later than 4 weeks from the completion of this initial treatment course.</p> <p>The PASI assessment for continuing treatment must be performed on the same affected area as assessed at baseline.</p> <p>(3) Continuing treatment.</p> <p>Following the completion of an initial treatment course with a specific biological medicine, a patient may qualify to receive up to 24 weeks of continuing treatment with that drug providing they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing biological medicine treatment with the same drug in courses of up to 24 weeks providing they continue to sustain the response. It is recommended that a patient is reviewed for response following a minimum of 12 weeks of therapy and no later than 4 weeks from the completion of the most recent course of treatment.</p> <p>A patient must be assessed for response to a course of continuing therapy, and the assessment must be submitted to Services Australia where applicable. Where a response assessment is not submitted where applicable, the patient will be deemed to have failed to respond to treatment with that biological medicine, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.</p> <p>Infliximab, adalimumab and etanercept only:</p> <p>For the first continuing treatment course of PBS-subsidised biological medicine treatment, it is recommended that a patient is reviewed for response following a minimum of 12 weeks of therapy under the Initial 1 or Initial 2 treatment restrictions.</p> <p>For second and subsequent continuing courses of PBS-subsidised biological medicine treatment, it is recommended that a patient is reviewed for response following a minimum of 12 weeks of therapy and no later than 4 weeks from the completion of the most recent course of treatment.</p> <p>(4) Swapping therapy.</p> <p>Once initial treatment with the first PBS-subsidised biological medicine is approved, a patient may swap to an alternate biological medicine without having to requalify with respect to the indices of disease severity (i.e. a PASI score of greater than 15), or the prior non-biological therapy requirements, except if the patient has had a break in therapy of more than 5 years who would need to requalify with respect to the indices of disease severity.</p> <p>A patient who is not able to complete a minimum of 12 weeks of an initial treatment course will be deemed to have failed treatment with that biological medicine unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.</p> <p>A patient may trial an alternate biological medicine at any time, regardless of whether they are receiving therapy (initial or continuing) with a biological medicine at the time of the application. However, they cannot swap to a particular biological medicine if they have failed to respond to prior treatment with that particular biological medicine within the same cycle or have experienced treatment failure with that particular biological medicine that required permanent treatment withdrawal.</p> <p>To ensure a patient receives the maximum treatment opportunities allowed under these arrangements, it is important that they are assessed for response to every course of treatment.</p> <p>(5) Baseline measurements to determine response.</p> <p>A response to treatment is to be determined by comparison of current disease activity measurements relative to the baseline PASI assessment submitted with the first authority application for a biological medicine. However, prescribers may provide new baseline PASI assessments any time that an initial or change or recommencement treatment application is submitted within a treatment cycle and this</p>
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		<p>revised baseline PASI score will be used to assess the patient's response to the PBS-subsidised treatment.</p> <p>To ensure consistency in determining response, the same body area assessed at the baseline PASI assessment must be assessed for demonstration of response to treatment for the purposes of all continuing treatments.</p> <p>(6) Recommencement of treatment after a 5-year break in PBS-subsidised therapy.</p> <p>A patient who wishes to trial a second or subsequent treatment cycle following a break in PBS-subsidised biological therapy of at least 5 years, must qualify under Initial 3 treatment according to the criteria of the relevant restriction and index of disease severity. A PASI assessment must be conducted prior to application and patient must have a PASI score of greater than 15 for whole body. For the face, hand, foot at least 2 of the 3 PASI symptom subscores for erythema, thickness and scaling are rated as severe or very severe; or the skin area affected is 30% or more of the face, palm of a hand or sole of a foot. The PASI assessment must be no older than 4 weeks at the time of application.</p>
PR level		<p>Administrative Advice: No increase in the maximum quantity or number of units may be authorised.</p>
		<p>Administrative Advice: No increase in the maximum number of repeats may be authorised.</p>
		<p>Administrative Advice: Special Pricing Arrangements apply.</p>
		<p>Indication: Severe chronic plaque psoriasis</p>
		<p>Treatment Phase: <i>Grandfather treatment, Whole body (initial PBS-subsidised supply for continuing treatment in a patient commenced on non-PBS-subsidised therapy)</i></p>
		<p>Clinical criteria:</p>
		<p>Patient must have severe chronic plaque psoriasis where lesions had been present for at least 6 months from the time of initial diagnosis prior to initiating non-PBS-subsidised treatment</p>
		<p>AND</p>
		<p>Clinical criteria:</p>
		<p>Patient must have received non-PBS-subsidised treatment with this drug for this PBS indication prior to [insert date of listing]</p>
		<p>AND</p>
		<p>Clinical criteria:</p>
		<p><i>Patient must have had a documented history of a Psoriasis Area and Severity Index (PASI) score of greater than 15 prior to commencing non-PBS- subsidised treatment with this drug,</i></p>
		<p>AND</p>
		<p>Clinical criteria:</p>
		<p><i>Patient must have demonstrated an adequate response to their most recent course of non-PBS-subsidised treatment with this drug,</i></p>
		<p>AND</p>
		<p>Clinical criteria:</p>
		<p>The treatment must be as systemic monotherapy (other than methotrexate),</p>
		<p>AND</p>
		<p>Clinical criteria:</p>
		<p>Patient must not receive more than 24 weeks of treatment under this restriction.</p>
		<p>Treatment criteria:</p>
		<p>Must be treated by a dermatologist.</p>
		<p>Population criteria:</p>
		<p>Patient must be at least 18 years of age</p>

