6.20 TILDRAKIZUMAB, Injection 100 mg in 1 mL single dose pre-filled syringe, Ilumya®, Sun Pharma

1 Purpose of submission

1.1 The Category 3 submission requested an Authority Required listing for tildrakizumab (TIL) 200 mg for the continuing treatment of adults with severe chronic plaque psoriasis. This new listing is a request to increase the pack size and dose of the existing TIL 100 mg PBS listings.

1.2 Listing was requested on the basis of a cost-minimisation approach vs tildrakizumab 100 mg.

Table 1: Key components of the clinical issue addressed by the submission (as stated in the submission)

Component	Description
Population	Adults with severe chronic plaque psoriasis who have achieved at least a PASI75 response with tildrakizumab 100 mg
Intervention	Tildrakizumab 200 mg Q12 weekly (consisting of 2 x 100 mg injections)
Comparator	Tildrakizumab 100 mg Q12 weekly
Outcomes	PASI75 at week 28, safety
Clinical claim	Treatment with tildrakizumab 200 mg under the continuing treatment PBS restriction is non-inferior to tidrakizumab 100 mg in terms of efficacy and safety.

Source: compiled from Section 1 and 2 of the submission as no PICO table was presented.
PASI75 = Psoriasis Activity and Severity Index score reduced by at least 75%; Q = every

2 Background

Registration status

2.1 TIL 100 mg subcutaneous injection at Weeks 0 and 4 and then every 12 weeks was registered by the TGA on 10 September 2018. The approved indication was 'for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy'. On 22 July 2025 the TGA approved an amendment to the dose and administration section of the Product Information (PI) to include the following: "At the physician's discretion, in patients with high disease burden or in patients above 90 kg of body weight who had unsatisfactory response at 100 mg, a dose of 200 mg may be tried".

Previous PBAC considerations

2.2 The PBAC considered a submission for TIL 100 mg and TIL 200 mg in July 2018. At that time the TGA registration for both doses had not been finalised and the PBAC noted that there were no significant differences between TIL 200 mg and TIL 100 mg with respect to Psoriasis Area and Severity Index (PASI) responses at Week 12/16 (paragraph

7.3, tildrakizumab Public Summary Document [PSD], July 2018 PBAC Meeting). The TGA approval was for the 100 mg dose only, and that dose then became the PBS-listed dose.

For more detail on PBAC's view, see section 7 PBAC outcome.

3 Requested listing

3.1 The submission requested a General Schedule (s85) listing of TIL 200 mg as an alternative to TIL 100 mg for the continuing treatment of severe chronic plaque psoriasis affecting the whole body, the face, hand or foot, and for balance of supply. The submission stated that in patients who achieved at least a PASI75 response to initiating treatment to TIL 100 mg, the dose could be escalated to 200 mg as a continuing treatment to target deeper levels of response (e.g. PASI90 or PASI100).

3.2 The submission requested identical restrictions for TIL 200 mg as the currently listed TIL 100 mg and, as such, the full restrictions have not been reproduced in Table 2 below.

Table 2: Sponsor requested listing

MEDICINAL PRODUCT medicinal product pack	Max. qty packs	Max. qty units	№. of Rpts	Available brands
TILDRAKIZUMAB				
tildrakizumab 100 mg,1 mL syringe	1	2	1	Ilumya
tildrakizumab 100mg, 2 x 1 mL syringe	1	2	1	Ilumya
Category / Program: ☒ GENERAL - General Schedule (Code GE)				
Prescriber type: ☒ Medical Practitioners				
Restriction type: ☒ Authority Required (written/online PBS authorities systems)				
Treatment Phase: Continuing treatment, Whole body				
Treatment Phase: Continuing treatment, Face, hand, foot				
Treatment Phase: Continuing treatment, Whole body or Continuing treatment, Face, hand, foot - balance of supply				

3.3 The submission did not propose additional clinical criteria to manage dose escalation, stating that the decision to escalate would be based on the physician's discretion. This aligned with the TGA approved PI (see paragraph 2.1).

3.4 The current PBS restrictions for TIL 100 mg (and thus, the proposed restrictions for TIL 200 mg) include an Administrative Advice stating that an adequate response to treatment is defined as a PASI score which is reduced by 75% or more (PASI75), or is sustained at this level, when compared to baseline for this treatment cycle.

For more detail on PBAC's view, see section 7 PBAC outcome.

4 Population and disease

4.1 Plaque psoriasis is a chronic, immune-mediated, painful and disabling disease of the skin, characterised by disfiguring scaling and erythematous plaques that may cause significant reductions in quality of life.

4.2 TIL is an antibody that binds to the p19 sub-unit of IL-23, inhibiting IL-23-mediated inflammation. Guselkumab and risankizumab also bind to the p19 subunit of IL-23.

4.3 The current treatment algorithm for TIL 100 mg restates the current PBS restriction for TIL: treatment with 100 mg at Weeks 0, 4, 16 and 28 and then 12 weekly if a PASI75 response is achieved. The proposed treatment algorithm, which included TIL 200 mg, was 100 mg at Weeks 0, 4, 16 and 28 and then either 100 mg or 200 mg 12 weekly if a PASI75 response is achieved, with no indication of which patients should receive the 200 mg dose.

