

5.04 GUSELKUMAB, Injection 100 mg in 1 mL single use pre-filled syringe, Tremfya[®], Janssen-Cilag Pty Ltd

1 Purpose of Application

- 1.1 Authority Required (in writing) listing for guselkumab for treatment of severe chronic plaque psoriasis (CPP) in patients meeting specified PBS criteria. The PBAC has not previously considered guselkumab (GUS).
- 1.2 The basis for the request listing was a cost-minimisation analysis versus ustekinumab (UST). Other biologic disease-modifying anti-rheumatic drugs (bDMARDs) currently listed on the PBS for CPP include: adalimumab (ADA), etanercept (ETN), infliximab (IFX); secukimumab (SEC) and ixekizumab (IXE). Biosimilars are also available on PBS for infliximab and etanercept. The submission also presented supportive comparative evidence against adalimumab.

Table 1: Key components of the clinical issue addressed by the submission

Component	Description
Population	Adult patients with severe CPP who have failed conventional therapy
Intervention	Guselkumab (100 mg subcutaneously at Weeks 0, 4 and every 8 weeks thereafter, until loss of response or unacceptable toxicity)
Comparator	Primary: ustekinumab (recommended dose: 45 mg administered at weeks 0 and 4, then every 12 weeks thereafter, Alternatively, 90 mg administered over Weeks 0 and 4, then every 12 weeks thereafter may be used in patients with a body weight greater than 100 kg). Supplementary: Adalimumab (initially 80 mg, then 40 mg fortnightly starting 1 week after 1st dose).
Outcomes	PASI 75 and PASI 90 response
Clinical claim	The submission claimed that in patients with severe CPP, guselkumab is no worse than ustekinumab at improving PASI 90 and PASI 75 response rates, and no worse than ustekinumab in terms of safety. Guselkumab was more effective than adalimumab at improving PASI 75 and PASI 90 response rates based on direct comparative evidence to Week 48, and no worse than adalimumab in terms of safety.

Abbreviations: CPP = chronic plaque psoriasis; IGA = Investigator's Global Assessment; PASI = Psoriasis Area Severity Index.
Source: Table 1-1, p3 of the submission.

2 Requested listing

- 2.1 An identical listing to that of existing biologic therapies in CPP was requested by the submission. The requested quantities (including repeats) would permit for up to 28 weeks of initial treatment (4 doses) followed by 24 weeks of continuing therapy (3 doses) on each prescription.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
GUSELKUMAB Injection 100 mg in 1 mL pre-filled syringe	1	3 ^a 2 ^b	\$██████#	Tremfya® Janssen-Cilag Pty Ltd
Category/Program:	General Schedule (Code GE)			
PBS indication:	Severe chronic plaque psoriasis			
Treatment phase:	Initial treatment, and continuing treatment			
Restriction:	<input checked="" type="checkbox"/> Authority Required - In Writing			
Treatment criteria:	Must be treated by a dermatologist			
Clinical criteria:	As per current PBS listed ustekinumab.			

^a Initial treatment; ^b Continuing treatment.

Note: Calculated in the submission based on cost-minimisation of ex-manufacturer prices to effective price of ustekinumab over 104 weeks of treatment.

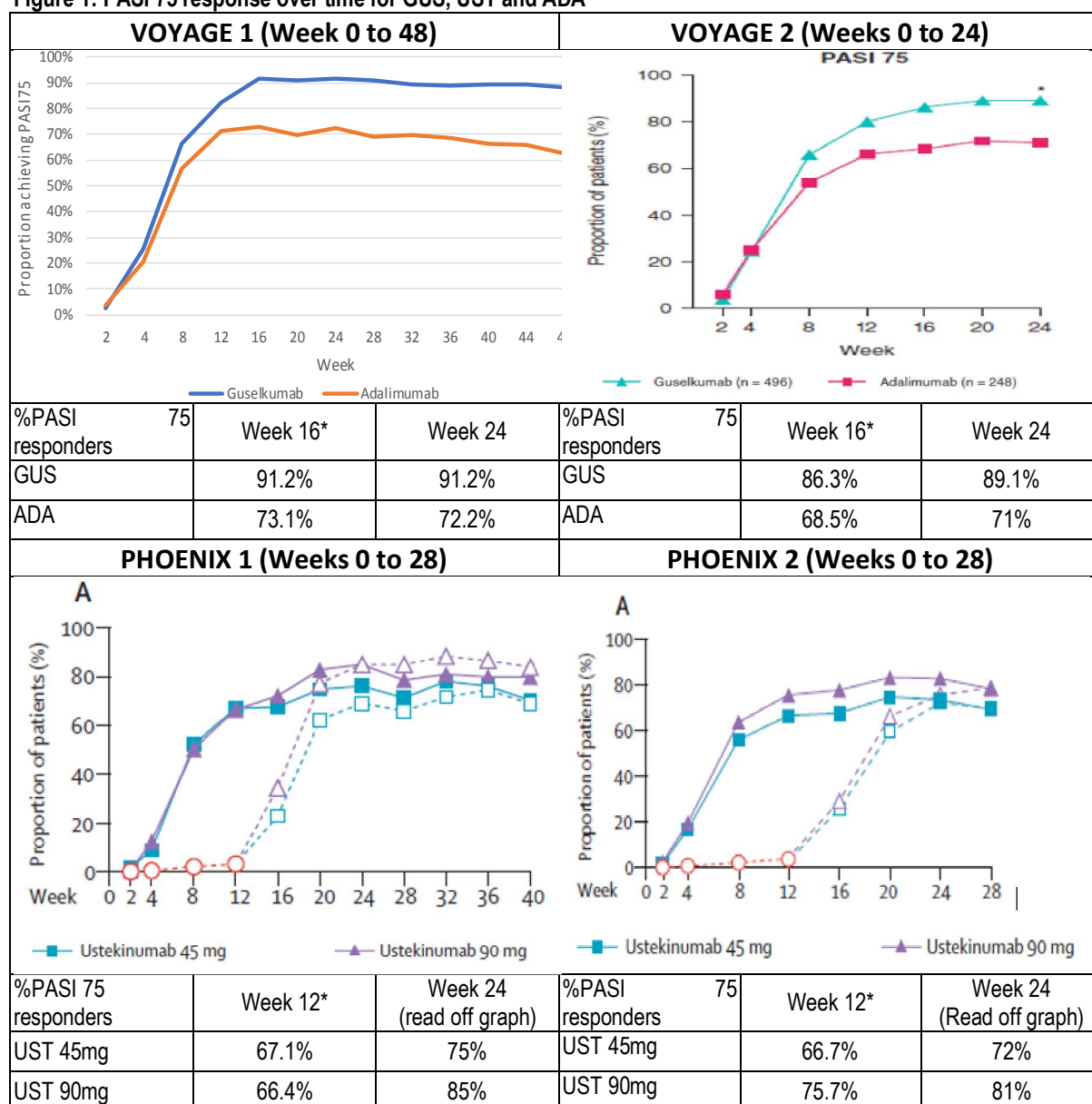
Source: Table 1-5, p18 of the submission.

- 2.2 No special pricing arrangements have been detailed in the submission. The proposed price for guselkumab was derived based on a cost-minimisation analysis versus the effective ustekinumab price over 104 weeks (2 years) of treatment. The sponsor for guselkumab is also the sponsor for ustekinumab.
- 2.3 The maximum quantity and the number of repeats requested would be sufficient to complete a 28-week initial treatment course of guselkumab (4 doses), and a 24-week continuing treatment course of guselkumab (3 doses). The requested treatment durations for continuing therapy is consistent with all listed biologics for severe CPP (all provide up to 24 weeks of therapy). The initial treatment period was similar to ustekinumab (also 28 weeks) but differed to infliximab (22 weeks) and 16 weeks for the others agents. The appropriateness of the proposed duration for initial therapy of 28 weeks is discussed in 2.7 below.
- 2.4 The submission stated that guselkumab would not be interchangeable with ustekinumab or any other PBS-listed bDMARD, due to unique pharmacokinetic, pharmacodynamic, and immunogenicity profiles.
- 2.5 The submission proposed that a grandfather clause be incorporated in the listing, to allow approximately █████ patients in a guselkumab Patient Familiarisation Program (PFP) to transition to PBS subsidised guselkumab. Furthermore, one ongoing trial (ECLIPSE trial of GUS versus SEC) is expected to be completed in September 2018. The submission stated that approximately █████ Australian patients in the trial would need to be grandfathered across to PBS supply. All grandfathered patients will be required to meet the requested PBS eligibility criteria. The sponsor requested in the Pre-PBAC response that Australian patients from the VOYAGE trials (████ from VOYAGE-1 and █████ from VOYAGE-2) be grandfathered across to PBS supply, noting that their participation in the trials is expected to conclude in 2020 which is more than 12 months after a potential PBS listing for guselkumab.
- 2.6 The requested PBS restriction was narrower than the proposed TGA indication with stricter criteria for prior failed therapies and disease severity, for example, only █████% and █████% of patients from the guselkumab trials (VOYAGE-1 and VOYAGE-2 respectively) had failed therapy with three or more conventional systemic therapies

fitting the PBS eligibility criteria. However, the evidence is comparable to that for all other biologics listed on the PBS. Overall, the requested restriction was appropriate, except for the assessment of the initial response (see 2.7 below).

- 2.7 The requested quantities (plus repeats) would permit up to 28 weeks of initial treatment with guselkumab. The submission argued (p18) that this was appropriate as it was consistent with initial treatment period of ustekinumab for severe CPP and would provide patients with the best chance of achieving a PASI response for continuing treatment eligibility. Dose response curves for guselkumab, ustekinumab and adalimumab (initial treatment period of 16 weeks with assessment of response at 12 weeks) from the included trials were examined during the evaluation for PASI 75 response over time (see Figure 1).

Figure 1: PASI 75 response over time for GUS, UST and ADA



Source: constructed during the evaluations from data presented in Figure 2.8, p120 of the submission, Figure 3, p427 of VOYAGE 2 trial Reich 2017, Figure 4, panel A of PHOENIX 1 trial Leonardi 2008, Figure 3, Panel A, p1679 of PHOENIX 2 trial, Papp 2008.

2.8 The data suggested, for guselkumab, very few additional patients became PASI 75 responders beyond Week 16 (end of trial double blind period). The guselkumab dose response curves were also found to be reasonably similar in trajectory to the adalimumab curves. Through the PBS, continuing eligibility to adalimumab is assessed after only 12 weeks of initial therapy (versus 24 weeks proposed for guselkumab). The dose response curves for guselkumab and adalimumab also contrasted with the curves for ustekinumab, which illustrated that quite a number of patients became PASI 75 responders between Week 12 (end of trial double blind period) and Week 24 (time point for PBS assessment of response) in both PHOENIX 1 and 2 trials.

- 2.9 The primary endpoints in the included guselkumab trials (VOYAGE-1 and -2) were measured at 16 weeks, which is significantly shorter than the proposed length of the initial treatment period of 28 weeks. Based on the dosing regimen of guselkumab at Weeks 0, 4 and 8 weekly thereafter, with next doses due at Weeks 12, 20 and 28, it might be more appropriate to allow only up to 20 weeks of initial treatment, with response assessment between Week 12 and 16. The PSCR accepted the evaluation in the Commentary and agreed to 20 weeks of initial therapy with the response assessment at week 16.

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

3 Background

Registration status

- 3.1 The submission was made under the TGA/PBAC Parallel Process. At the time of evaluation for PBAC consideration, the TGA delegate's overview was available. The proposed indication for guselkumab is: "treatment of moderate to severe plaque psoriasis, scalp, nail, and hand and foot psoriasis, and improvement of health-related quality of life in adult patients who are candidates for systemic therapy or phototherapy". The TGA delegate's request for ACM advice dated 2 January 2018, stated that the pre ACM preliminary assessment conducted by the delegate has identified no reason why guselkumab should be not be approved for registration, subject to negotiation of the PI and other conditions of registration. The ACM discussed this request on 2 February 2018. The ACM outcome was not available at the PBAC meeting.