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	<p>Prescribing Instructions: An adequate response to treatment is defined as: A Psoriasis Area and Severity Index (PASI) score which is reduced by 75% or more, or is sustained at this level, when compared with the baseline value taken prior to receiving non-PBS-subsidised treatment.</p>
	<p>Prescribing Instructions: The authority application must be made in writing and must include: (1) a completed authority prescription form(s); and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice) which includes the following: (i) the completed current and previous Psoriasis Area and Severity Index (PASI) calculation sheets including the dates of assessment of the patient's condition at baseline (prior to initiation of non-PBS-subsidised therapy with this drug) and the most recent PASI assessment; and (ii) details of previous phototherapy and systemic drug therapy [dosage (where applicable), date of commencement and duration of therapy].</p>
	<p>Prescribing Instructions: The most recent PASI assessment must be no more than 4 weeks old at the time of application.</p>
	<p>Prescribing Instructions: If a patient fails to demonstrate a response to treatment with this drug under this restriction they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition.</p>
	<p>Administrative Advice: A Grandfathered patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the continuing treatment criteria.</p>
	<p>Administrative Advice: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.</p>
	<p>Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
<p>Restriction Summary [new] / Treatment of Concept: [new]</p>	
<p>Concept ID (for internal Dept. use)</p>	<p>Category / Program: GENERAL – General Schedule (Code GE)</p>
	<p>Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners</p>
	<p>Restriction type: <input checked="" type="checkbox"/> Authority Required (in writing only via post/HPOS upload)</p>
<p>PR level</p>	<p>Administrative Advice: TREATMENT OF ADULT PATIENTS WITH SEVERE CHRONIC PLAQUE PSORIASIS The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of the biological medicines adalimumab, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab and ustekinumab for adult patients with severe chronic plaque psoriasis. Therefore, where the term 'biological medicines' appears in notes and restrictions, it refers to adalimumab, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab only.</p>