4.4 Current Australian guidelines suggest that treatment should be modified if the response is inadequate (defined by an individual patient) but do not express a preference for increases in dose or frequency of administration versus adding topical treatments or changing to a different medication.

4.5 Current UK guidelines suggest that the dose of a biologic treatment may be increased or the dose interval reduced "when an inadequate primary response might be due to insufficient drug exposure (e.g. in people who are obese and/or whose psoriasis

relapses during the treatment cycle and/or if the drug level is known to be subtherapeutic)".[1]

4.6 Current US guidelines suggest consideration of an increased dose for all biologic treatments in "partially responding" patients but do not define partial response.[2]

For more detail on PBAC's view, see section 7 PBAC outcome.

5 Comparator

5.1 The comparator proposed for TIL 200 mg 12 weekly was TIL 100 mg 12 weekly.

For more detail on PBAC's view, see section 7 PBAC outcome.

6 Consideration of the evidence

Sponsor hearing

6.1 There was no hearing for this item.

Consumer input

6.2 The PBAC noted and welcomed input from one medical organisation, the Australasian College of Dermatologists, which advocated for increasing the maintenance dose of TIL to 200 mg to provide an opportunity to improve outcomes in patient with severe disease or obesity.

Clinical trials

6.3 The submission presented the same three randomised controlled trials that were used in the July 2018 submission. Details of the trials are provided in Table 3.

6.4 Since July 2018, the PBAC has again considered these trials, together with additional trial data, systematic reviews and network meta-analyses of biologic treatments for psoriasis, in its considerations of bimekizumab in March 2023 and risankizumab in November 2023.

[1] Smith CH, Yiu ZZN, Bale T, et al. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2020: a rapid update. *BJ Dermatol* 2020; 183:628-637.

[2] Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol* 2019; https://doi.org/10.1016/j.jaad.2018.11.057

Table 3: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
reSURFACE 1	A 64-week, Phase 3, Randomized, Placebo-controlled, Parallel Design Study to Evaluate the Efficacy and Safety/Tolerability of Subcutaneous Tildrakizumab (SCH 900222/MK-3222), Followed by an Optional Long-Term Safety Extension Study, in Subjects With Moderate-to-Severe Chronic Plaque Psoriasis. 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.	February 2017 *Lancet* 2017; 390: 276-288.
reSURFACE 2	A 52-week, Phase 3, Randomized, Active Comparator and Placebo-controlled, Parallel Design Study to Evaluate the Efficacy and Safety/Tolerability of Subcutaneous Tildrakizumab (SCH 900222/MK-3222), Followed by an Optional Long-Term Safety Extension Study, in Subjects With Moderate-to-Severe Chronic Plaque Psoriasis. 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.	February 2017 *Lancet* 2017; 390: 276-288
Phase IIb trial	Randomized, double-blinded, placebo-controlled, parallel-design, dose-range finding study of subcutaneous tildrakizumab (SCH 900222/MK-3222) in subjects with moderate-to-severe chronic plaque psoriasis. Papp K, Thaci D, Reich K et al. Tildarkizumab (MK3222), an anti-interleukin-23p19 monoclonal antibody, improves psoriasis in a Phase IIb randomised placebo controlled trial.	February 2015 *Br J Dermatol. 2015; 173:930-939.*

Source: Table 2, PSD tildrakizumab July 2018 PBAC Meeting.

6.5 The key features of the randomised trials are summarised in Table 4**Error! Reference source not found.**.

Table 4: Key features of the included evidence

Trial	N	Design/duration	Risk of bias	Patient population	Outcome(s)
reSURFACE 1	772	R, DB, MC; 64 weeks Patients crossed over (PBO to TIL and TIL to PBO) at Week 12.	Low	Moderate to severe CPP; PGA ≥3, PASI score > 12, BSA ≥ 10%	PASI75 & PGA 0/1 & ≥ two-grade improvement in PGA at Week 12.
reSURFACE 2	1090	R, DB, MC; 52 weeks PBO patients crossed over to TIL at Week 12.	Low		
Phase IIb	355	R, DB, MC; 52 weeks PBO patients crossed over to TIL at Week 16. .	Low		PASI75 at Week 16

Source: Table 3, PSD tildrakizumab July 2018 PBAC Meeting.
BSA = body surface area; CPP = chronic plaque psoriasis; DB = double blind; MC = multicentre; PASI = Psoriasis Area Severity Index; PBO = placebo; R = randomised; PGA = physician global assessment; TIL = tildrakizumab