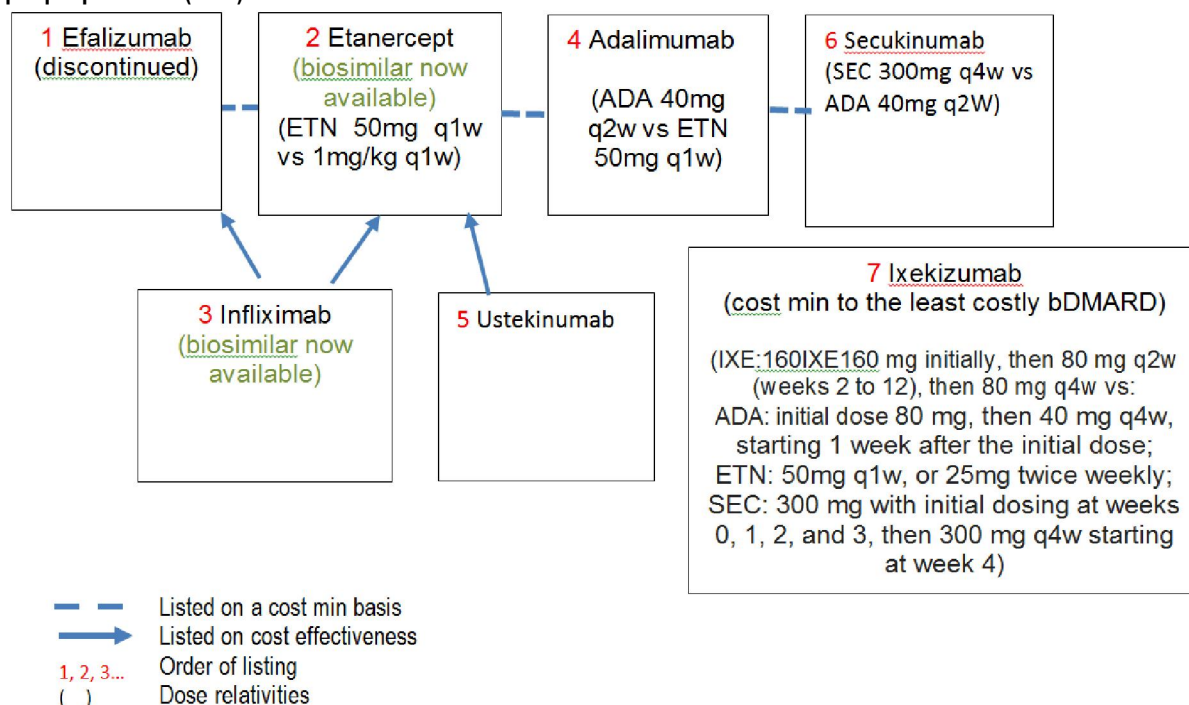
For more detail on PBAC's view, see section 7 PBAC outcome.

4 Population and disease

- 4.1 Psoriasis manifests as chronic inflammation of the skin, characterised by disfiguring, scaling and erythematous plaques that may be painful and severely pruritic and may cause significant reductions in quality of life (QoL). The target population proposed for guselkumab is the same as that for other biologics on the PBS for severe CPP. The initial treatment criteria for PBS-subsidised biologic therapy for whole body psoriasis requires patients to have a PASI > 15 and have failed to achieve an adequate response, are intolerant or contraindicated to at least three of the four systemic therapies (methotrexate, cyclosporine, acitretin and phototherapy [either PUVA or UVB]).
- 4.2 Guselkumab is proposed as an alternative bDMARD in the treatment of severe chronic plaque psoriasis. If accepted, guselkumab will become one of several bDMARDs listed on PBS for patients with severe CPP who have failed to achieve adequate response to non-biologic therapies. The addition of guselkumab to the clinical management algorithm will not alter current practice. The submission suggested that guselkumab would mostly replace therapy with ustekinumab followed by adalimumab. However, given the therapeutic relativities of listed

biologics (see Figure 2 below) and that clinicians are free to choose among them, guselkumab could replace any of the listed bDMARDs.

Figure 2: Diagrammatic representation of the therapeutic relativities of biological agents listed on PBS for chronic plaque psoriasis (CPP)



Source: constructed during the evaluation based on PBS public summary documents and therapeutic relativity sheets.

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

5 Comparator

- 5.1 The submission nominated ustekinumab as the main comparator (and the only comparator considered in the cost-minimisation analysis). This was based on ustekinumab being the most commonly used PBS-subsidised biologic for severe CPP (47% market share); and guselkumab being an exclusive IL-23 inhibitor, having a similar mechanism of action to ustekinumab an IL-12/23 inhibitor. The submission nominated adalimumab (ADA) as a supplementary efficacy comparator, based on adalimumab being the active comparator (up to 48 weeks) in the main trials supporting the submission (the VOYAGE-1 and 2 trials).
- 5.2 The ESC and PBAC considered that any of the biologic agents on the PBS for CPP may be replaced and hence be a relevant comparator. The ESC noted that infliximab and etanercept, are now less costly than ustekinumab. If treatment with guselkumab is substantially more costly than these alternative therapies, the PBAC could only recommend listing of guselkumab if it is satisfied that guselkumab provides, for some patients, a significant improvement in efficacy or reduction of toxicity over the alternative therapies (National Health Act 1953, Section 101(3B)).

- 5.3 The PBAC and ESC noted that etanercept, adalimumab, secukinumab and ixekizumab have been cost-minimised against each other or against the least expensive biological. The PBAC and ESC noted that the submission claimed superiority for guselkumab versus adalimumab, and thus it may be reasonable to claim for some patients there is a significant improvement in efficacy versus these alternative therapies. However counter to this, the analysis presented in the Draft report to the PBAC for the post-market review (PMR) of the use of biologics in the treatment of severe chronic plaque psoriasis suggests that all PBS biologics were effective against placebo with ixekizumab having the highest point estimate and etanercept the lowest. Specifically, given the evidence presented in this submission ESC considered that guselkumab may be non-inferior, or possibly inferior, in terms of efficacy compared with ixekizumab.
- 5.4 The PBAC and ESC noted that ustekinumab was listed on a cost-effective basis versus etanercept, and the submission claimed non-inferiority for guselkumab versus ustekinumab.
- 5.5 The ESC noted that infliximab was listed on a cost-effective basis versus etanercept, and that the submission did not include a clinical claim for guselkumab versus infliximab. The Pre-PBAC response stated that the sponsor would be amenable to listing on a cost minimisation basis to infliximab. The Pre-PBAC response presented an indirect comparison of the meta-analysed results from the pivotal trials for infliximab (EXPRESS 1 and EXPRESS 2) and guselkumab (VOYAGE 1 and VOYAGE 2). This analysis has not been evaluated and PBAC noted that not all potentially relevant infliximab trials were included in the analysis.

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 comments

- 6.2 The PBAC noted and welcomed the input from individuals (5) and health care professionals (9) via the Consumer Comments facility on the PBS website. The comments described a range of benefits of treatment with guselkumab including improved compliance, the ability to use alternative therapy when existing therapy has failed and being a more effective treatment.

Clinical trials

- 6.3 The submission was based on an indirect comparison of two placebo-and active controlled trials of guselkumab (VOYAGE-1 and -2) and two placebo-controlled trials of ustekinumab (PHOENIX-1 and -2). During the course of the evaluation, data were extracted from five additional placebo-controlled trials of ustekinumab (Igarashi 2012, LOTUS and PEARL, AMAGINE-2 and AMAGINE-3) and meta-analysed with

included trials. These trials were inappropriately excluded by the submission and had previously been considered by the PBAC in other listing decisions for CPP (see ixekizumab July 2016 PSD).

- 6.4 One identified head-to-head randomised trial (NAVIGATE) comparing guselkumab and ustekinumab in CPP was also excluded by the submission, but included during the evaluation. The submission considered the trial not applicable to the PBS setting, as patients who failed ustekinumab were either re-randomised to treatment with guselkumab, or re-treatment with ustekinumab, the latter is not permitted within a PBS biological treatment cycle (whereby patients can only fail treatment with the same biologic once). Although this exclusion was not entirely unreasonable, some patients in NAVIGATE may still be representative of the proposed PBS population, particularly since patients in the guselkumab arm of the trial would be representative of those most likely to take up guselkumab on PBS. The NAVIGATE trial was included as supportive evidence during the evaluation, however given the trial design the results are likely to favour guselkumab and were not meta-analysed with the other guselkumab trials.
- 6.5 Details of the trials presented in the submission and those additionally evaluated during the evaluation are provided in Table 2.

Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
GUS vs PBO and ADA		
VOYAGE-1 (GUS ₁)	A Phase 3, Multicentre, Randomized, Double-blind, Placebo and Active Comparator-controlled Study Evaluating the Efficacy and Safety of Guselkumab for the Treatment of Subjects with Moderate to Severe Plaque-type Psoriasis. Blauvelt A, Papp K, Griffiths C et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: Results from the phase III, double-blinded, placebo- and active comparator-controlled VOYAGE 1 trial.	October 2016 <i>J Am Acad Dermatol.</i> 2017; 76: 405-417.
VOYAGE-2 (GUS ₂)	A Phase 3, Multicentre, Randomized, Double-blind, Placebo and Active Comparator-controlled Study Evaluating the Efficacy and Safety of Guselkumab for the Treatment of Subjects with Moderate to Severe Plaque-type Psoriasis with Randomized Withdrawal and Retreatment Reich K, Armstrong A, Foley P et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the treatment of patients with moderate to severe psoriasis with randomized withdrawal and retreatment: Results from the phase III, double-blind, placebo- and active comparator controlled VOYAGE 2 trial.	October 2016 <i>J Am Acad Dermatol.</i> 2017; 76: 418-431.
GUS vs UST		
NAVIGATE (GUS ₃)	Langley R, Tsai T, Flavin S et al. Efficacy and safety of guselkumab in patients with psoriasis who have an inadequate response to ustekinumab: Results of the randomized, double-blind, phase III NAVIGATE trial.	<i>Brit J Dermatol.</i> 2017; doi: 10.1111/bjd.15750
UST vs PBO		
PHOENIX 1 (UST ₁)	Leonardi C, Kimball A, Papp K et al. Efficacy and safety of ustekinumab, human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomised, double blind, placebo-controlled trial (PHOENIX 1)	<i>Lancet</i> 2008; 371: 1665-1674.
PHOENIX 2 (UST ₂)	Papp K, Langley R, Lebwohl G et al. Efficacy and safety of ustekinumab, human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 52-week results from a randomised, double blind, placebo-controlled trial (PHOENIX 2)	<i>Lancet</i> 2008; 371: 1675-1684.
PEARL (UST ₃)	Tsai T, Ho, J, Song M et al. Efficacy and safety of ustekinumab for the treatment of moderate-to-severe psoriasis: A phase III, randomized, placebo-controlled trial in Taiwanese and Korean patients (PEARL).	<i>J Dermatol Sci</i> 2011; 63: 154-163.
LOTUS (UST ₄)	Zhu X, Zheng M, Song M et al. Efficacy and safety of ustekinumab in Chinese patients with moderate to severe plaque-type psoriasis: Results from a phase 3 clinical trial (LOTUS).	<i>J Drugs Dermatol.</i> 2013; 12 (2): 166-174.
Igarashi 2012 (UST ₅)	Igarashi A, Kato T, Kato M et al. Efficacy and safety of ustekinumab in Japanese patients with moderate-to-severe plaque-type psoriasis: Long-term results from a phase 2/3 clinical trial.	<i>J Dermatol.</i> 2012; 39: 242-252..
AMAGINE-2 (UST ₆)	Lebwohl M, Strober B, Menter A et al. Phase 3 studies comparing brodalumab with ustekinumab in psoriasis.	<i>NEJM</i> 2015; 373 (14): 1318-1328
AMAGINE-3 (UST ₇)		

Abbreviations: ADA=adalimumab, GUS=guselkumab, PBO=placebo, UST=ustekinumab.
Source: Table 2.6, pp60-64 of the submission.

6.6 The key features of the included trials (including those added during the evaluation) are summarised in Table 3.

Table 3: Key features of evidence included in the submission and during the evaluation

Trial	N	Design/ duration of follow-up	Within trial risk of bias	Patient population	Key Outcomes
GUS vs PBO and ADA					
GUS ₁ (VOYAGE-1)	837	R, DB, MC, 48 wks. PBO patients crossed over to GUS at Wk 16. Switching not permitted for ADA group.	Low	Moderate to severe CPP;	IGA 0/1, PASI 90, PASI 75 at Wk 16. Versus ADA PASI 75 and PASI 90 at Wks 24 and 48 (VOYAGE 1 only)
GUS ₂ (VOYAGE-2)	992	R, DB, MC, 28 wks PBO patients crossed over to GUS at Week 16.	Low	IGA _≥ 3, PASI score _≥ 12, BSA _≥ 10%	
UST vs PBO					
UST ₁ (PHOENIX 1)	766	R, DB MC, 40 wks. PBO patients crossed-over to UST at Week 12. Wk 40 to 72: randomised withdrawal phase ^b	Low	Moderate to severe CPP;	PASI 75 at Wk 12. Maintenance of PASI response thru to trial end.
UST ₂ (PHOENIX 2)	1230	R, DB, MC, 28 wks, PBO patients crossed-over to UST at Week 12. Wk28 -52: randomised dose intensification phase.	Low	PASI score _≥ 12, BSA _≥ 10%	
UST ₃ (PEARL)	121	R, DB, MC, 36 wks (efficacy results up to 28 weeks). PBO patients crossed-over to UST at Week 12.	Low	Same as UST ₁ and UST ₂ , but in Korean or Taiwanese pts	
UST ₄ (LOTUS)	322	R, DB, MC, 36 wks (efficacy results up to 28 weeks). PBO patients crossed-over to UST at Week 12.	Low	Same as UST ₁ and UST ₂ , but in Chinese pts	
UST ₅ (Igarashi 2012)	158	R, DB, MC, 72 wks (efficacy results up to 64 wks), PBO patients crossed-over to UST at Week 12.	Low	Same as UST ₁ and UST ₂ , but in Japanese pts	
UST ₆ (AMAGINE-2)	1831	R, DB, MC, 52 wks. Trial compared brodalumab, UST and PBO.	Low	Moderate to severe CPP;	PASI 75 & sPGA (0,1) at Wk 12.
UST ₇ (AMAGINE-3)	1881	PBO patients crossed-over to brodalumab at Week 12.	Low	PASI score _≥ 12, BSA _≥ 10%, sPGA _≥ 3	Maintenance of PASI response thru to Wk 52.
GUS vs UST					
GUS ₃ (NAVIGATE)	268 ^a	MC, initial open label UST for 16 wks, non-responders then re-randomised to either DB GUS or UST for a further 36 weeks (wk52)	Low	Moderate to severe CPP; IGA _≥ 3, PASI score _≥ 12, BSA _≥ 10%; pts with an inadequate response (IGA _≥ 2) to UST after 16 weeks	IGA 0/1 & _≥ two-grade improvement in IGA; PASI 90 at wk52

Abbreviations: ADA=adalimumab, BSA=body surface area; DB=double blind; GUS=guselkumab; IGA = Investigator's Global Assessment (3 and 4 corresponds to moderate and severe CPP, respectively, 0-2 correspond to clear to mild); MC=multicentre; PASI = Psoriasis Area Severity Index; PBO = placebo, PC=placebo control, pts=patients; R=randomised; sPGA=static physician global assessment; UST=ustekinumab, CPP=chronic plaque psoriasis.