	<p>A patient is eligible for PBS-subsidised treatment with only 1 of the above biological medicines at any 1 time.</p> <p>A patient who received PBS-subsidised adalimumab, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab treatment prior to 1 February 2019 is considered to start their first cycle as of 1 February 2019.</p> <p>A patient receiving PBS-subsidised treatment for chronic plaque psoriasis is able to commence a 'treatment cycle', where they may trial biological medicines without having to experience a disease flare, when swapping to an alternate biological medicine. Under these arrangements, within a single cycle, a patient may receive long-term treatment with a biological medicine as long as they sustain a response to therapy.</p> <p>Within the same treatment cycle, a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised biological medicine more than once. Therefore, once a patient fails to meet the response criteria for a PBS-subsidised biological medicine, they must change to an alternate biological medicine if they wish to continue PBS-subsidised biological treatment.</p> <p>Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment, including serious infusion or injection related reactions, Steven's Johnson Syndrome, development of a demyelinating lesion, progressive multifocal leukoencephalopathy and malignancy related to treatment with the biological medicine, is not considered as a treatment failure.</p> <p>A patient must be assessed for response to each course of treatment according to the criteria included in the relevant continuing treatment restriction.</p> <p>Once a patient has either failed or ceased to sustain a response to treatment 3 times, they are deemed to have completed a treatment cycle and they must have, at a minimum, a 5-year break in PBS-subsidised biological medicine therapy before they are eligible to commence the next cycle.</p> <p>The duration of the break in therapy will be measured from the date the last prescription for PBS-subsidised treatment was approved in the most recent cycle to the date of the first application for initial treatment with a biological medicine under the new cycle.</p> <p>A patient who has failed fewer than 3 biological medicines in a treatment cycle and who has a break in therapy of more than 5 years may commence a new treatment cycle under Initial 3 treatment restriction.</p> <p>A patient who has failed fewer than 3 biological medicines in a treatment cycle and who has a break in therapy of less than 5 years may commence a further course of treatment within the same treatment cycle under Initial 2 treatment restriction.</p> <p>There is no limit to the number of treatment cycles a patient may undertake in their lifetime.</p> <p>How to prescribe PBS-subsidised biological medicine treatment for severe chronic plaque psoriasis.</p> <p>There are separate restrictions for both the initial and continuing treatment for psoriasis affecting the whole body, versus psoriasis affecting the face, hands and feet.</p> <p>(1) Initial treatment.</p> <p>An application for initial treatment should be made where:</p> <ul style="list-style-type: none"> (i) a patient has not received prior PBS-subsidised biological medicine treatment for this condition and wishes to commence such therapy (Initial 1 - New patient); or (ii) a patient who has received prior PBS-subsidised biological medicine therapy for this condition (initial or continuing) and wishes to trial an alternate biological medicine (Initial 2 - Change or Recommencement of treatment after a break in biological medicine of less than 5 years) [further details are under (4) 'Swapping therapy' below]; or (iii) a patient wishes to recommence treatment with a specific biological medicine following a break in PBS-subsidised therapy of less than 5 years with the same medicine (Initial 2 - Change or Recommencement of treatment after a break in biological medicine of less than 5 years). (iv) a patient wishes to recommence treatment with a biological medicine following a break in PBS-subsidised therapy of more than 5 years (Initial 3 - Recommencement of treatment after a break in biological medicine of more than 5 years). <p>An application for initial treatment will be limited to provide for a maximum of 16 weeks of therapy for adalimumab, etanercept, ixekizumab, and secukinumab, 20 weeks of therapy for guselkumab, 22 weeks of therapy for infliximab and 28 weeks of therapy for risankizumab, tildrakizumab and ustekinumab.</p>
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	<p>It is recommended that a patient is reviewed for response following a minimum of 12 weeks of therapy and no later than 4 weeks from the completion of their course of initial treatment to ensure uninterrupted biological medicine supply.</p> <p>Grandfather patients (risankizumab and <i>tildrakizumab</i> only).</p> <p>A patient who commenced treatment with risankizumab for chronic plaque psoriasis prior to 1 August 2022, or <i>tildrakizumab</i> prior to [date of listing], and who continues to receive treatment at the time of application, may qualify for treatment under the Initial treatment Grandfather treatment restriction.</p> <p>(2) Assessment of response to initial treatment.</p> <p>When prescribing initial treatment with a biological medicine, it is recommended that a PASI assessment is conducted after at least 12 weeks of treatment and no later than 4 weeks from the completion of this initial treatment course.</p> <p>The PASI assessment for continuing treatment must be performed on the same affected area as assessed at baseline.</p> <p>(3) Continuing treatment.</p> <p>Following the completion of an initial treatment course with a specific biological medicine, a patient may qualify to receive up to 24 weeks of continuing treatment with that drug providing they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing biological medicine treatment with the same drug in courses of up to 24 weeks providing they continue to sustain the response. It is recommended that a patient is reviewed for response following a minimum of 12 weeks of therapy and no later than 4 weeks from the completion of the most recent course of treatment.</p> <p>A patient must be assessed for response to a course of continuing therapy, and the assessment must be submitted to Services Australia where applicable. Where a response assessment is not submitted where applicable, the patient will be deemed to have failed to respond to treatment with that biological medicine, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.</p> <p>Infliximab, adalimumab and etanercept only:</p> <p>For the first continuing treatment course of PBS-subsidised biological medicine treatment, it is recommended that a patient is reviewed for response following a minimum of 12 weeks of therapy under the Initial 1 or Initial 2 treatment restrictions.</p> <p>For second and subsequent continuing courses of PBS-subsidised biological medicine treatment, it is recommended that a patient is reviewed for response following a minimum of 12 weeks of therapy and no later than 4 weeks from the completion of the most recent course of treatment.</p> <p>(4) Swapping therapy.</p> <p>Once initial treatment with the first PBS-subsidised biological medicine is approved, a patient may swap to an alternate biological medicine without having to requalify with respect to the indices of disease severity (i.e. a PASI score of greater than 15), or the prior non-biological therapy requirements, except if the patient has had a break in therapy of more than 5 years who would need to requalify with respect to the indices of disease severity.</p> <p>A patient who is not able to complete a minimum of 12 weeks of an initial treatment course will be deemed to have failed treatment with that biological medicine unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.</p> <p>A patient may trial an alternate biological medicine at any time, regardless of whether they are receiving therapy (initial or continuing) with a biological medicine at the time of the application. However, they cannot swap to a particular biological medicine if they have failed to respond to prior treatment with that particular biological medicine within the same cycle or have experienced treatment failure with that particular biological medicine that required permanent treatment withdrawal.</p> <p>To ensure a patient receives the maximum treatment opportunities allowed under these arrangements, it is important that they are assessed for response to every course of treatment.</p> <p>(5) Baseline measurements to determine response.</p> <p>A response to treatment is to be determined by comparison of current disease activity measurements relative to the baseline PASI assessment submitted with the first authority application for a biological medicine. However, prescribers may provide new baseline PASI assessments any time that an initial or change or recommencement treatment application is submitted within a treatment cycle and this</p>
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		<p>revised baseline PASI score will be used to assess the patient's response to the PBS-subsidised treatment.</p> <p>To ensure consistency in determining response, the same body area assessed at the baseline PASI assessment must be assessed for demonstration of response to treatment for the purposes of all continuing treatments.</p> <p>(6) Recommencement of treatment after a 5-year break in PBS-subsidised therapy.</p> <p>A patient who wishes to trial a second or subsequent treatment cycle following a break in PBS-subsidised biological therapy of at least 5 years, must qualify under Initial 3 treatment according to the criteria of the relevant restriction and index of disease severity. A PASI assessment must be conducted prior to application and patient must have a PASI score of greater than 15 for whole body. For the face, hand, foot at least 2 of the 3 PASI symptom subscores for erythema, thickness and scaling are rated as severe or very severe; or the skin area affected is 30% or more of the face, palm of a hand or sole of a foot. The PASI assessment must be no older than 4 weeks at the time of application.</p>
PR level		<p>Administrative Advice: No increase in the maximum quantity or number of units may be authorised.</p>
		<p>Administrative Advice: No increase in the maximum number of repeats may be authorised.</p>
		<p>Administrative Advice: Special Pricing Arrangements apply.</p>
		<p>Indication: Severe chronic plaque psoriasis</p>
		<p>Treatment Phase: <i>Grandfather treatment- Face, hand and foot (initial PBS-subsidised supply for continuing treatment in a patient commenced on non-PBS-subsidised therapy)</i></p>
		<p>Clinical criteria:</p>
		<p>Patient must have severe chronic plaque psoriasis of the face, or palm of a hand or sole of a foot, where lesions have been present for at least 6 months from the time of initial diagnosis prior to initiating non-PBS-subsidised treatment</p>
		<p>AND</p>
		<p>Clinical criteria:</p>
		<p>Patient must have received non-PBS-subsidised treatment with this drug for this PBS indication prior to [insert date of listing]</p>
		<p>AND</p>
		<p>Clinical criteria:</p>
		<p>Patient must have had a documented history of disease, prior to commencing non-PBS- subsidised treatment with this drug, classified as severe due to a plaque or plaques on the face, palm of a hand or sole of a foot where: (i) at least 2 of the 3 Psoriasis Area and Severity Index (PASI) symptom subscores for erythema, thickness and scaling are were rated as severe or very severe; or (ii) the skin area affected is was 30% or more of the face, palm of a hand or sole of a foot,</p>
		<p>AND</p>
		<p>Clinical criteria:</p>
		<p><i>Patient must have demonstrated an adequate response to their most recent course of non-PBS-subsidised treatment with this drug (face, hand and foot),</i></p>
		<p>AND</p>
		<p>Clinical criteria:</p>
		<p>The treatment must be as systemic monotherapy (other than methotrexate),</p>
		<p>AND</p>
		<p>Clinical criteria:</p>
		<p>Patient must not receive more than 24 weeks of treatment under this restriction.</p>
		<p>Treatment criteria:</p>
		<p>Must be treated by a dermatologist.</p>
		<p>Population criteria:</p>