6.6 The interventions compared in the trials are listed in Table 5.

Table 5: Interventions in the submitted trials

Trials	Treatment	Dosage regimen	Duration of PBO control period	Duration of follow-up
reSURFACE 1	TIL 200	200 mg at Weeks 0 and 4, and Q12W thereafter	12 weeks	64 weeks
	TIL 100	100 mg at Weeks 0 and 4, and Q12W thereafter		
	PBO	Placebo at Weeks 0 and 4, followed by TIL at Weeks 12, 16		
reSURFACE 2	TIL 200	200 mg at Weeks 0, 4 and 16; PBO twice weekly until Week 12, then once weekly	12 weeks	52 weeks
	TIL 100	100 mg at Weeks 0, 4 and 16; PBO twice weekly until Week 12, then once weekly		
	PBO	Placebo at Weeks 0 and 4; PBO twice weekly until Week 12 then once weekly, followed by TIL at Weeks 12, 16		
Phase IIb	TIL100	100 mg at Weeks 0 and 4, and TIL 25 mg or 100 mg Q12W from week 16 onwards if have PASI75 response, otherwise TIL 200 mg Q12W	16 weeks	52 weeks
	TIL 200	200 mg at Weeks 0 and 4, from Week 16 onwards TIL 100 or 200 mg Q12W		
	PBO	Placebo at Weeks 0 and 4, at Week 16 TIL 25 mg Q12W thereafter if have PASI75 response, otherwise TIL 100 mg Q12W		

Source: Table A2.4.5, p83 of the Commentary on the July 2018 Submission.
ETN = etanercept, PASI75 = Psoriasis Activity and Severity Index score reduced by at least 75%; PBO=placebo, Q12W = every 12 weeks; TIL = tildrakizumab

Comparative effectiveness

6.7 The PBAC did not previously consider the results for TIL 100 mg vs TIL 200 mg in detail but noted that 'there were no significant differences between TIL 200 mg and TIL 100 mg with respect to PASI responses at Week 12/16 (the timepoints at which comparative efficacy was assessed) (paragraph 7.3, tildrakizumab PSD, July 2018 PBAC meeting).

6.8 A summary of the key results that were presented in the July 2018 submission is reproduced in Table 6.

Table 6: PASI responses at Weeks 12/16 - TIL 200 mg vs TIL 100 mg (direct comparisons)

	TIL 200 mg	TIL 100 mg	Odds ratio^ (95% CI)	Relative risk^ (95% CI)	Risk difference^ (95% CI)
At Weeks 12/16					
PASI75					
reSURFACE 1	192/308 (62.3%)	197/309 (63.8%)	0.94 (0.68, 1.30)	0.98 (0.87, 1.10)	-0.01 (-0.09, 0.06)
reSURFACE 2	206/314 (65.6%)	188/307 (61.2%)	1.21 (0.87, 1.67)	1.07 (0.95, 1.21)	0.04 (-0.03, 0.12)
Phase IIb trial[a]	64/86 (74.4%)	59/89 (66.3%)	1.48 (0.77, 2.84)	1.12 (0.93, 1.36)	0.08 (-0.05, 0.22)
		Meta-analysis	1.11 (0.89, 1.37)	1.04 (0.96, 1.12)	0.04 (-0.03, 0.12)
PASI90					
reSURFACE 1	109/308 (35.4%)	107/309 (34.6%)	1.03 (0.74, 1.44)	1.02 (0.82, 1.27)	0.01 (-0.07, 0.08)
reSURFACE 2	115/314 (36.6%)	119/307 (38.8%)	0.91 (0.66, 1.26)	0.94 (0.77, 1.16)	-0.02 (-0.10, 0.05)
Phase IIb trial[a]	44/86 (51.2%)	34/89 (38.2%)	1.69 (0.93, 3.09)	1.34 (0.96, 1.87)	0.13 (-0.02, 0.28)
		Meta-analysis	1.07 (0.81, 1.43)	1.05 (0.88, 1.24)	0.02 (-0.05, 0.08)
PASI100					
reSURFACE 1	43/308 (14.0%)	43/309 (13.9%)	1.00 (0.64, 1.58)	1.00 (0.68, 1.48)	0.00- (-0.05, 0.06)
reSURFACE 2	37/314 (11.8%)	38/307 (12.4%)	0.95 (0.58, 1.53)	0.95 (0.62, 1.46)	-0.01 (-0.06, 0.05)
Phase IIb trial[a]	14/86 (16.3%)	13/89 (14.6%)	1.14 (0.50, 2.58)	1.11 (0.56, 2.23)	0.02 (-0.09, 0.12)
		Meta-analysis	1.00 (0.73, 1.36)	1.00 (0.76, 1.30)	0.00 (-0.04, 0.03)
At Week 28					
PASI75					
reSURFACE 1	236/288 (81.9%)	229/285 (80.4%)	1.17 (0.73, 1.69)	1.02 (0.94, 1.10)	0.02 (-0.0-5, 0.08)
reSURFACE 2	217/293 (74.1%)	216/290 (74.5%)	0.98 (0.67, 1.42)	0.99 (0.90, 1.09)	0.00 (-0.08, 0.07)
		Meta-analysis	1.03 (0.78, 1.37)	1.01 (0.95, 1.07)	0.01 (-0.04, 0.05)
PASI90					
reSURFACE 1	170/288 (59.0%)	147/285 (51.6%)	1.35 (0.97, 1.88)	1.14 (0.99, 1.33)	0.07 (-0.01, 0.16)
reSURFACE 2	169/293 (57.7%)	161/290 (55.5%)	1.09 (0.79, 1.52)	1.04 (0.90, 1.20)	0.02 (-0.06, 0.10)
		Meta-analysis	1.21 (0.96, 1.53)	1.09 (0.98, 1.21)	0.05 (-0.01, 0.10)
PASI100					
reSURFACE 1	91/288 (31.6%)	67/285 (23.5%)	**1.50 (1.04, 2.18)**	**1.34 (1.03, 1.76)**	**0.08 (0.01, 0.15)**
reSURFACE 2	79 /293 (27.0%)	66/290 (22.8%)	1.25 (0.86, 1.83)	1.18 (0.89, 1.57)	0.04 (-0.03, 0.11)
		Meta-analysis	**1.37 (1.06, 1.79)**	**1.27 (1.04, 1.54)**	**0.06 (0.01, 0.11)**