^a This is the number of patients with an inadequate response to UST at Week 16, who were randomised to GUS or to continue UST.

^b UST patients who attained PASI 75 were re-randomised to withdrawal or continuing treatment and PBO group patients switched back to PBO. Patients could restart treatment if lost at least PASI 50 response.

^c partial responders in the UST groups (i.e. those that attained PASI 50 by not PASI 75) were re-randomised to standard (q12w) or more intensive (q12w) dosing regimen. Placebo group patients all underwent non-randomised adjustment to q8w dosing.

Source: compiled during the evaluation from trial publications.

6.7 All trials were multicentre, double-blind RCTs. Overall, the risks of bias in the placebo-controlled phase of the trials were considered low. All the included trials however had multiple phases, beyond the initial placebo-controlled phase (16 and 12 weeks for the guselkumab and ustekinumab trials, respectively) since patients in the placebo groups were switched onto active treatments, placebo outcomes from

subsequent periods would be subject to bias. For this reason, appropriately, main trial outcomes were all assessed at the end of the placebo-controlled periods.

- 6.8 In the guselkumab trials, switching was not permitted for those randomised to the active comparator (ADA). As a result, directly comparative efficacy results comparing guselkumab and adalimumab were available for up to 48 and 24 weeks in the VOYAGE 1 and 2 trials respectively. In the VOYAGE-2 trial, a randomised withdrawal and retreatment also occurred between Weeks 28 and 72. As this did not present a comparison of interest it was appropriately not presented in the submission.
- 6.9 The guselkumab and ustekinumab trials examined during the evaluation enrolled similar patient populations, consisting of adult patients with moderate to severe plaque psoriasis (PASI score > 12, and body surface area involvement > 10%). The guselkumab trials in addition required patients to have an Investigator Global Assessment (IGA) score > 3. The IGA grades lesions for induration, erythema and scaling. An IGA score of 3 and 4 corresponds to moderate and severe, respectively, and IGA scores of 0-2 correspond to clear to mild symptoms. The NAVIGATE trial was conducted in a second line (ustekinumab ‘non-responsive’) population.
- 6.10 As noted above, the guselkumab and ustekinumab trial populations differed to the requested PBS population (which has stricter requirements for number of prior failed therapies and severity) but overall the trial populations were similar to other trials of biologics previously considered by the PBAC and were generally representative of the likely PBS population.
- 6.11 The dosing regimens of guselkumab and adalimumab in the trials were consistent with those recommended in the (draft) PIs. For ustekinumab however, except for the AMAGINE-2 and -3 trials which administered ustekinumab based on the recommended weight based dosing (45mg for patients ≤ 100 kg and 90mg for patients >100kg), the doses used in the ustekinumab trials generally deviated from that recommended in the PI. In order to pool results across these trials, some assumptions were required to determine if correct doses were administered. The submission also presented outcomes for ustekinumab from the PHOENIX trials as a proportion of those correctly dosed based on the TGA recommended doses.

Comparative effectiveness

- 6.12 The PBAC has previously based recommendations for listing of biologics for the treatment of CPP on the proportion of patients i) achieving and ii) maintaining a PASI 75 response (≥75% improvement from baseline in the Psoriasis Activity and Severity Index score). This is consistent with the PBS eligibility criteria for continued treatment with biologics. PASI 75 response was reported in all included trials (primary outcome in the ustekinumab trials and secondary outcome in the guselkumab trials). In addition, results were reported for PASI 90 and PASI 100 response (90% or 100% improvement from baseline in PASI score respectively) and response based on investigator assessment.

- 6.13 Appropriately, the submission's clinical claims were based on the outcomes of PASI 75 and PASI 90 response and only these outcomes were compared in the indirect comparisons versus ustekinumab. However, results were compared after 24 weeks of active treatment (but using Week 16 or 12 (i.e. prior to cross over) placebo response rates in the guselkumab and ustekinumab trials respectively as common reference). The submission argued this was more appropriate than using the primary trial end points as it better aligns with the proposed times that eligibility for continuing treatment will be assessed on the PBS.
- 6.14 Given this approach require the acceptance that placebo response at Week 24 will be identical to those observed at Weeks 16 or 12, a more appropriate approach might be to compare results prior to cross over (Week 16 in the guselkumab trials and Week 12 in the ustekinumab trials). Past PBAC considerations of biologics in CPP have also mainly considered efficacy outcomes measured at the end of the trial placebo control periods. For ustekinumab, this was at Week 12 (see ixekizumab July 2016, secukinumab March 2015 and ustekinumab November 2009 PSDs). In the ustekinumab November 2009 submission, it was also noted the PBAC accepted a longer initial treatment period (with one additional dose) for ustekinumab as the submission was able to additionally demonstrate cost effectiveness versus etanercept despite the longer 28 week initiation period (ustekinumab November 2009 PSD). Data from the ustekinumab trials also indicated a sizeable number of patients attained PASI 75 response between Weeks 12 and 24 (when response would be assessed on PBS).
- 6.15 The submission presented four risk statistics when performing the indirect comparisons using the Bucher 1997 methodology: risk difference (RD), odds ratio (OR), relative risk (RR) expressed in terms of proportion of responders and RR expressed in terms of non-responders. The main reason to also present RR in terms of non-response was that due to asymmetry in the variance of the RR statistic, and thus results of indirect comparisons using RR (in both direction and size) can change depending on whether the outcome is framed in terms of a loss or gain. In contrast, variances for RD and OR are symmetric. The submission argued that the choice to frame in terms of loss or gain would depend on which has the highest baseline risk in the common comparator arms. In the VOYAGE and PHOENIX trials, given the placebo PASI response rates were low (<10%), then expressing RR in terms of non-response would be more appropriate.
- 6.16 The submission further claimed that this approach was also adopted for the November 2009 PBAC submission for ustekinumab and was considered to be appropriate by the evaluation. This claim was not able to be verified. The PSD for the ustekinumab November 2009 submission reported results using OR and the Commentary reported results in RR, OR and RD based on response rather than non-response. Recent submissions of bDMARDs for CPP have also presented results using all three risk statistics (RD, RR, and OR in terms of response; ixekizumab July 2016 and secukinumab March 2015).

- 6.17 In a paper by Eckermann, Coory and Willan (2009) (also referenced by the submission), the authors suggested that rather than RR, OR given its symmetric properties should be used to estimate relative treatment effects in indirect comparisons. The Report of the Indirect Comparisons Working Group to the PBAC (pp47-48) further suggested if the choice of the measure of comparative treatment effect affects conclusions, then the submission should show the range of conclusions that can be drawn from the different measures.
- 6.18 Given all indirect comparisons versus ustekinumab were updated during the evaluation to both incorporate additional evidence as well as to provide an alternate set of results assessing results at the end of placebo control period for both sets of trials (Week 16 for guselkumab and Week 12 for ustekinumab), results were re-estimated using mainly OR and RD. Results in RR (in terms of response) were also re-estimated to allow comparability with other previous submissions considered by the PBAC.
- 6.19 Tables 4 and 5 summarise results of indirect and direct comparison for PASI 75 and PASI 90 responses at Week 16 for the guselkumab trials and Week 12 for the ustekinumab trials. As discussed, the evidence base was expanded during the evaluation to also include the NAVIGATE trial (direct comparative evidence of guselkumab vs ustekinumab in patients who have failed ustekinumab) and the PEARL; LOTUS; Igarashi 2012, AMAGINE-2 and AMAGINE-3 trials comparing ustekinumab and placebo. The evidence versus ustekinumab was indirect, using placebo as common reference, whereas comparative results versus adalimumab was direct since the VOYAGE 1 and 2 trials also included adalimumab as an active comparator (for up to either 24 (VOYAGE 2) or 48 weeks (VOYAGE 1)).
- 6.20 For the indirect comparisons, the submission nominated a non-inferiority margin of - 10% for PASI 90 or PASI 75 between guselkumab and ustekinumab based on results estimated using the RD statistic. This was sourced from the VOYAGE trials, which nominated a non-inferiority margin of 10% (lower bound of the 95% CI for the difference in proportions in guselkumab minus adalimumab for PASI 90 or PASI 75 > - 10%).

Table 4: Initial PASI 75 response at Weeks 16/12 across the trials

Trial	Drug n/N (%)	Control n/N (%)	OR (95% CI) [^]	RD [95% CI] [^]	NNT (95%CI)
GUS vs PBO Wk16					
GUS1	300/329 (91.2)	10/174 (5.7)	169.7 (80.7, 356.8)	0.85 (0.81, 0.90)	1 (1, 1)
GUS2	428/496 (86.3)	20/248 (8.1)	71.8 (42.5, 121.9)	0.78 (0.74, 0.83)	1 (1, 1)
Pooled	728/825 (88.2)	30/422 (7.1)	105.8 (45.7, 244.9)	0.82 (0.75, 0.89)	1 (1, 1)
UST 45mg (<100kg) vs PBO Wk 12					
UST1					
UST2					
UST3	41/61 (67.2)	3/60 (5.0)	39.0 (10.9, 139.83)	0.62 (0.49, 0.75)	2 (1, 2)
UST4	132/160 (82.5)	18/162 (11.1)	37.7 (19.9, 71.34)	0.71 (0.64, 0.79)	1 (1, 2)
UST5	38/64 (59.4)	2/31 (6.5)	21.2 (4.7, 96.6)	0.53 (0.38, 0.68)	2 (1, 3)
Pooled			49.4 (34.12, 71.6)	0.68 (0.63, 0.72)	1 (1, 2)
UST 90mg (>100kg) vs PBO Wk 12					
UST1					
UST2					
Pooled					
UST Label vs PBO Wk 12					
UST6	210/300 (70.0)	25/309 (8.1)	26.5 (16.4, 42.74)	0.62 (0.56, 0.68)	2 (1, 2)
UST7	217/313 (69.3)	19/315 (6.0)	35.2 (20.9, 59.4)	0.63 (0.58, 0.69)	2 (1, 2)
Pooled	427/613 (69.7)	44/624 (7.1)	30.2 (21.2, 42.9)	0.63 (0.58, 0.67)	2 (1, 2)
UST(all)					
Indirect : GUS versus UST					
<i>GUS versus UST45mg</i>					
<i>GUS versus UST90mg</i>					
<i>GUS versus UST Label</i>			3.5 (1.4, 8.8)	0.19 (0.11, 0.27)	5 (4, 9)
<i>GUS versus UST (all doses pooled)</i>					
Direct : GUS versus ADA Wk16					
GUS1	300/329 (91.2)	244/334 (73.1)	3.8 (2.4, 6.0)	0.18 (0.12, 0.24)	6 (4, 8)
GUS2	428/496 (86.3)	170/248 (68.5)	2.9 (2.0, 4.2)	0.18 (0.11, 0.24)	6 (4, 9)
Pooled	728/825 (88.2)	414/582 (71.1)	3.2 (2.4, 4.3)	0.18 (0.14, 0.22)	6 (5, 7)

Italics indicate results estimated during the evaluation; Bold typography indicates statistically significant differences.

Abbreviations: GUS₁=VOYAGE-1; GUS₂=VOYAGE-2; GUS₃=NAVIGATE; UST₁=PHOENIX-1; UST₂=PHOENIX-2; UST₃=PEARL; UST₄=LOTUS; UST₅=Igarashi 2012; UST₆=AMAGINE-2; UST₇=AMAGINE-3; UST Label refers to weight-based dosing for UST (UST 45 mg for patients ≤ 100 kg; UST 90 mg for patients > 100 kg); Wk=week; PBO=placebo, UST=ustekinumab, GUS=guselkumab, ADA=adalimumab.

[^] estimated using random effects meta-analysis using RevMan Version 5.3

* From IPD data supplied by the submission (from subgroup of patients in the trial who received the TGA approved UST dose: 45mg for patients weighing ≤ 100 kg and UST 90 mg for patients weighing > 100 kg). Placebo data also presented according to weight (comparison of UST 45 mg to PBO in patients weighing ≤ 100 kg and UST 90 mg to PBO in patients weighing > 100 kg).