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	Patient must be at least 18 years of age
	<p>Prescribing Instructions: An adequate response to treatment is defined as the plaque or plaques assessed prior to biological treatment showing:</p> <p>(i) a reduction in the Psoriasis Area and Severity Index (PASI) symptom subscores for all 3 of erythema, thickness and scaling, to slight or better, or sustained at this level, as compared to the baseline values; or</p> <p>(ii) a reduction by 75% or more in the skin area affected, or sustained at this level, as compared to the baseline value for this treatment cycle.</p>
	<p>Prescribing Instructions: The authority application must be made in writing and must include:</p> <p>(1) a completed authority prescription form(s); and</p> <p>(2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice) which includes the following:</p> <p>(i) the completed current and previous Psoriasis Area and Severity Index (PASI) calculation sheets, and the face, hand, foot area diagrams including the dates of assessment of the patient's condition at baseline (prior to initiation of therapy with this drug) and the most recent PASI assessment; and</p> <p>(ii) details of previous phototherapy and systemic drug therapy [dosage (where applicable), date of commencement and duration of therapy]</p>
	<p>Prescribing Instructions: The most recent PASI assessment must be no more than 4 weeks old at the time of application.</p>
	<p>Prescribing Instructions: If a patient fails to demonstrate a response to treatment with this drug under this restriction they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition within this treatment cycle.</p>
	<p>Administrative Advice: <i>Where treatment has been commenced via non-PBS supply, the current PASI score of greater than 15 in (a) refers to a PASI measurement taken prior to commencing non-PBS supply of a biological medicine with the PBS indication of severe chronic plaque psoriasis, but following the specified prior therapies (i.e. phototherapy, methotrexate, ciclosporin, acitretin, apremilast). As a result, the PASI score can be more than 4 weeks old at the time of this application in these circumstances. For continuing treatment after this application, continued PBS subsidy is to be through either the Continuing treatment phase listing, or, an Initial 2 treatment phase listing.</i></p>
	<p>Administrative Advice: A Grandfathered patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the continuing treatment criteria.</p>
	<p>Administrative Advice: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.</p>
	<p>Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