Source: Table 2.3.1 pp41 and 42 of the Commentary on the JULY 208 submission.

CI = confidence interval; PASI75 = Psoriasis Activity and Severity Index score reduced by at least 75%; PASI90 = Psoriasis Activity and Severity Index score reduced by at least 90%; PASI100 = Psoriasis Activity and Severity Index score reduced by 100%; TIL = tildrakizumab

^ Estimated during the evaluation using RevMan Version 5.3

[a] Results at Week 16.

6.9 In the reSURFACE 1 and reSURFACE 2 trials, patients randomised to the TIL 100 mg dose until Week 28 and who achieved a PASI50 response, but not a PASI75 response, were re-randomised to either continue TIL 100 mg or receive TIL 200 mg until Week 52. Data on their responses following re-randomisation were not included in the published reports, the July 2018 submission, or the current submission. In the current submission the reason given for not including this data was that these patients would not be eligible for continuing treatment under the current PBS restriction; however, the results are relevant to the likelihood of an increased dose of TIL producing an increased response in continuing treatment.

6.10 The outcomes for patients who had a PASI50 but not PASI75 response to TIL 100 mg and were randomised to continue either TIL 100 mg or TIL 200 mg were included in the EMA

Evaluation Report for TIL.[3] In pooled data from reSURFACE 1 and 2 the proportion with PASI75 at Week 52 was 23/40 (57.5%) among those continuing on TIL 100 mg and 24/40 (60.0%) among those increasing to TIL 200 mg.

6.11 Improvements to PASI90 and PASI100 were more common among those continuing on TIL 100 mg: 11/40 (27.5%) and 6/40 (15.0%) reached PASI90 in the continuing TIL 100 mg and increasing to TIL 200 mg groups respectively, and 7/40 (17.5%) and 2/40 (5.0%) reached PASI100 in the continuing TIL 100 mg and increasing to TIL 200 mg groups respectively.

6.12 The proportions of initially unresponsive patients responding at PASI75, PASI90 and PASI100 after 52 weeks were less than the proportion of all randomised patients responding at Week 28 (75-80%, 50-55% and 23-24%, respectively, see Table 7). These results do not support a claim that dose escalation is an effective strategy in patients with an unsatisfactory initial response to TIL 100 mg.

6.13 Although randomisation in the reSURFACE trials was stratified by body weight less than or greater than 90 kg, response data for these groups was not presented in the submission in 2018, or in the present submission.

6.14 A *post-hoc* re-analysis of the reSURFACE trials (Thaci, 2022[4]) provided data on the effect of body weight on responses. This analysis was not included in the submission.

6.15 Interpretation of the *post-hoc* re-analysis is complicated because the specified primary outcome in the trials (PASI75) was not used, instead responses were defined as PASI < 3 or DLQI 0 or 1. The results are shown in Table 7. Numbers of patients in each group are shown in Table 8.

Table 7: Responses (PASI < 3 and DLQI 0 or 1) at week 28 according to body weight in pooled reSURFACE 1 and 2.

	PASI < 3, % responders (95% CI)		DLQI 0 or 1, % responders (95% CI)	
	TIL 100 mg	TIL 200 mg	TIL 100 mg	TIL 200 mg
< 90 kg	69.0 (63.7, 73.9)	70.0 (64.8, 74.8)	56.0 (50.5, 61.4)	62.1 (56.7, 67.2)
≥ 90 kg	59.2 (53.0, 65.2)	66.3 (60.1, 72.1)	49.0 (42.8, 55.2)	55.4 (49.1, 61.6)
< 120 kg	66.4 (62.2, 70.4)	68.7 (64.6, 72.6)	54.3 (50.0, 58.6)	59.6 (55.3, 53.7)
≥ 120 kg	48.8 (35.3, 62.4)	65.2 (50.4, 78.1)	40.0 (27.3, 53.8)	55.4 (40.7, 69.5)

Source: Thaci 2022, Table 1.
CI = confidence interval; DLQI = dermatology life quality index; PASI = Psoriasis Area and Severity Index; TIL = tildrakizumab

[3] Assessment Report EMA/CHMP/664213/2018.
[4] Thaci D, Gerdes S, Gaarn du Jardin K, Perrot J-L, Puig L. Efficacy of tildrakizumab across different body weights in moderate-to-severe psoriasis over 5 years: Pooled analyses from the reSURFACE pivotal studies. *Dermatol Ther (Heidelb)* 2022; 12:2325-2341.