Source: constructed during the evaluation using results reported in Table 2.49, p156 of submission; Attachment TEFMS8910A, p412 of CSR for VOYAGE-1, Attachment TEFMS678A, p509 of CSR for VOYAGE-2; Table 2, p158 of PEARL publication; Table 2, p170 of LOTUS publication; Table 2, p247 of Igarashi 2012; Table 2, p1323 of AIMAGINE-2 and -3 publication. PHOENIX 1 and 2 trials: Data sourced from Week 12 results from Attachment 3.45-3.46, pp.400-401; Attachment 3.53, pp.408-409; Attachment 3.54, pp.410-411 of PHOENIX-1 Week 52 CSR; Attachment 3.31, p295; Attachment 3.32, p296 of PHOENIX-2 Week 28 CSR.

Table 5: Initial PASI 90 response at Weeks 16/12 across the trials

Trial	Drug n/N (%)	Control n/N (%)	OR (95% CI) ^a	RD (95% CI) ^a	NNT (95%CI)
GUS vs. PBO Wk16					
GUS1	241/329 (73.3)	5/174 (2.9)	92.6 (36.8, 232.8)	+ 0.70 (0.65, 0.76)	1 (1, 2)
GUS2	347/496 (70.0)	6/248 (2.4)	93.9 (40.9, 215.9)	+ 0.68 (0.63, 0.72)	1 (1, 2)
Pooled	588/825 (71.3)	11/422 (2.6)	93.3 (50.3, 173.1)	+ 0.69 (0.65, 0.72)	1 (1, 2)
UST 45mg (<100kg) vs PBO Wk 12					
UST1					
UST2					
UST3	30/61 (49.2)	1/60 (1.7)	57.1 (7.4, 438.8)	+ 0.48 (0.35, 0.60)	2 (2, 3)
UST4	107/160 (66.9)	5/162 (3.1)	63.49 (24.5, 163.8)	+ 0.64 (0.56, 0.72)	2 (1, 2)
UST5	21/64 (32.8)	1/31 (3.2)	14.7 (1.87, 114.9)	+ 0.30 (0.17, 0.43)	3 (2, 6)
Pooled					
UST 90mg (>100kg) vs PBO Wk 12					
UST1					
UST2					
Pooled					
UST (all)					
Indirect : GUS vs UST					
GUS versus UST 45mg					
GUS versus UST 90mg					
GUS versus UST (all doses pooled)					
Direct: GUS vs ADA Wk16					
GUS1	241/329 (73.3)	166/334 (49.7)	2.8 (2.0, 3.8)	+ 0.24 (0.16, 0.31)	4 (3, 6)
GUS2	347/496 (70.0)	116/248 (46.8)	2.7 (1.9, 3.6)	+ 0.23 (0.16, 0.31)	4 (3, 6)
Pooled	588/825 (71.3)	282/582 (48.5)	2.7 (2.2, 3.4)	+ 0.23 (0.18, 0.29)	4 (3, 6)
Direct: GUS vs UST Wk 12 (UST failures)					
GUS3	65/135 (48.1)	30/133 (22.6)	3.19 (1.88, 5.41)	+ 0.26 (0.15, 0.37)	4 (3, 7)

Italics indicate results estimated during the evaluation; Bold typography indicates statistically significant differences.

Abbreviations: GUS₁=VOYAGE-1; GUS₂=VOYAGE-2; GUS₃=NAVIGATE; UST₁=PHOENIX-1; UST₂=PHOENIX-2; UST₃=PEARL;

UST₄=LOTUS; UST₅=Igarashi 2012; UST₆=AMAGINE-2; UST₇=AMAGINE-3; UST Label refers to weight-based dosing for UST (UST 45 mg for patients ≤ 100 kg; UST 90 mg for patients > 100 kg), Wk=week; PBO=placebo, UST=ustekinumab, GUS=guselkumab, ADA=adalimumab.

^a estimated using random effects meta-analysis using RevMan Version 5.3

* From IPD data supplied by the submission (from subgroup of patients in the trial who received the TGA approved UST dose: 45mg for patients weighing ≤ 100 kg and UST 90 mg for patients weighing > 100 kg). Placebo data also presented according to weight (comparison of UST 45 mg to PBO in patients weighing ≤ 100 kg and UST 90 mg to PBO in patients weighing > 100 kg).

Source: constructed during the evaluation using results reported in Table 2.31, Table 2.34, pp127-130 of submission; Attachment TEFMS8910A, p412 of CSR for VOYAGE-1, Attachment TEFMS678A, p509 of CSR for VOYAGE-2; Table 2, p158 of PEARL publication; Table 2, p170 of LOTUS publication; Table 2, p247 of Igarashi 2012. AMAGINE-2 and -3: study publication did not report PASI 90 results. PHOENIX-1 and PHOENIX-2 trials: data sourced from Week 12 results from Attachment 3.45-3.46, pp.400-401; Attachment 3.53, pp.408-409; Attachment 3.54, pp.410-411 of PHOENIX-1 Week 52 CSR; Attachment 3.31, p295; Attachment 3.32, p296 of PHOENIX-2 Week 28 CSR; Table 2 of NAVIGATE publication.

6.21 As the Commentary updated a number of comparisons (with added data and alternate assessment time points), Table 6 presents a qualitative summary of results of indirect comparisons for PASI 75 and PASI 90 outcomes. As pointed out by the submission, results of indirect comparisons using RR is prone to framing and the conclusions varied depending on if the outcomes were framed as losses or gains.

Table 6: Qualitative summary of indirect comparison results for PASI 75 and PASI 90 at 16/12 weeks and 24 weeks for all risk statistics

Treatment with numerically superior result	PASI 75				PASI 90			
	OR	RR (response)	RR (non-response)	RD	OR	RR (response)	RR (non-response)	RD
All trials 16/12 weeks								
UST45mg	<i>GUS</i>	<i>UST</i>	<i>NE</i>	<i>GUS</i> (✓)	<i>GUS</i>	<i>GUS</i>	<i>NE</i>	<i>GUS</i> (✓)
UST 90mg	<i>GUS</i>	<i>UST</i>	<i>NE</i>	<i>GUS</i> (✓)	<i>GUS</i>	<i>GUS</i>	<i>NE</i>	<i>GUS</i> (✓)
UST label	<i>GUS</i>	<i>GUS</i>	<i>NE</i>	<i>GUS</i> (✓)	<i>NE</i>	<i>NE</i>	<i>NE</i>	<i>NE</i>
UST (all doses pooled)	<i>GUS</i>	<i>GUS</i>	<i>NE</i>	<i>GUS</i> (✓)	<i>GUS</i>	<i>GUS</i>	<i>NE</i>	<i>GUS</i> (✓)
All trials 24 weeks								
UST45mg	<i>GUS</i>	<i>UST</i>	<i>NE</i>	<i>GUS</i> (✓)	<i>GUS</i>	<i>UST</i>	<i>NE</i>	<i>GUS</i> (✓)
UST 90mg	<i>UST</i>	<i>UST</i>	<i>NE</i>	<i>GUS</i> (✓)	<i>GUS</i>	<i>UST</i>	<i>NE</i>	<i>GUS</i> (✓)
UST label	<i>GUS</i>	<i>GUS</i>	<i>NE</i>	<i>GUS</i> (✓)	<i>NE</i>	<i>NE</i>	<i>NE</i>	<i>NE</i>
UST 45mg (PHOENIX trials only)*	<i>GUS</i>	<i>UST</i>	<i>GUS</i>	<i>GUS</i> (✓)	<i>UST</i>	<i>UST</i>	<i>GUS</i>	<i>GUS</i> (✓)
UST 90mg (PHOENIX trials only)*	<i>UST</i>	<i>UST</i>	<i>GUS</i>	<i>GUS</i> (✓)	<i>GUS</i>	<i>UST</i>	<i>GUS</i>	<i>GUS</i> (✓)
UST (all doses pooled)	<i>GUS</i>	<i>UST</i>	<i>NE</i>	<i>GUS</i> (✓)	<i>GUS</i>	<i>UST</i>	<i>NE</i>	<i>GUS</i> (✓)

Bold typography indicates that the indirect comparison reached statistical significance favouring the named drug. Italics represent comparisons that were conducted during the evaluation.

* Submissions' results.

Abbreviations: NE=not estimated. ✓ the lower 95%CI meets the -10% non-inferiority margin in RD. X=the lower 95%CI does not meet the -10% non-inferiority margin in RD.

Source compiled during the evaluation.

Summary of efficacy results

GUSELKUMAB versus USTEKINUMAB

- 6.22 Both guselkumab and ustekinumab were significantly more effective than placebo in terms of proportions of patients attaining either PASI 90 or PASI 75 responses. This was also affirmed by result of investigator assessed responses (IGA in the guselkumab trials and sPGA in the ustekinumab trials).
- 6.23 Based on indirect comparisons using placebo as common reference (assessed at the end of trial placebo controlled periods) guselkumab was numerically superior to ustekinumab 45mg, 90mg with respect to both PASI 75 and PASI 90 responses when comparisons were conducted using OR or RD. The results also reached statistical significance in the RD statistic for both PASI 75 and PASI 90 responses for all comparisons. In the OR statistic, the results were also significant for guselkumab versus ustekinumab (labelled dosing) and ustekinumab (all doses pooled) for PASI 75. Using the RR statistic, no statistically significant differences were detected between guselkumab in any of the ustekinumab comparisons, and the direction of effect varied depending on which dosage of ustekinumab was compared.
- 6.24 At 24 weeks, results of indirect comparisons using placebo response measured at Weeks 16/12 for the guselkumab and ustekinumab trials as common comparator gave similar conclusions based on RD for both PASI 75 and PASI 90 with results favouring guselkumab, although fewer comparisons were statistically significant, all met the non-inferiority margin of -10%. Using OR, the results were more varied, favouring guselkumab for some comparisons and ustekinumab for others. However, none of the results that favoured ustekinumab reached statistical significance.

Results for response expressed in RR, like OR were also varied, but the comparison versus ustekinumab 90mg for PASI 75 did reach statistical significance RR (response) (95%CI): [REDACTED] suggesting fewer responders with guselkumab than ustekinumab 90mg.

- 6.25 In the second line population, the NAVIGATE trial reported a composite outcome of proportion of patients with IGA 0/1 and > 2-grade improvement. Guselkumab was statistically more effective than ustekinumab, however given the trial was conducted in ustekinumab non-responders, the results would naturally favour guselkumab.
- 6.26 Overall, the results suggest that a conclusion of non-inferiority of guselkumab versus ustekinumab would be reasonable.
- 6.27 The results from the indirect comparisons however need to be considered with caution, as a number of differences across trials (e.g., prior biologic experience and proportions of patients with psoriatic arthritis) could impact on the transitivity assumption and impact on the validity of the indirect comparison results. The placebo group PASI 75 response was also found to differ across the trials ranging from 3.1% and 3.7% (PHOENIX- 1 and -2 ustekinumab trials), to 5.7% and 8.1% (in VOYAGE-1 and -2 guselkumab trials) up to 11.1% (in the LOTUS ustekinumab trial).

GUSELKUMAB versus ADALIMUMAB

- 6.28 Compared to adalimumab, at 16 weeks, significantly more patients randomised to guselkumab attained PASI 75 and PASI 90 responses in both VOYAGE-1 and -2 trials (pooled results: RD (95%CI): 0.18 (0.14, 0.22) and 0.23 (0.18, 0.29) for PASI 75 and PASI 90 respectively). Significantly better response to guselkumab versus adalimumab was also maintained at Weeks 24 and 48. This conclusion was also supported by IGA results indicating a higher proportion of patients had attained an IGA 0/1 rating (indicating clear to minimal symptoms) at Week 24 and 48.

Comparative harms

- 6.29 Based on direct comparative data up to Week 16, guselkumab appears to have a similar safety profile compared to placebo and adalimumab (any adverse events (AE), serious AE, discontinuations due to AE, infections). Longer term data (to Week 48) versus adalimumab also indicated a similar conclusion. In an ustekinumab non-responsive population (NAVIGATE), although the incidence of AEs were higher in the guselkumab treatment arm versus ustekinumab, the differences were not statistically significant. Like ustekinumab, the most frequently reported AEs for guselkumab were nasopharyngitis, upper respiratory tract infections and headaches.
- 6.30 The results of the indirect comparison of safety outcomes for guselkumab vs ustekinumab at the end of the placebo-controlled periods Weeks 16/12 are presented in Table 7. Despite a significantly higher discontinuation rate due to AE for guselkumab (based on the RR statistic only), the results would appear to support a conclusion of non-inferior safety for guselkumab versus ustekinumab.