- 3.3 Grandfather restrictions were requested for patients participating in two tildrakizumab clinical trials: TILD-18-20 (Clinicaltrials.gov NCT03897088) and TILD-18-19 (Clinicaltrials.gov NCT03897075). The submission estimated that < 500 patients from TILD-18-20 and < 500 patients from TILD-18-19 would require PBS access through the grandfathering restriction if recommended by the PBAC. TILD-18-20 had been completed (with patients receiving ongoing compassionate access through the sponsor). TILD-18-19 is an ongoing clinical trial and is expected to be completed in May 2024.
- 3.4 The submission requested a grandfather criterion for patients who met the requirement of a Psoriasis Area and Severity Index (PASI) score of >15 at baseline when entering the clinical trials but would not satisfy this initial treatment criterion when transitioning from the clinical trial to PBS treatment. The PBAC noted the clinical trials presented in both this submission and the July 2018 submission had an inclusion criterion of PASI score >12.

4 Consideration of the evidence

Sponsor hearing

- 4.1 There was no hearing for this item.

Consumer comments

- 4.2 The PBAC noted and welcomed the input from The Australasian College of Dermatologists which stated that the addition of the grandfathering restriction would enable patients to continue with timely, affordable and quality treatment.

Clinical trials

- 4.3 The submission included three clinical trials of tildrakizumab, comparing key eligibility criteria rather than outcomes. Two of the trials (Papp et al and Reich et al) were included in the submission considered by the PBAC in July 2018, and one was a new trial published in 2021. Details of the trials provided in the submission are presented in the table below.

Table 1: Trials provided in the submission

Trial ID	Publication title	Publication citation
reSURFACE 1 (TIL ₁) and reSURFACE 2 (TIL ₂)	Reich K, Papp K, Blauvelt A, et al. Tildrakizumab versus placebo or etanercept for chronic plaque psoriasis (reSURFACE 1 and reSURFACE 2): Results from two randomised controlled, phase 3 trials.	Lancet 2017; 390: 276-288
Phase IIb trial (TIL ₃)	Papp K, Thaci D, Reich K et al. Tildrakizumab (MK-3222), an anti-interleukin-23p19 monoclonal antibody, improves psoriasis in a phase IIb randomised placebo-controlled trial.	British Journal of Dermatology 2015; 173: 930-939
NCT01722331 and NCT01729754	Thaci D, Piaserico S, Warren RB et al. Five-year efficacy and safety of tildrakizumab in patients with moderate-to-severe psoriasis who respond at week 28: pooled analyses of two randomized phase III clinical trials.	British Journal of Dermatology 2021; 185: 323-334

- 4.4 The submission included details of the eligibility criteria for the three published clinical trials presented in the 2018 submission and the two trials for which the new grandfathering restriction was requested.