Table 8: Number of patients in each of the body weight and dose groups in Table 7.

	TIL 100 mg	TIL 200 mg
< 90 kg	332	343
≥ 90 kg	261	254
< 120 kg	536	547
≥ 120 kg	57	50

Source: Thaci, 2022, Figure 2.
TIL = tildrakizumab

6.16 There was no clear benefit of the TIL 200 mg dose in patients weighing over 90 kg versus those weighing under 90 kg. In patients weighing over 120 kg, there appeared to be a trend towards better outcomes with the TIL 200 mg dose, but this was not a pre-specified analysis, the differences were not statistically significant, and the number of patients in this weight group was small.

6.17 Further, it should be noted that this analysis relates to the initial treatment phase, not to continuing treatment.

Comparative harms

6.18 Adverse events reported during Weeks 0-12 of the reSURFACE 1 and 2 trials are shown in Table 9.

Table 9: Adverse events in pooled reSURFACE 1 and 2 trials

	TIL 100 mg N = 615	TIL 200 mg N = 622	Placebo N = 310
Patients with any AE, n (%)	282 (46%)	285 (46%)	160 (52%)
Serious AEs, n (%)	9 (1.5%)	14 (2%)	5 (2%)
Discontinued because of AE, n (%)	3 (0.5%)	8 (2%)	3 (1%)
Nasopharyngitis, n (%)	65 (11%)	55 (9%)	20 (6%)
Severe Infections, n (%)	1 (<0.5%)	2 (<0.5%)	1 (<0.5%)
Malignancy, n (%)	1 (<0.5%)	1 (<0.5%)	0
Non-melanoma skin cancer, n (%)	1 (<0.5%)	1 (<0.5%)	0
MACE, n (%)	1 (<0.5%)	0	0

Source: Reich et al, 2017, Tables 6 and 7.
AE = adverse event; MACE = major adjudicated cardiovascular event; TIL = tildrakizumab

6.19 Adverse events seen in pooled data from the reSURFACE 1 and 2 and in the four-year open label extension studies are shown in Table 10. As IL-23 plays a role in immune surveillance of tumours and regulation of inflammatory processes, an increased risk of malignancy and cardio-vascular event with long-term use of IL-23 antagonists has been suggested.

6.20 These data do not exclude an increased risk of malignancy and cardio-vascular events with TIL and also do not suggest that the risk is materially higher with TIL 200 mg vs TIL 100 mg.

Table 10: Adverse events in pooled reSURFACE 1 and 2 plus 4-year extension studies.

	TIL 100 mg N = 872	TIL 200 mg N = 928
Serious AE, n (%)	249 (29%)	245 (26%)
AE leading to discontinuation, n (%)	52 (6%)	40 (4%)
Severe Infection, n (%)	38 (4%)	48 (6%)
Malignancy excluding NMSC, n (%)	21 (2%)	17 (2%)
NMSC, n (%)	14 (2%)	16 (2%)
MACE, n (%)	15 (2%))	24 (3%)
Injection-site reaction, n (%)	67 (8%)	86 (9%)
Death, n (%)	11 (1%)	5 (0.5%)
AE leading to discontinuation, n (%)	52 (6%)	40 (4%)

Source: Thaci, 2022, Table 3.
AE = adverse event; MACE = major adjudicated cardio-vascular event; NMSC = non-melanoma skin cancer; TIL = tildrakizumab

Benefits/harms

6.21 A benefits and harms table is not presented as the submission made a claim of non-inferiority.

Clinical claim

6.22 The submission described TIL 200 mg as non-inferior in terms of effectiveness compared to TIL 100 mg. No evidence was presented that demonstrated that an increase of the continuing treatment dose from TIL 100 mg to TIL 200 mg is associated with improved outcomes.

6.23 The submission described TIL 200 mg as non-inferior in terms of safety compared to TIL 100 mg.

6.24 The PBAC considered that the claim non-inferior comparative effectiveness was reasonable.

6.25 The PBAC considered that the claim of non-inferior comparative safety was reasonable.

Economic analysis

6.26 The submission presented a cost minimisation approach to the economic evaluation, calculated over a 2-year time horizon. The only costs included in the evaluation were the drug costs. The assumptions and components of the evaluation are shown in Table 11.