Table 7: Summary of safety indirect comparisons: GUS vs UST – placebo-controlled periods (16 weeks for GUS; 12 weeks for UST)

	Pooled Indirect RR ^a (95% CI)	Pooled Indirect RD ^a (95% CI)	Conclusion for GUS vs UST
GUS vs UST 45 mg			
Any AE	0.97 (0.84, 1.13)	-0.01 (-0.08, 0.06)	No significant difference
Discontinuation due to AE	5.15 (1.03, 25.77)	0.02 (-0, 0.04)	<i>Significant difference using RR but not on RD</i>
Serious AE	1.78 (0.53, 5.97)	0.01 (-0.01, 0.03)	No significant difference
Severe AE	0.80 (0.18, 3.51)	-0.01 (-0.03, 0.01)	No significant difference
Infections	0.93 (0.71, 1.23)	-0.02 (-0.08, 0.04)	No significant difference
GUS vs UST 90 mg			
Any AE	1.05 (0.89, 1.23)	0.03 (-0.04, 0.10)	No significant difference
Discontinuation due to AE	1.81 (0.46, 7.03)	0.01 (-0.01, 0.03)	No significant difference
Serious AE	1.59 (0.46, 5.51)	0.01 (-0.01, 0.03)	No significant difference
Severe AE	0.43 (0.06, 3.21)	-0.01 (-0.04, 0.02)	No significant difference
Infections	1.05 (0.78, 1.41)	0.01 (-0.05, 0.07)	No significant difference
GUS vs UST 45mg for < 100 kg; 90 mg for < 100 kg^{a, b}			
Any AE	0.97 (0.84, 1.12)	-0.01 (-0.08, 0.06)	No significant difference
Discontinuation due to AE	2.73 (0.62, 12.00)	0.01 (-0.01, 0.03)	No significant difference
Serious AE	2.05 (0.67, 6.22)	0.01 (-0.01, 0.03)	No significant difference
Infections	0.92 (0.70, 1.22)	-0.02 (-0.08, 0.04)	No significant difference

Italics indicate results estimated during the evaluation, bold typography indicates statistically significant results.

Abbreviations: AE, adverse event; CI, confidence interval; RR, Relative Risk.

^a Used the UST 45 mg results from the Asian studies (Igarashi 2012, PEARL and LOTUS)

^b The submission did not report severe AE data for patients who received UST according to the weight-based dosing regimen (Table 2.62, p173 of submission).

[^] estimated during the evaluation in RevMan Version 5.3 following the Bucher 1997 method.

Source: Estimated during the evaluation using results reported in Tables 2.60-2.62, pp,172-173 of submission.

Benefits/harms

6.31 A summary of the comparative benefits for guselkumab versus nominated comparators is presented in Table 8. A summary of comparative harms of guselkumab versus comparators is not presented given the results support non-inferior safety.

Table 8: Summary of comparative benefits and harms for GUS and nominated comparators

Trial	Drug	common reference /comparator	OR (95%CI)	Event rate/100 patients*	RD (95% CI)			
Benefits: GUS versus UST								
PASI 75 response at Week 16 (GUS) and Week 12 (UST) using placebo as common reference								
	GUS n/N	PBO n/N	UST n/N	OR ^a (95% CI)	Event rate/100 patients*			RD (95% CI)
					GUS	PBO	UST	
GUS (pooled)	728/825	30/422	-	105.78 (45.70, 244.85)	88.2	7.1	-	0.82 (0.75, 0.89)
UST (all doses)	█	█	█	█	█	█	█	█
Indirect comparison: GUS vs UST (all doses)								
PASI 90 response at Week 16 (GUS) and Week 12 (UST) using placebo as common reference								
GUS (pooled)	588/825	11/422	-	93.32 (50.3, 173.11)	71.3	2.6	-	0.69 (0.65, 0.72)
UST (all doses)	█	█	█	█	█	█	█	█
Indirect comparison: GUS vs UST all doses								
Benefits: GUS vs ADA								
	GUS n/N	ADA n/N	OR ^a (95% CI)	Event rate/100 patients*		RD (95% CI)		
				GUS	ADA			
PASI 75 (Week 16)								
GUS (pooled)	728/825	414/582	3.23 (2.43, 4.30)	88.2	71.1	0.18 (0.14, 0.22)		
PASI 75 (Week 24)								
GUS (pooled)	742/825	417/582	3.61 (2.69, 4.86)	89.9	71.6	0.19 (0.14, 0.23)		
PASI 75 (Week 48)								
GUS ₁	289/329	209/334	4.32 (2.90, 6.43)	87.8	62.6	0.25 (0.19, 0.32)		
PASI 90 (Week 16)								
GUS (pooled)	588/825	282/582	2.71 (2.16, 3.40)	71.3	48.5	0.23 (0.18, 0.29)		
PASI 90 (Week 24)								
GUS (pooled)	637/825	313/582	2.98 (2.08, 4.27)	77.2	53.8	0.24 (0.17, 0.31)		
PASI 90 (Week 48)								
GUS ₁	251/329	160/334	3.50 (2.51, 4.88)	76.3	47.9	0.28 (0.21, 0.35)		

Abbreviations: GUS=guselkumab; GUS (pooled) = VOYAGE-1 and VOYAGE-2; GUS₁=VOYAGE-1; PBO = placebo; OR=odds ratio; RD = risk difference; RR = risk ratio; UST= ustekinumab; UST (all doses) refers to weight-based dosing for UST (UST 45 mg for patients ≤ 100 kg; UST 90 mg for patients > 100 kg, with resulted pulled across all included trials (for UST: UST₁=PHOENIX-1; UST₂=PHOENIX-2; UST₃=PEARL; UST₄=LOTUS; UST₅=Igarashi 2012; UST₆=AMAGINE-2; UST₇=AMAGINE-3).

* Maximum duration of exposure during placebo-controlled phases: 16 weeks for GUS trials; 12 weeks for UST trials. Maximum duration of exposure during DB phases: 48 weeks for VOYAGE-1; 28 weeks for VOYAGE-2.

^a The OR is used here instead of the RR, due to the non-symmetry of the variance of the RR; which can lead to different estimates depending on framing of outcomes as positive or negative outcomes.

Source: Compiled during the evaluation.

6.32 On the basis of indirect evidence presented by the submission, for every 100 patients treated with guselkumab in comparison to ustekinumab over a maximum duration of exposure of 16 weeks for guselkumab and 12 weeks for ustekinumab, it is expected:

- Approximately 16 additional patients would achieve a PASI 75 response versus ustekinumab (all doses pooled); and
- Approximately 23 additional patients would achieve a PASI 90 response versus ustekinumab (all doses pooled).

- 6.33 On the basis of direct evidence presented by the submission, for every 100 patients treated with guselkumab in comparison to adalimumab over a maximum duration of exposure of 48 weeks, it is expected:
- Approximately 18, 19 and 25 additional patients would achieve a PASI 75 response at Weeks 16, 24 and 48 respectively, and
 - Approximately 23, 24 and 28 additional patients would achieve a PASI 90 response at Weeks 16, 24 and 48 respectively.

Clinical claim

- 6.34 The submission described guselkumab as:
- non-inferior (and likely superior) in terms of effectiveness and non-inferior in terms of safety compared to ustekinumab and
 - superior in terms of effectiveness and non-inferior in terms of safety compared to adalimumab.
- 6.35 The safety claims and the efficacy claims of non-inferiority against ustekinumab and superiority versus adalimumab appear to be adequately supported by the results presented in the submission. The evidence however would not adequately support a conclusion of superior efficacy for guselkumab versus ustekinumab as the claim relied on indirect comparisons and there were a number of differences across the included trials that could impact on the transitivity assumption (see 5.25 above). The ESC noted the PSCR confirmed the clinical claim in the submission is that guselkumab is non-inferior to ustekinumab.
- 6.36 The PBAC agreed with the ESC consideration that;
- the claim of non-inferior efficacy and safety versus ustekinumab to be reasonable; and
 - the claim of superior efficacy and non-inferior safety versus adalimumab to be reasonable.
- 6.37 The PBAC restated that even though the clinical evidence supported the clinical claim made by the submission, the PBAC considered that the comparative evidence provided was not informative as the comparators were incorrect.

Economic analysis

- 6.38 The submission presented a cost-minimisation analysis comparing guselkumab with ustekinumab. The analysis compared total costs over a 2-year treatment period (without discounting and despite different initiation periods). Consistent with the clinical claim, a cost-minimisation analysis comparing guselkumab with adalimumab was not presented.
- 6.39 The equi-effective doses were estimated as guselkumab 100 mg at Weeks 0, 4 and every 8 weeks thereafter, and ustekinumab weight-based dosing (45 mg for patients weighing ≤ 100 kg, and 90 mg for patients weighing > 100 kg) at Weeks 0, 4 and every 12 weeks thereafter. The guselkumab dosing was based on trial evidence from

the VOYAGE 1 and 2 trials. The dosing for ustekinumab was based on the weight-based dosing recommended in the PI for ustekinumab. The PHOENIX trials for ustekinumab vs placebo did not assess the efficacy and safety of ustekinumab according to the weight-based dosing, however post hoc analysis by the submission using individual patient data (IPD) did analyse results for those correctly dosed (based on the recommended TGA approved dosing). Furthermore, [REDACTED]

[REDACTED], application of weight-based dosing does not affect the overall cost of ustekinumab.

- 6.40 The submission did not count the continuation dose at Week 28 for both guselkumab and ustekinumab in the cost minimisation analysis, this was corrected during the evaluation. The revised Approved Ex-Manufacturer Price (AEMP) of guselkumab cost-minimised to ustekinumab over a 104-week period was estimated to be \$ [REDACTED]0 (versus an AEMP of \$ [REDACTED] estimated by the submission).
- 6.41 The Commentary included a cost-minimisation analysis using the effective AEMP for the 45 mg vial of ustekinumab. The ESC agreed with the PSCR that the AEMP for ustekinumab is \$4,232.31 and [REDACTED].
- 6.42 The submission assumed that there would be no additional administration costs for guselkumab, despite its more frequent dosing regimen compared to ustekinumab. This assumption may not be appropriate. Over two years, there would be on average additional 4 injections per patient with guselkumab. Given the PBAC had previously accepted that 10 % of patients may require assistance with subcutaneous administration of bDMARDs (golimumab for ankylosing spondylitis (AS) March 2010, paragraph 4 Section 12; golimumab for psoriatic arthritis (PsA) March 2010 PSD, paragraph 5 Section 12; golimumab for RA March 2010 PSD, paragraph 2 Section 10, paragraph 4 c 12), a similar assumption was made during the evaluation. It was assumed that 10% of guselkumab and ustekinumab patients will require a level 'A' General Practitioner consultation per injection (MBS item 3), incurring \$16.95 per visit. The PSCR states that patients with chronic plaque psoriasis are less likely to require assistance with administration compared to patients with arthritic type conditions. The PSCR argues that extrapolating the assumed percentage requiring assistance from spondylitis and arthritis submissions to CPP is inappropriate as CPP does not involve joints, and therefore should not require the same degree of assistance. The ESC acknowledged that fewer than 10% of patient with psoriasis may require assistance with the administration of guselkumab.

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

- 6.43 Using the requested DPMQ of \$ [REDACTED] per injection, and assuming [REDACTED] guselkumab injections per patient per year will be used in the maintenance treatment phase, the drug cost of guselkumab was estimated to be \$ [REDACTED] per patient per year. PBS treatment is only permitted to continue if the patients achieve and maintain a PASI 75 response. Using the DPMQ for ustekinumab of \$4,346.86 and assuming 4.33

ustekinumab injections per patient per year dispensed in the maintenance treatment phase, the drug cost of ustekinumab was estimated to be \$18,836 for maintenance.

Estimated PBS usage & financial implications

6.44 This submission was not considered by DUSC. The submission used a market share approach to estimate the financial implications of listing of guselkumab for CPP. Historical PBS usage data were used to estimate the number of prescriptions for all listed bDMARDs and to project utilisations in the next six years as summarised in Table 9. The key assumptions in the submission’s estimates were:

- Guselkumab would only substitute for ustekinumab (█% of project utilisations in Year 1 and █% from Year 2 onwards) and adalimumab (█% in Year 1 and █% from Year 2 onwards),
- The requested listing would not increase the current growth of bDMARDs for CPP,
- The reduction in costs for ustekinumab, adalimumab was estimated based on the average published DPMQs.

Table 9: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of scripts dispensed ^{a,b}	█	█	█	█	█	█
Estimated financial implications of GUS						
Cost to PBS/RPBS	\$█	\$█	\$█	\$█	\$█	\$█
Cost to PBS/RPBS less co-payments	\$█	\$█	\$█	\$█	\$█	\$█
Estimated financial implications for UST and ADA						
Cost to PBS/RPBS	\$█	\$█	\$█	\$█	\$█	\$█
Cost to PBS/RPBS less co-payments	\$█	\$█	\$█	\$█	\$█	\$█
Net financial implications						
Net cost to PBS/RPBS	\$█	\$█	\$█	\$█	\$█	\$█
Net cost to MBS/DHS/other	\$█	\$█	\$█	\$█	\$█	\$█
Net cost to PBS/RPBS/MBS/DHS	\$█	\$█	\$█	\$█	\$█	\$█

^a Assuming one initial GUS script is equivalent to 1.33 UST scripts and 0.89 ADA scripts. The GUS: ADA equivalence assumed 4.5 ADA scripts in the initial treatment period of 16 weeks. This should be 5 scripts, 2x40mg at Week 0, and 40mg fortnightly starting at Week1.

Assuming one continuing GUS script is equivalent to 1.5 UST scripts and 0.5 ADA scripts.