Economic analysis

- 4.5 No changes to the price of tildrakizumab were proposed. The submission stated that as tildrakizumab is currently listed on the PBS and the request was to reinstate the original grandfathering restriction, cost-effectiveness had already been established and no economic evaluation was presented.
- 4.6 The submission stated that the current special pricing arrangement (SPA) should still apply for the requested updated listing.

Drug cost/patient/year: \$ [REDACTED]

- 4.7 The estimated drug cost/patient per year was \$ [REDACTED], based on an effective price of \$ [REDACTED] and one prescription dispensed every 12 weeks (4 times a year).

Estimated PBS usage and financial implications

- 4.8 The estimated financial implications were based on an estimated treatment duration on the PBS of approximately 5 years, and a dosing regimen of 100 mg administered subcutaneously every 12 weeks.
- 4.9 The estimated financial implications to the PBS/RPBS are presented in Table 2.
- 4.10 The submission estimated that an additional < 500 patients (< 500 patients from TILD-18-20 and < 500 patients from TILD-18-19) would be supplied tildrakizumab through the grandfather listings over the first 6 years of listing (< 500 in Year 1 to < 500 in Year 6). It was unclear if these patients were included in the financial forecast for the July 2018 submission.
- 4.11 The submission stated that the estimated net financial impact to the PBS/RPBS for the listing of a grandfathering restriction for tildrakizumab is \$0 to < \$10 million over 6 years (Year 1 \$0 to < \$10 million to Year 6 \$0 to < \$10 million) (see Table 2).

Table 2: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of patients treated	1	1	1	1	1	1
Number of scripts dispensed ^a	1	1	1	1	1	1
Estimated financial implications of the grandfather restriction for tildrakizumab (published AEMP)						
Cost to PBS/RPBS (\$)	2	2	2	2	2	2
Patient co-payment (\$)	2	2	2	2	2	2
Cost to PBS/RPBS less co-payment (\$)	2	2	2	2	2	2
SPA Rebate (\$)						
	2	2	2	2	2	2
Estimated financial implications of the grandfather restriction for tildrakizumab (effective AEMP)						
Cost to PBS/RPBS less co-payment (\$)	2	2	2	2	2	2
Net financial implications						
Net cost to PBS/RPBS (\$)	2	2	2	2	2	2

Source: Attachment 4 – UCM of the Submission, Submission main body, Table 2, p.3

^a Assuming 4.32 prescriptions per patient per year as estimated by the submission.

Abbreviations: AEMP = approved ex-manufacturer price; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme; SPA = special pricing arrangement

The redacted values correspond to the following ranges:

¹ < 500

² \$0 to < \$10 million

4.12 As a Category 3 submission, the financial estimates were not independently evaluated.

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

5 PBAC Outcome

5.1 The PBAC did not recommend adding a new grandfathering restriction to the existing PBS-listing for tildrakizumab injection 100 mg in 1 mL single dose pre-filled syringe (Ilumya) for the treatment of severe CPP for patients enrolled in two new clinical trials.

5.2 The PBAC noted that the clinical trials presented in both this submission and the July 2018 submission had an inclusion criterion of PASI score >12, however the current PBS clinical criteria for initial treatment with tildrakizumab states that the condition must have a PASI score >15. The PBAC therefore considered that it was uncertain whether the patients in the clinical trials would have been eligible for treatment with tildrakizumab through the PBS prior to starting the trials.

5.3 The PBAC noted that the sponsor had previously agreed to the removal of the original grandfathering restrictions, and that the intent of a grandfathering restriction is to allow access to subsidised treatment for eligible patients who start therapy before the requested PBS listing is implemented. The PBAC considered that patients who start therapy as part of clinical trials that commence after the medicine has been PBS listed are not ‘grandfathered’ patients.

5.4 The PBAC recalled its previous recommendation to extend the grandfathered listing beyond 12 months for risankizumab for severe CPP to allow patients to transition to

PBS-subsidised treatment from a clinical trial that finished after the standard grandfathering period elapsed. However, the PBAC recalled that the situation differed in that the patients had been enrolled in the trial at the time of the original submission and were accounted for when the PBAC made its recommendation for the listing (paragraphs 2.4 and 7.8, risankizumab, PSD, July 2019 PBAC Meeting).

5.5 The PBAC noted that this submission is eligible for an Independent Review.

Outcome:

Not recommended

6 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.

7 Sponsor's Comment

The sponsor had no comment.