Table 11: Key assumptions and components of the economic evaluation

Component	Claim or assumption
Therapeutic claim: effectiveness	The clinical evaluation showed that TIL 200 mg Q12W is non-inferior to TIL 100 mg Q12W in terms of efficacy.
Therapeutic claim: safety	The clinical evaluation showed that TIL 200 mg Q12W is non-inferior to TIL 100 mg Q12W in terms of safety.
Evidence base	Direct comparison of TIL 200 mg Q12W versus TIL 100 mg Q12W from reSURFACE 1, reSURFACE 2 and Papp et al. (2025)
Equi-effective doses	TIL 200 mg Q12W ≡ TIL 100 mg Q12W
Direct medicine costs	Cost of TIL 100 mg and TIL 200 mg
Other costs or cost offsets	No additional costs of cost-offsets are considered

Source: Table 3.1-1, p16 of the submission.
Q12W = every 12 weeks; TIL = tildrakizumab

6.27 The equi-effective doses were estimated as:

TIL 200 mg every 12 weeks = TIL 100 mg every 12 weeks

6.28 The submission stated that listing TIL 200 mg would not change any aspect of resource use. The only difference identified was that patients being treated with 200 mg instead of 100 mg would require 17.33 injections versus 8.67 over two years. However, as the submission proposed a flat pricing structure for the 2 pack sizes, the cost of the treatment over 2 years was the same. The results are shown in Table 12.

Table 12: Result of the CMA over 2 years (confidential effective AEMP)

	TIL 100 mg Q12W	TIL 200 mg Q12W	Increment
Administrations	8.67	17.33	8.67
Packs	8.67	8.67	0
Effective ex-manufacturer per pack	$[redacted]	$[redacted]	-
Total cost of treatment	$[redacted]	$[redacted]	$0.00

Source: Table 3.4.2, p19 of the submission.
AEMP = approved ex-manufacturer price; Q12W = every 12 weeks; TIL = tildrakizumab

Drug cost/patient/year: $[redacted]

6.29 As shown in **Error! Reference source not found.**, the cost of treatment with TIL 200 mg Q12W over 2 years is the same as treatment with TIL 100 mg Q12W. The estimated cost per patient per year of TIL 200 mg (and TIL 100 mg) is $[redacted] (effective ex-manufacturer price), assuming 100% compliance.

Estimated PBS usage & financial implications

6.30 This submission was not considered by DUSC. The submission presented a market share approach to estimate the utilisation and cost of listing for TIL 200 mg. The key inputs are shown in Table 13.

Table 13: Key inputs for financial estimates

Parameter	Value applied and source	Comment
Predicted utilisation of TIL 100 mg under the continuing treatment restriction	Observed: Services Australia PBS item report for item number 11613F in calendar years 2019 to 2024. Extrapolation: Logarithmic trendline fitted to the number of services in calendar years 2019 to 2024. Estimated services **Year** / **Services** 2026 / [redacted][1] 2027 / [redacted][1] 2028 / [redacted][1] 2029 / [redacted][1] 2030 / [redacted][1] 2031 / [redacted][1]	-
TIL 200 mg predicted uptake	Sponsor assumption **Year** / **Uptake** 2026 / [redacted]% 2027 / [redacted]% 2028 / [redacted]% 2029 / [redacted]% 2030 / [redacted]% 2031 / [redacted]%	Unable to be verified. Includes the assumption that there is effectively no market expansion, patients simply switch from the TIL 100 mg to the TIL 200 mg dose so that the uptake of the 200 mg is offset by the reduction in 100 mg dose.
Effective DPMQ of TIL	1 x 100 mg/mL injection, 1 mL: $[redacted] 2 x 100 mg/mL injection, 1 mL: $[redacted]	-
Patient copayment	PBS: $24.86 RPBS: $5.29	-

Source: Table 4.2.1, p21 of the submission.
DPMQ = dispensed price for maximum quantity; TIL = tildrakizumab
The redacted values correspond to the following ranges:
[1] 5,000 to < 10,000

6.31 The estimates of use and the financial impact of listing TIL 200 mg on the PBS/RPBS are shown in Table 14.

Table 14: Estimated use and financial implications for TIL 200 mg (effective price)

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of scripts dispensed	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Estimated financial implications for TIL 200 mg						
Cost to PBS/RPBS less copayments	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]
Estimated financial implications for TIL 100mg						
Cost offsets to PBS/RPBS less copayments	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]
Net financial implications						
Net cost to PBS/RPBS	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]

Source: Table 4.3.6, p25 of the submission.
TIL = tildrakizumab
The redacted values correspond to the following ranges: [1] 500 to < 5,000
[2] $0 to < $10 million

6.32 The total cost to the PBS/RPBS of listing TIL 200 mg was estimated to be $0 to < $10 million in Year 6, but with a net cost of $0 over the first 6 years of listing.

6.33 The estimates are based on the assumption that there will be simple switching of patients from the TIL 100 mg to TIL 200 mg dose.

6.34 The submission requested a Special Pricing Arrangement (SPA) in line with the existing SPA for the 100 mg pack. The requested effective price for TIL 200 mg (i.e. 2 x 100 mg injections) is the same as the current effective price for TIL 100 mg (i.e. 1 x 100 mg injection).

For more detail on PBAC's view, see section 7 PBAC outcome.