^b The submission estimated 4.5 ADA initial scripts. This appeared to be the result of counting the subsequent doses from Week 2 instead of Week 1 as recommended in the PI (“Dosing schedule” worksheet). This has been corrected to 5 ADA initial scripts.

Source: Tables 4-6-4-12, pp242-250 of the submission.

The redacted table shows that at Year 6, the estimated number of scripts dispensed was in the range of 10,000 – 50,000 per year and the net cost to the PBS would be less than \$10 million per year.

6.45 The predicted use and financial impacts for the proposed listing may not be accurate for the following reasons:

- the submission did not account for additional costs associated with SC administration with guselkumab despite requiring more frequent dosing compared to ustekinumab (q8w versus q12w), and
- the estimated overall cost to the PBS over the first 6 years relied on

published price for adalimumab and an ustekinumab effective price that is equivalent to its DPMQ.

- 6.46 The PBAC noted the net expected cost to government would be higher if guselkumab should substitute for less expensive biologics.

Quality Use of Medicines

- 6.47 The Sponsor stated in the submission that patients, prescribers, dispensers and dermatology nurses, will be provided with appropriate education, resources and support to promote appropriate prescribing and use. Further, the Sponsor outlined a plan for a patient support program delivered by trained nurses to patients focusing on quality use of medicines.

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

7 PBAC Outcome

- 7.1 The PBAC did not recommend the Section 85 Authority Required listing of guselkumab for the treatment of severe chronic plaque psoriasis (CPP). In making its decision the PBAC considered that ustekinumab was an inappropriate choice as the main comparator.
- 7.2 The submission proposed ustekinumab as the main comparator on the basis of being the most commonly used PBS-subsidised biological for severe CPP (47% market share); and guselkumab being an exclusive IL-23 inhibitor, having a similar mechanism of action to ustekinumab an IL-12/23 inhibitor. The PBAC disagreed with the justification provided to support the nominated comparator and considered that any of the biologic agents on the PBS for CPP may be replaced and hence be a relevant comparator. If treatment with guselkumab is substantially more costly than these alternative therapies, the PBAC could only recommend listing of guselkumab if it is satisfied that guselkumab provides, for some patients, a significant improvement in efficacy or reduction of toxicity over the alternative therapies (National Health Act 1953, Section 101(3B)).
- 7.3 The PBAC noted that the submission nominated adalimumab (ADA) as a supplementary efficacy comparator, based on adalimumab being the active comparator (up to 48 weeks) in the main trials supporting the submission (the VOYAGE-1 and 2 trials).
- 7.4 The PBAC recalled etanercept, adalimumab, secukinumab and ixekizumab were cost-minimised against each other or the least expensive biological. The PBAC noted that the submission claimed superior efficacy for guselkumab versus adalimumab, and thus it may be reasonable to claim for some patients there is a significant improvement in efficacy versus these alternative therapies. However, the PBAC also noted ESC's reference to the findings of the draft post-market review (PMR) of the use of biologics in the treatment of severe CPP which shows that ixekizumab may be the most effective of the PBS listed biologics. Given this, the PBAC considered that a comparison versus ixekizumab would also be informative.

- 7.5 Infliximab and ustekinumab were each listed on a cost effectiveness basis against etanercept. ESC raised that the submission did not include a clinical claim for guselkumab versus infliximab even though infliximab was listed on a cost-effectiveness basis against etanercept, and infliximab is now less costly than ustekinumab. The PBAC agreed with ESC that infliximab was a relevant comparator. The Pre-PBAC response stated that the sponsor would be amenable to listing on a cost-minimisation basis versus infliximab. The PBAC noted that the indirect comparison of the meta-analysed results from the pivotal trials for infliximab (EXPRESS 1 and EXPRESS 2) and guselkumab (VOYAGE 1 and VOYAGE 2) presented in the Pre-PBAC response had not been evaluated and considered that not all potentially relevant infliximab trials were included in the analysis. The PBAC considered that this comparison would need to be presented in a major submission to enable it to be fully evaluated.
- 7.6 The submission was based on an indirect comparison of two placebo and active controlled trials of guselkumab and two placebo-controlled trials of ustekinumab. The PBAC noted that the bias in each of the trials was low, however some transitivity issues were noted across the trials. The PBAC noted that the trial populations were broader than the requested PBS population, however were similar overall to the trial populations previously considered by the PBAC.
- 7.7 The PBAC considered that the safety and efficacy claims of non-inferiority against ustekinumab, and superior efficacy and non-inferior safety versus adalimumab appear to be adequately supported by the results presented in the submission. However, the PBAC considered that additional comparisons are required for the Committee to be satisfied that guselkumab is not substantially more costly than alternative therapies for which a significant improvement in efficacy or reduction of toxicity has not been demonstrated for some patients.
- 7.8 The submission assumed that there will be minimal difference in resource use for administration of guselkumab versus ustekinumab. A proportion of patients who are unable to self-inject may require the assistance from a health care professional. Given guselkumab is administered more frequently than ustekinumab (8 weekly versus 12 weekly) there would be additional administration costs. The Pre Sub-Committee Response (PSCR) claimed that patients with chronic plaque psoriasis are less likely to require assistance with administration compared to patients with arthritic type conditions. The PBAC and ESC considered that fewer than 10% of patients with psoriasis may require assistance with administration.
- 7.9 The PBAC noted the net expected cost to government would be higher than estimated (approximately an additional \$10 - 20 million over 6 years) if guselkumab should substitute for listed biologics with a lower treatment cost compared to ustekinumab.
- 7.10 The PBAC considered that any resubmission must be a major submission and should address the comparator issues as raised above.
- 7.11 The PBAC noted that this submission is eligible for an Independent Review.

Outcome:

Rejected

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

9 Sponsor's Comment

The sponsor had no comment.

Addendum to March 2018 PBAC Minutes

**7.16 GUSELKUMAB,
Injection 100 mg in 1 mL single use pre-filled syringe,
Tremfya[®], Janssen-Cilag Pty Ltd**

10 Background

- 10.1 The sponsor submitted a minor resubmission for the July 2018 PBAC meeting which did not include a formal comparison against an alternative bDMARD and instead, stated acceptance of a cost minimisation approach to ixekizumab.
- 10.2 The sponsor considered that as guselkumab demonstrated superiority over adalimumab in the March 2018 submission, it would be eligible for a price premium over adalimumab. However, the sponsor acknowledged that in accepting a cost-minimisation approach for listing versus ixekizumab, guselkumab will also be considered therapeutically equivalent to and cost-minimised versus adalimumab and secukinumab.
- 10.3 The resubmission presented equi-effective doses and total costs per patient based on the proposed published guselkumab price and the published prices for ixekizumab, adalimumab and secukinumab. The sponsor noted that adalimumab and secukinumab have special pricing arrangements and acknowledged that the cost-minimisation would be performed at the effective price level.
- 10.4 The sponsor considered that differences in the frequency of administration, and potential associated differences in administration costs, do not need to be accounted for in the cost-minimisation analysis. In support of this the sponsor notes the PBAC and ESC considered that fewer than 10% of patients with psoriasis may require assistance with administration (paragraph 7.9, March 2018 Public Summary Document (PSD)).

11 PBAC Outcome

- 11.1 The PBAC recommended an Authority Required listing of guselkumab on a cost-minimisation basis against the lowest cost biological agent available for severe CPP. In making this recommendation, the PBAC accepted any of the current PBS listed bDMARDs for severe CPP could be an alternative therapy to guselkumab.
- 11.2 The PBAC noted that six alternative bDMARDs were listed on the PBS for the treatment of severe CPP at the time of the July 2018 meeting; specifically: adalimumab, etanercept, infliximab, ixekizumab, secukinumab and ustekinumab. The PBAC noted that tildrakizumab for the same indication was also considered at the same meeting. The PBAC considered that the clinical need for an additional bDMARD was low however the PBAC acknowledged the addition of another drug

may be useful to some patients.

- 11.3 The PBAC recalled that the safety and efficacy claims of non-inferiority against ustekinumab, and superior efficacy and non-inferior safety versus adalimumab appear to be adequately supported by the evidence presented in the March 2018 submission. The PBAC also recalled that it considered in March 2018 that comparisons of guselkumab to ixekizumab (paragraph 7.4, March 2018 PSD) and infliximab (paragraph 7.5) would have been informative. The PBAC noted that while the sponsor was agreeable to a cost minimisation approach to either ixekizumab or infliximab, no formal comparison against these or alternative bDMARDs was presented in the resubmission. In the absence of these comparisons, and noting that etanercept, adalimumab, secukinumab and ixekizumab were cost-minimised against each other or the least expensive biological, the PBAC considered it would be appropriate for guselkumab to also be cost-minimised to the least expensive biological agent for this condition.
- 11.4 The PBAC considered the equi-effective doses between guselkumab and the alternative bDMARDs could be derived from the product information and with reference to previously recommended equi-effective doses collated in the PBS Therapeutic Relativity Sheets.
- 11.5 The PBAC advised that it would be appropriate to provide grandfathered PBS supply to those patients receiving non-PBS subsidised guselkumab including those from the existing patient familiarisation program (approximately ■■■ patients) and the soon to be completed ECLIPSE study (approximately ■■■ patients). All grandfathered patients will be required to meet the PBS eligibility criteria and the grandfather provision will be removed from the listing after 12 months in line with standard procedure.
- 11.6 The PBAC recalled that at the March 2018 meeting the sponsor also requested inclusion of a grandfather clause for patients from the Voyage trials which are due to conclude in 2020. The PBAC advised that an additional submission would be required closer to the date of trial completion in order to transition those patients to PBS subsidised guselkumab.
- 11.7 Under section 101(3BA) of the *National Health Act 1953*, the PBAC advised that guselkumab may be treated as interchangeable on an individual patient basis with adalimumab, etanercept, infliximab, ixekizumab, secukinumab, tildrakizumab and ustekinumab for the treatment of severe CPP.
- 11.8 The PBAC advised that guselkumab is not suitable for prescribing by nurse practitioners.
- 11.9 The PBAC advised that the restriction is complex and will include an update to the administrative note which will flow on to the other biologic agents used for severe CPP.
- 11.10 The PBAC recommended that the Early Supply Rule should apply for the continuing treatment phase only.
- 11.11 The PBAC noted that this submission is not eligible for an Independent Review as it

received a positive recommendation.

Outcome:

Recommended

12 Recommended listing

3.1 Add item:

Name, Restriction, Manner of administration and form	Max. Qty	No.of Rpts	Proprietary Name and Manufacturer	
GUSELKUMAB Injection 100 mg in 1 mL pre-filled syringe	1	2	Tremfya®	Janssen- Cilag

Category/Program	GENERAL – General Schedule (Code GE)
Condition	Severe chronic plaque psoriasis
PBS indication	Severe chronic plaque psoriasis
Treatment phase	Initial treatment – Initial 1, Whole body (new patient (no prior biological agent) or patient recommencing treatment after a break of 5 years or more)
Restriction Level/Method	Authority Required - written
Clinical criteria	<p>Patient must have severe chronic plaque psoriasis where lesions have been present for at least 6 months from the time of initial diagnosis, AND Patient must not have received any prior PBS-subsidised treatment with a biological agent for this condition; OR Patient must not have received PBS-subsidised treatment with a biological agent for at least 5 years, if they have previously received PBS-subsidised treatment with a biological agent for this condition and wish to commence a new Treatment Cycle, AND Patient must have failed to achieve an adequate response, as demonstrated by a Psoriasis Area and Severity Index (PASI) assessment, to at least 3 of the following 4 treatments: (i) phototherapy (UVB or PUVA) for 3 treatments per week for at least 6 weeks; and/or (ii) methotrexate at a dose of at least 10 mg weekly for at least 6 weeks; and/or (iii) cyclosporin at a dose of at least 2 mg per kg per day for at least 6 weeks; and/or (iv) acitretin at a dose of at least 0.4 mg per kg per day for at least 6 weeks, AND Patient must have signed a patient and prescriber acknowledgement indicating they understand and acknowledge that PBS-subsidised treatment will cease if they do not meet the predetermined response criterion for ongoing PBS-subsidised treatment, as outlined in the restriction for continuing treatment (whole body), AND The treatment must be as systemic monotherapy (other than methotrexate), AND Patient must not receive more than 20 weeks of treatment under this restriction. Must be treated by a dermatologist.</p>
Population criteria	Patient must be aged 18 years or older.
Prescribing Instructions:	<p>For the purposes of this restriction 'biological agent' means adalimumab, etanercept, <i>guselkumab</i>, infliximab, ixekizumab, secukinumab or ustekinumab. Where treatment with methotrexate, cyclosporin or acitretin is contraindicated according to the relevant TGA-approved Product Information, or where phototherapy is contraindicated,</p>