7 PBAC Outcome

7.1 The PBAC recommended the listing of tildrakizumab (TIL) 200 mg (100 mg/mL injection, 2 x 1 mL syringe) for the treatment of severe chronic plaque psoriasis for continuing treatment only. The PBAC considered that TIL 200 mg was non-inferior compared to TIL 100 mg in terms of efficacy and safety. The PBAC considered that the cost minimisation approach presented in the submission was reasonable and noted that the listing of TIL 200 mg on the PBS would be cost neutral.

7.2 The PBAC considered that the nominated comparator, TIL 100 mg, was reasonable.

7.3 The PBAC noted that the submission was based on three randomised controlled trials, reSURFACE 1, reSURFACE 2 and a Phase IIb trial, all of which compared TIL 200 mg with TIL 100 mg and placebo from initiation.

7.4 The PBAC noted that there was no significant difference in comparative effectiveness between TIL 100 mg and TIL 200 mg, measured in Psoriasis Activity and Severity Index (PASI) scores, at 12/16 weeks after initiation of treatment. The PBAC noted that data provided in the submission did not demonstrate that an increase of the continuing dose from TIL 100 mg to TIL 200 mg in patients is associated with improved outcomes. The PBAC considered that TIL 200 mg was non-inferior to TIL 100 mg in the continuing treatment phase.

7.5 The PBAC considered that treating clinicians, at their discretion, may escalate the dose from TIL 100 mg to TIL 200 mg in any patient who has achieved a 75% PASI response at the initial or continuing phase. The PBAC considered that these patients may achieve a deeper response with a higher dosage, noting that the magnitude of benefit may be modest.

7.6 The PBAC also stated that for patients to continue on the TIL 200 mg, they must have demonstrated an adequate response at the TIL 200 mg continuing phase. As such, the PBS restrictions include the following clinical criteria.

- Patient must be both: (i) experienced an adequate response following the most recent course of treatment at the 100 mg dosage regimen and (iii) the treating physician determined that a more satisfactory response can be achieved at the 200 mg dosage regimen; or
- Patient must have demonstrated an adequate response to the most recent course of treatment with this drug at the 200 mg dosage regimen

7.7 In terms of safety, the PBAC considered that TIL 200 mg was non-inferior to TIL 100 mg.

7.8 The PBAC considered that the cost minimisation approach presented in the submission was appropriate. The PBAC advised the equi-effective doses were:

TIL 100 mg = TIL 200 mg.

7.9 The PBAC, noting the flat pricing structure for TIL 100 mg and TIL 200 mg, considered that the addition of TIL 200 mg to the PBS would be cost neutral.

7.10 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because tildrakizumab 200 mg is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over tildrakizumab 100 mg, 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 2022* for Pricing Pathway A were not met.

7.11 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:
Recommended

8 Recommended listing

Add new medicinal product pack as follows:

Continuing treatment – Whole body

MEDICINAL PRODUCT medicinal product pack		PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
TILDRAKIZUMAB						
tildrakizumab 100 mg/mL injection, 2 x 1 mL syringe		*NEW MP*	*1*	*2*	*1*	*Ilumya*
Concept ID (for internal Dept. use)		**Category / Program:** ☒ GENERAL - General Schedule (Code GE)				
		Prescriber type: ☒ Medical Practitioners				
		Restriction type: ☒ Authority Required (Written/Online PBS Authorities systems)				
Prescribing rule level		**Administrative Advice – ABRIGED:** TREATMENT OF ADULT PATIENTS WITH SEVERE CHRONIC PLAQUE PSORIASIS				
		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 chronic plaque psoriasis				
		Treatment Phase: Continuing treatment, Whole body				
		Clinical criteria:				
		Patient must have received this drug as their most recent course of PBS-subsidised biological medicine treatment for this condition				
		AND				

	Clinical criteria:
	Patient must be both: (i) experienced an adequate response following the most recent course of treatment at the 100 mg dosage regimen and (ii) the treating physician determined that a more satisfactory response can be achieved at the 200 mg dosage regimen; or
	Patient must have demonstrated an adequate response to the most recent course of treatment with this drug at the 200 mg dosage regimen
	AND
	Clinical criteria:
	The treatment must be as systemic monotherapy (other than methotrexate)
	AND
	Clinical criteria:
	Patient must not receive more than 24 weeks of treatment under this restriction
	Population criteria:
	Patient must be aged 18 years or older
	Treatment criteria:
	Must be treated by a dermatologist
	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 for this treatment cycle.
	Prescribing Instructions: The authority application must be made in writing and must include: (a) a completed authority prescription form(s); and (b) a completed Severe Chronic Plaque Psoriasis PBS Authority Application - Supporting Information Form which includes the completed Psoriasis Area and Severity Index (PASI) calculation sheet including the date of the assessment of the patient's condition. The most recent PASI assessment must be no more than 4 weeks old at the time of application. Approval will be based on the PASI assessment of response to the most recent course of treatment with this drug.
	Prescribing Instructions: An application for the continuing treatment must be accompanied with the assessment of response conducted following a minimum of 12 weeks of therapy and no later than 4 weeks from cessation of the most recent course of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment
	Prescribing Instructions: Where a response assessment is not conducted within the required timeframe, the patient will be deemed *to not have responded* to treatment with this drug, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.
	Prescribing Instructions: If a patient *does not* 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.
	Prescribing Instructions: A patient may re-trial this drug after a minimum of 5 years have elapsed between the date the last prescription for a PBS-subsidised biological medicine was approved in this cycle and the date of the first application under a new cycle under the Initial 3 treatment restriction.

	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

Continuing treatment – Face, hand, foot

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
TILDRAKIZUMAB					
tildrakizumab 100 mg/mL injection, 2 x 1 mL syringe	*NEW MP*	*1*	*2*	*1*	*Ilumya*

Concept ID (for internal Dept. use)		**Category / Program:** ☒ GENERAL - General Schedule (Code GE)
		Prescriber type: ☒ Medical Practitioners
		Restriction type: ☒ Authority Required (Written/Online PBS Authorities systems)
Prescribing rule level		**Administrative Advice – ABRIGED:** TREATMENT OF ADULT PATIENTS WITH SEVERE CHRONIC PLAQUE PSORIASIS
		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 chronic plaque psoriasis
		Treatment Phase: Continuing treatment, Face, hand, foot
		Clinical criteria:
		Patient must have received this drug as their most recent course of PBS-subsidised biological medicine treatment for this condition
		AND
		Clinical criteria:
		Patient must be both: (i) experienced an adequate response following the most recent course of treatment at the 100 mg dosage regimen and (ii) the treating physician determined that a more satisfactory response can be achieved at the 200 mg dosage regimen; or
		Patient must have demonstrated an adequate response to the most recent course of treatment with this drug at the 200 mg dosage regimen
		AND
		Clinical criteria:
		The treatment must be as systemic monotherapy (other than methotrexate)
		AND
		Clinical criteria:
		Patient must not receive more than 24 weeks of treatment under this restriction
		Population criteria:
		Patient must be aged 18 years or older
		Treatment criteria:
		Must be treated by a dermatologist

	Prescribing Instructions: An adequate response to treatment is defined as the plaque or plaques assessed prior to biological treatment showing: (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 (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.
	Prescribing Instructions: The authority application must be made in writing and must include: (a) a completed authority prescription form(s); and (b) a completed Severe Chronic Plaque Psoriasis PBS Authority Application - Supporting Information Form which includes the completed Psoriasis Area and Severity Index (PASI) calculation sheet and face, hand, foot area diagrams including the date of the assessment of the patient's condition.
	Prescribing Instructions: The most recent PASI assessment must be no more than 4 weeks old at the time of application.
	Prescribing Instructions: Approval will be based on the PASI assessment of response to the most recent course of treatment with this drug.
	Prescribing Instructions: The PASI assessment for continuing treatment must be performed on the same affected area as assessed at baseline.
	Prescribing Instructions: An application for the continuing treatment must be accompanied with the assessment of response conducted following a minimum of 12 weeks of therapy and no later than 4 weeks from cessation of the most recent course of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment
	Prescribing Instructions: Where a response assessment is not conducted within the required timeframe, the patient will be deemed *to not have responded* to treatment with this drug, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.
	Prescribing Instructions: If a patient *does not* 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.
	Prescribing Instructions: A patient may re-trial this drug after a minimum of 5 years have elapsed between the date the last prescription for a PBS-subsidised biological medicine was approved in this cycle and the date of the first application under a new cycle under the Initial 3 treatment restriction.
	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

Continuing treatment – Whole Body or Continuing treatment – Face, hand, foot – Balance of Supply

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
TILDRAKIZUMAB					
tildrakizumab 100 mg/mL injection, 2 x 1 mL syringe	*NEW MP*	*1*	*2*	*1*	*Ilumya*

Concept ID (for internal Dept. use)		**Category / Program:** ☒ GENERAL - General Schedule (Code GE)
		Prescriber type: ☒ Medical Practitioners
		Restriction type: ☒ Authority Required (telephone/online PBS Authorities system)
Prescribing rule level		**Administrative Advice – ABRIGED:** TREATMENT OF ADULT PATIENTS WITH SEVERE CHRONIC PLAQUE PSORIASIS
		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 chronic plaque psoriasis
		Treatment Phase: Continuing treatment, Whole body or Continuing treatment, Face, hand, foot - balance of supply
		Clinical criteria:
		Patient must have received insufficient therapy with this drug under the continuing treatment, Whole body restriction to complete 24 weeks treatment; or
		Patient must have received insufficient therapy with this drug under the continuing treatment, Face, hand, foot restriction to complete 24 weeks treatment
		AND
		Clinical criteria:
		The treatment must be as systemic monotherapy (other than methotrexate)
		AND
		Clinical criteria:
		The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restrictions
		Treatment criteria:
		Must be treated by a dermatologist
		Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

9 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.

10 Sponsor's Comment

The sponsor had no comment.