	<p>details must be provided at the time of application.</p> <p>Where intolerance to treatment with phototherapy, methotrexate, cyclosporin or acitretin developed during the relevant period of use, which was of a severity to necessitate permanent treatment withdrawal, details of the degree of this toxicity must be provided at the time of application.</p> <p>The following criterion indicates failure to achieve an adequate response to prior treatment and must be demonstrated in the patient at the time of the application:</p> <p>(a) A current Psoriasis Area and Severity Index (PASI) score of greater than 15, as assessed, preferably whilst still on treatment, but no longer than 1 month following cessation of the most recent prior treatment.</p> <p>(b) A PASI assessment must be completed for each prior treatment course, preferably whilst still on treatment, but no longer than 1 month following cessation of each course of treatment.</p> <p>(c) The most recent PASI assessment must be no more than 1 month old at the time of application.</p> <p>The authority application must be made in writing and must include:</p> <p>(a) a completed authority prescription form; and</p> <p>(b) a completed Severe Chronic Plaque Psoriasis PBS Authority Application - Supporting Information Form which includes the following:</p> <p>(i) the completed current and previous Psoriasis Area and Severity Index (PASI) calculation sheets including the dates of assessment of the patient's condition; and</p> <p>(ii) details of previous phototherapy and systemic drug therapy [dosage (where applicable), date of commencement and duration of therapy]; and</p> <p>(iii) the signed patient and prescriber acknowledgements.</p>
<p>Administrative Advice:</p>	<p>Details of the toxicities, including severity, which will be accepted as a reason for exempting a patient from the requirement for 6 weeks treatment with phototherapy, methotrexate, cyclosporin or acitretin can be found on the Department of Human Services website (www.humanservices.gov.au)</p> <p>A PASI assessment of the patient's response to this initial course of treatment must be made after at least 12 weeks of treatment so that there is adequate time for a response to be demonstrated. This assessment, which will be used to determine eligibility for continuing treatment, must be submitted to the Department of Human Services no later than 1 month from the date of completion of this initial course of treatment. Where a response assessment is not undertaken and submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with this drug.</p> <p>In circumstances where it is not possible to submit a response assessment within these timeframes, please call the Department of Human Services on 1800 700 270 to discuss.</p> <p>It is recommended that an application is posted to the Department of Human Services no later than 2 weeks prior to the patient completing their current treatment course to ensure continuity of treatment for those patients who meet the continuation criterion for PBS-subsidised treatment with this drug.</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p> <p>No increase in the maximum number of repeats may be authorised. No increase in the maximum number of units may be authorised.</p>

Public Summary Document – March 2018 PBAC Meeting

	Special Pricing Arrangements apply.
Category/Program	GENERAL – General Schedule (Code GE)
Prescriber type	Dermatologists
Condition	Severe chronic plaque psoriasis
PBS indication	Severe chronic plaque psoriasis
Treatment phase	Treatment Phase: Initial treatment – Initial 2, Whole body (change or recommencement of treatment after a break of less than 5 years)
Restriction Level/Method	Authority Required - written
Clinical criteria	<p>Patient must have a documented history of severe chronic plaque psoriasis, AND Patient must have received prior PBS-subsidised treatment with a biological agent for this condition in this Treatment Cycle, AND Patient must not have already failed, or ceased to respond to, PBS-subsidised treatment with 3 biological agents for this condition within this Treatment Cycle, AND Patient must not have failed, or ceased to respond to, PBS-subsidised therapy with this drug for the treatment of this condition in the current Treatment Cycle, AND The treatment must be as systemic monotherapy (other than methotrexate), AND Patient must not receive more than 20 weeks of treatment under this restriction. AND Must be treated by a dermatologist.</p>
Population criteria	Patient must be aged 18 years or older.
Prescribing Instructions	<p>For the purposes of this restriction 'biological agent' means adalimumab, etanercept, <i>guselkumab</i> infliximab, ixekizumab, secukinumab or ustekinumab. The authority application must be made in writing and must include: (a) a completed authority prescription form; and (b) a completed Severe Chronic Plaque Psoriasis PBS Authority Application - Supporting Information Form which includes the following: (i) the completed current Psoriasis Area and Severity Index (PASI) calculation sheets including the dates of assessment of the patient's condition; and (ii) details of prior biological treatment, including dosage, date and duration of treatment. Applications for patients who have demonstrated a response to PBS-subsidised treatment with this drug within this Treatment Cycle and who wish to recommence treatment with this drug within the same Cycle following a break in therapy, will only be approved where evidence of the patient's response to their most recent course of PBS-subsidised treatment with this drug has been submitted within 1 month of cessation of treatment. 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 prebiological treatment baseline value for this Treatment Cycle.</p>
Administrative Advice:	A PASI assessment of the patient's response to this initial course of treatment must be made after at least 12 weeks of treatment so that there is adequate time for a response to be demonstrated. This assessment, which will be used to determine eligibility for continuing treatment, must be submitted to the Department of Human Services no later than 1 month from the date of completion of this initial course of treatment. Where a response assessment is not undertaken and submitted to the Department of Human Services within these

	<p>timeframes, the patient will be deemed to have failed to respond to treatment with this drug. In circumstances where it is not possible to submit a response assessment within these timeframes, please call the Department of Human Services on 1800 700 270 to discuss.</p> <p>Patients who fail to demonstrate a response to treatment with 3 biological agents are deemed to have completed this Treatment Cycle and must cease PBS-subsidised therapy. These patients may recommence a new Biological Treatment Cycle after a minimum of 5 years has elapsed between the date the last prescription for a PBS-subsidised biological agent was approved in this Cycle and the date of the first application under the new Cycle.</p> <p>It is recommended that an application is posted to the Department of Human Services no later than 2 weeks prior to the patient completing their current treatment course to ensure continuity of treatment for those patients who meet the continuation criterion for PBS-subsidised treatment with this drug.</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p> <p>No increase in the maximum number of repeats may be authorised. No increase in the maximum number of units may be authorised. Special Pricing Arrangements apply.</p>
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Category/Program	GENERAL – General Schedule (Code GE)
Condition	Severe chronic plaque psoriasis
PBS indication	Severe chronic plaque psoriasis
Treatment phase	Treatment Phase: Initial treatment – Initial 1, Face, hand, foot (new patient (no prior biological agent) or patient recommencing treatment after a break of 5 years or more)
Restriction Level/Method	Authority Required - written
Clinical criteria	<p>Patient must have severe chronic plaque psoriasis of the face, or palm of a hand or sole of a foot where the plaque or plaques have been present for at least 6 months from the time of initial diagnosis, AND Patient must not have received any prior PBS-subsidised treatment with a biological agent for this condition; OR Patient must not have received PBS-subsidised treatment with a biological agent for at least 5 years, if they have previously received PBS-subsidised treatment with a biological agent for this condition and wish to commence a new Treatment Cycle, AND Patient must have failed to achieve an adequate response, as demonstrated by a Psoriasis Area and Severity Index (PASI) assessment, to at least 3 of the following 4 treatments: (i) phototherapy (UVB or PUVA) for 3 treatments per week for at least 6 weeks; and/or (ii) methotrexate at a dose of at least 10 mg weekly for at least 6 weeks; and/or (iii) cyclosporin at a dose of at least 2 mg per kg per day for at least 6 weeks; and/or (iv) acitretin at a dose of at least 0.4 mg per kg per day for at least 6 weeks, AND Patient must have signed a patient and prescriber acknowledgement indicating they understand and acknowledge that PBS-subsidised treatment will cease if they do not meet</p>

	<p>the predetermined response criterion for ongoing PBS-subsidised treatment, as outlined in the restriction for continuing treatment (face, hand, foot),</p> <p>AND</p> <p>The treatment must be as systemic monotherapy (other than methotrexate),</p> <p>AND</p> <p>Patient must not receive more than 20 weeks of treatment under this restriction.</p> <p>AND</p> <p>Must be treated by a dermatologist.</p>
Population criteria	Patient must be aged 18 years or older
Prescriber Instructions:	<p>For the purposes of this restriction 'biological agent' means adalimumab, etanercept, <i>guselkumab</i>, infliximab, ixekizumab, secukinumab or ustekinumab.</p> <p>Where treatment with methotrexate, cyclosporin or acitretin is contraindicated according to the relevant TGA-approved Product Information, or where phototherapy is contraindicated, details must be provided at the time of application.</p> <p>Where intolerance to treatment with phototherapy, methotrexate, cyclosporin or acitretin developed during the relevant period of use, which was of a severity to necessitate permanent treatment withdrawal, details of the degree of this toxicity must be provided at the time of application.</p> <p>The following criterion indicates failure to achieve an adequate response to prior treatment and must be demonstrated in the patient at the time of the application:</p> <p>(a) Chronic plaque psoriasis classified as severe due to a plaque or plaques on the face, palm of a hand or sole of a foot where:</p> <p>(i) at least 2 of the 3 Psoriasis Area and Severity Index (PASI) symptom subscores for erythema, thickness and scaling are rated as severe or very severe, as assessed, preferably whilst still on treatment, but no longer than 1 month following cessation of the most recent prior treatment; or</p> <p>(ii) the skin area affected is 30% or more of the face, palm of a hand or sole of a foot, as assessed, preferably whilst still on treatment, but no longer than 1 month following cessation of the most recent prior treatment;</p> <p>(b) A PASI assessment must be completed for each prior treatment course, preferably whilst still on treatment, but no longer than 1 month following cessation of each course of treatment.</p> <p>(c) The most recent PASI assessment must be no more than 1 month old at the time of application.</p> <p>The authority application must be made in writing and must include:</p> <p>(a) a completed authority prescription form; and</p> <p>(b) a completed Severe Chronic Plaque Psoriasis PBS Authority Application - Supporting Information Form which includes the following:</p> <p>(i) the completed current and previous Psoriasis Area and Severity Index (PASI) calculation sheets and face, hand, foot area diagrams including the dates of assessment of the patient's condition; and</p> <p>(ii) details of previous phototherapy and systemic drug therapy [dosage (where applicable), date of commencement and duration of therapy]; and</p> <p>(iii) the signed patient and prescriber acknowledgements.</p>
Administrative Advice:	<p>Details of the toxicities, including severity, which will be accepted as a reason for exempting a patient from the requirement for 6 weeks treatment with phototherapy, methotrexate, cyclosporin or acitretin can be found on the Department of Human Services website (www.humanservices.gov.au)</p> <p>A PASI assessment of the patient's response to this initial course of treatment must be made after at least 12 weeks of treatment so that there is adequate time for a response to be demonstrated. This assessment, which will be used to determine eligibility for continuing treatment, must be submitted to the Department of Human Services no later than 1 month</p>

	<p>from the date of completion of this initial course of treatment. The PASI assessment for continuing treatment must be performed on the same affected area as assessed at baseline. Where a response assessment is not undertaken and submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with this drug.</p> <p>In circumstances where it is not possible to submit a response assessment within these timeframes, please call the Department of Human Services on 1800 700 270 to discuss. It is recommended that an application is posted to the Department of Human Services no later than 2 weeks prior to the patient completing their current treatment course to ensure continuity of treatment for those patients who meet the continuation criterion for PBS-subsidised treatment with this drug.</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p> <p>No increase in the maximum number of repeats may be authorised. No increase in the maximum number of units may be authorised. Special Pricing Arrangements apply.</p>
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Category/Program	GENERAL – General Schedule (Code GE)
Condition	Severe chronic plaque psoriasis
PBS indication	Severe chronic plaque psoriasis
Treatment phase	Treatment Phase: Initial treatment – Initial 2, Face, hand, foot (change or recommencement of treatment after a break of less than 5 years)
Restriction Level/Method	Authority Required - written
Clinical criteria	<p>Patient must have a documented history of severe chronic plaque psoriasis of the face, or palm of a hand or sole of a foot, AND Patient must have received prior PBS-subsidised treatment with a biological agent for this condition in this Treatment Cycle, AND Patient must not have already failed, or ceased to respond to, PBS-subsidised treatment with 3 biological agents for this condition within this Treatment Cycle, AND Patient must not have failed, or ceased to respond to, PBS-subsidised therapy with this drug for the treatment of this condition in the current Treatment Cycle, AND The treatment must be as systemic monotherapy (other than methotrexate), AND Patient must not receive more than 20 weeks of treatment under this restriction.</p>

Population criteria	Patient must be aged 18 years or older
Treatment criteria	<p>Must be treated by a dermatologist.</p> <p>For the purposes of this restriction 'biological agent' means adalimumab, etanercept, <i>guselkumab</i>, infliximab, ixekizumab, secukinumab or ustekinumab.</p> <p>The authority application must be made in writing and must include:</p> <p>(a) a completed authority prescription form; and</p> <p>(b) a completed Severe Chronic Plaque Psoriasis PBS Authority Application - Supporting Information Form which includes the following:</p> <p>(i) the completed current Psoriasis Area and Severity Index (PASI) calculation sheets and face, hand, foot area diagrams including the dates of assessment of the patient's condition; and</p> <p>(ii) details of prior biological treatment, including dosage, date and duration of treatment.</p> <p>Applications for patients who have demonstrated a response to PBS-subsidised treatment with this drug within this Treatment Cycle and who wish to recommence treatment with this drug within the same Cycle following a break in therapy, will only be approved where evidence of the patient's response to their most recent course of PBS-subsidised treatment with this drug has been submitted within 1 month of cessation of treatment.</p> <p>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 pre-biological treatment 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 pre-biological treatment baseline value.</p>
Administrative Advice:	<p>A PASI assessment of the patient's response to this initial course of treatment must be made after at least 12 weeks of treatment so that there is adequate time for a response to be demonstrated. This assessment, which will be used to determine eligibility for continuing treatment, must be submitted to the Department of Human Services no later than 1 month from the date of completion of this initial course of treatment. The PASI assessment for continuing treatment must be performed on the same affected area as assessed at baseline. Where a response assessment is not undertaken and submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with this drug.</p> <p>In circumstances where it is not possible to submit a response assessment within these timeframes, please call the Department of Human Services on 1800 700 270 to discuss.</p> <p><u>Note</u></p> <p>Patients who fail to demonstrate a response to treatment with 3 biological agents are deemed to have completed this Treatment Cycle and must cease PBS-subsidised therapy. These patients may recommence a new Biological Treatment Cycle after a minimum of 5 years has elapsed between the date the last prescription for a PBS-subsidised biological agent was approved in this Cycle and the date of the first application under the new Cycle.</p> <p><u>Note</u></p> <p>It is recommended that an application is posted to the Department of Human Services no later than 2 weeks prior to the patient completing their current treatment course to ensure continuity of treatment for those patients who meet the continuation criterion for PBS-subsidised treatment with this drug.</p> <p><u>Note</u></p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p>

Public Summary Document – March 2018 PBAC Meeting

	<p>Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p> <p><u>Note</u> No increase in the maximum number of repeats may be authorised. No increase in the maximum number of units may be authorised. Special Pricing Arrangements apply.</p>
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Category/Program	GENERAL – General Schedule (Code GE)
Condition	Severe chronic plaque psoriasis
PBS indication	Severe chronic plaque psoriasis
Treatment phase	Treatment Phase: Initial treatment - Initial 1, Whole body or Face, hand, foot (new patient or patient recommencing treatment after a break of 5 years or more) or Initial 2, Whole body or Face, hand, foot (change or recommencement of treatment after a break of less than 5 years) - balance of supply
Restriction Level/Method	Authority Required - telephone
Clinical criteria	<p>Patient must have received insufficient therapy with this drug under the Initial 1, Whole body (new patient or patient recommencing treatment after a break of 5 years or more) restriction to complete 20 weeks treatment; OR</p> <p>Patient must have received insufficient therapy with this drug under the Initial 2, Whole body (change or recommencement of treatment after a break of less than 5 years) restriction to complete 20 weeks treatment; OR</p> <p>Patient must have received insufficient therapy with this drug under the Initial 1, Face, hand, foot (new patient or patient recommencing treatment after a break of 5 years or more) restriction to complete 20 weeks treatment; OR</p> <p>Patient must have received insufficient therapy with this drug under the Initial 2, Face, hand, foot (change or recommencement of treatment after a break of less than 5 years) restriction to complete 20 weeks treatment,</p> <p>AND</p> <p>The treatment must be as systemic monotherapy (other than methotrexate),</p> <p>AND</p> <p>The treatment must provide no more than the balance of up to 20 weeks treatment available under the above restrictions.</p> <p>AND</p> <p>Must be treated by a dermatologist.</p>
Administrative Advice:	<p><u>Note</u> Authority approval for sufficient therapy to complete a maximum of 20 weeks of treatment may be requested by telephone by contacting the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). No increase in the maximum number of repeats may be authorised. No increase in the maximum number of units may be authorised. Special Pricing Arrangements apply.</p>

Category/Program	GENERAL – General Schedule (Code GE)
Condition	Severe chronic plaque psoriasis
PBS indication	Severe chronic plaque psoriasis
Treatment phase	Treatment Phase: Continuing treatment, Face, hand, foot

Restriction Level/Method	Authority Required - written
Clinical criteria	<p>Patient must have a documented history of severe chronic plaque psoriasis of the face, or palm of a hand or sole of a foot, AND Patient must have received this drug as their most recent course of PBS-subsidised treatment with a biological agent for this condition in the current Treatment Cycle, AND Patient must have demonstrated an adequate response to their most recent course of treatment with this drug, AND The treatment must be as systemic monotherapy (other than methotrexate), AND Patient must not receive more than 24 weeks of treatment per continuing treatment course authorised under this restriction. AND Must be treated by a dermatologist</p>
Population criteria	Patient must be aged 18 years or older
	<p>For the purposes of this restriction 'biological agent' means adalimumab, etanercept, guselkumab, infliximab, ixekizumab, secukinumab or ustekinumab. 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 pre-biological treatment baseline values; or (ii) a reduction by 75% or more in the skin area affected, or sustained at this level, as compared to the pre-biological treatment baseline value. All applications for continuing treatment with this drug must include a measurement of response to the most recent course of PBS-subsidised therapy. This assessment must be submitted no later than 4 weeks from the cessation of that treatment course. If the application is the first application for continuing treatment with this drug, it must be accompanied by an assessment of response to a minimum of 12 weeks of treatment with the initial treatment course. Where a response assessment is not submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with this drug. The authority application must be made in writing and must include: (a) a completed authority prescription form; and (b) a completed Severe Chronic Plaque Psoriasis PBS Authority Application - Supporting Information Form which includes the following: (i) 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. The most recent PASI assessment must be no more than 1 month 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. The PASI assessment for continuing treatment must be performed on the same affected area assessed at baseline.</p>
Administrative Advice:	A PASI assessment of the patient's response must be conducted within 4 weeks prior to completion of this course of treatment. This assessment, which will be used to determine eligibility for further continuing treatment, must be submitted to the Department of Human Services no later than 1 month from the date of completion of this course of treatment. Where a response assessment is not undertaken and submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to

	<p>treatment with this drug.</p> <p>In circumstances where it is not possible to submit a response assessment within these timeframes, please call the Department of Human Services on 1800 700 270 to discuss.</p> <p>Patients who fail to demonstrate a response to treatment with 3 biological agents are deemed to have completed this Treatment Cycle and must cease PBS-subsidised therapy. These patients may recommence a new Biological Treatment Cycle after a minimum of 5 years has elapsed between the date the last prescription for a PBS-subsidised biological agent was approved in this Cycle and the date of the first application under the new Cycle.</p> <p>It is recommended that an application is posted to the Department of Human Services no later than 2 weeks prior to the patient completing their current treatment course to ensure continuity of treatment for those patients who meet the continuation criterion for PBS-subsidised treatment with this drug.</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p> <p>No increase in the maximum number of repeats may be authorised. No increase in the maximum number of units may be authorised. Special Pricing Arrangements apply.</p>
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Category/Program	GENERAL – General Schedule (Code GE)
Condition	Severe chronic plaque psoriasis
PBS indication	Severe chronic plaque psoriasis
Treatment phase	Treatment Phase: Continuing treatment, Whole body
Restriction Level/Method	Authority Required - written
Clinical criteria:	<p>Patient must have received insufficient therapy with this drug under the Continuing treatment, Whole body restriction to complete 24 weeks treatment; OR</p> <p>Patient must have received insufficient therapy with this drug under the Continuing treatment, Face, hand, foot restriction to complete 24 weeks treatment,</p> <p>AND</p> <p>The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restrictions,</p> <p>AND</p> <p>The treatment must be as systemic monotherapy (other than methotrexate).</p> <p>AND</p> <p>Must be treated by a dermatologist.</p>
Prescriber Instructions:	<p>For the purposes of this restriction 'biological agent' means adalimumab, etanercept, <i>guselkumab</i>, infliximab, ixekizumab, secukinumab or ustekinumab.</p> <p>An adequate response to treatment is defined as:</p> <p>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 prebiological treatment baseline value for this Treatment Cycle.</p> <p>All applications for continuing treatment with this drug must include a measurement of response to the most recent course of PBS-subsidised therapy. This assessment must be</p>

	<p>submitted no later than 4 weeks from the cessation of that treatment course. If the application is the first application for continuing treatment with this drug, it must be accompanied by an assessment of response to a minimum of 12 weeks of treatment with the initial treatment course.</p> <p>Where a response assessment is not submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with this drug.</p> <p>The authority application must be made in writing and must include:</p> <p>(a) a completed authority prescription form; and</p> <p>(b) a completed Severe Chronic Plaque Psoriasis PBS Authority Application - Supporting Information Form which includes the following:</p> <p>(i) the completed Psoriasis Area and Severity Index (PASI) calculation sheet including the date of the assessment of the patient's condition.</p> <p>The most recent PASI assessment must be no more than 1 month old at the time of application.</p> <p>Approval will be based on the PASI assessment of response to the most recent course of treatment with this drug.</p>
<p>Administrative Advice:</p>	<p>A PASI assessment of the patient's response must be conducted within 4 weeks prior to completion of this course of treatment. This assessment, which will be used to determine eligibility for further continuing treatment, must be submitted to the Department of Human Services no later than 1 month from the date of completion of this course of treatment. Where a response assessment is not undertaken and submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with this drug.</p> <p>Patients who fail to demonstrate a response to treatment with 3 biological agents are deemed to have completed this Treatment Cycle and must cease PBS-subsidised therapy. These patients may recommence a new Biological Treatment Cycle after a minimum of 5 years has elapsed between the date the last prescription for a PBS-subsidised biological agent was approved in this Cycle and the date of the first application under the new Cycle.</p> <p>In circumstances where it is not possible to submit a response assessment within these timeframes, please call the Department of Human Services on 1800 700 270 to discuss. Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p> <p>No increase in the maximum number of repeats may be authorised. No increase in the maximum number of units may be authorised. Special Pricing Arrangements apply.</p>

Grandfathered patients:

Category/Program	GENERAL – General Schedule (Code GE)
Condition	Severe chronic plaque psoriasis
PBS indication	Severe chronic plaque psoriasis
Treatment phase	Treatment Phase: Initial treatment – Initial 3, Whole body (initial PBS-subsidised supply for

	continuing treatment in a patient commenced on non-PBS-subsidised therapy)
Restriction Level/Method	Authority Required - written
Clinical criteria	<p>Patient must have a documented history of severe chronic plaque psoriasis, AND Patient must have been receiving treatment with this drug for this condition prior to [insert date], AND Patient must have had a Psoriasis Area and Severity Index (PASI) score of greater than 15 prior to commencing treatment with this drug, AND Patient must have demonstrated a response to treatment as specified in the criterion included in the restriction for continuing PBS-subsidised treatment with this drug (whole body), AND Patient must have signed a patient and prescriber acknowledgement indicating they understand and acknowledge that PBS-subsidised treatment will cease if they do not meet the predetermined response criterion for ongoing PBS-subsidised treatment, as outlined in the restriction for continuing treatment (whole body), AND The treatment must be as systemic monotherapy (other than methotrexate), AND Patient must not receive more than 24 weeks of treatment under this restriction. AND Must be treated by a dermatologist.</p>
Population criteria	Patients must be aged 18 years or older
Prescribing Instructions:	<p>The authority application must be made in writing and must include:</p> <ul style="list-style-type: none"> (a) a completed authority prescription form; and (b) a completed Severe Chronic Plaque Psoriasis PBS Authority Application - Supporting Information Form which includes the following: <ul style="list-style-type: none"> (i) the completed Psoriasis Area and Severity Index (PASI) calculation sheet including the date of the assessment of the patient's condition at baseline (prior to initiation of 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]; and (iii) the signed patient and prescriber acknowledgements. <p>The most recent PASI assessment must be no more than 1 month old at the time of application.</p> <p>A patient may qualify for PBS-subsidised treatment under this restriction once only</p>
Administrative Advice:	<p>A PASI assessment of the patient's response to this initial PBS-subsidised course of therapy must be conducted within 4 weeks prior to completion of this course of treatment. This assessment, which will be used to determine eligibility for continuing treatment, must be submitted to the Department of Human Services no later than 1 month from the date of completion of this initial course of treatment. Where a response assessment is not undertaken and submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with this drug.</p> <p>In circumstances where it is not possible to submit a response assessment within these timeframes, please call the Department of Human Services on 1800 700 270 to discuss.</p> <p>It is recommended that an application is posted to the Department of Human Services no later than 2 weeks prior to the patient completing their current treatment course to ensure continuity of treatment for those patients who meet the continuation criterion for PBS-subsidised treatment with this drug.</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to</p>

Public Summary Document – March 2018 PBAC Meeting

	<p>Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p> <p>No increase in the maximum number of repeats may be authorised. No increase in the maximum number of units may be authorised. Special Pricing Arrangements apply.</p>
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Category/Program	GENERAL – General Schedule (Code GE)
Condition	Severe chronic plaque psoriasis
PBS indication	Severe chronic plaque psoriasis
Treatment phase	Treatment Phase: Initial treatment – Initial 3, Face, hand, foot (initial PBS-subsidised supply for continuing treatment in a patient commenced on non-PBS-subsidised therapy)
Restriction Level/Method	Authority Required - written
Clinical criteria	<p>Patient must have a documented history of severe chronic plaque psoriasis of the face, or palm of a hand or sole of a foot, AND Patient must have been receiving treatment with this drug for this condition prior to [insert date], AND Patient must have had disease, prior to 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 were rated as severe or very severe; or (ii) the skin area affected was 30% or more of the face, palm of a hand or sole of a foot, AND Patient must have demonstrated a response to treatment as specified in the criterion included in the restriction for continuing PBS-subsidised treatment with this drug (face, hand, foot), AND Patient must have signed a patient and prescriber acknowledgement indicating they understand and acknowledge that PBS-subsidised treatment will cease if they do not meet the predetermined response criterion for ongoing PBS-subsidised treatment, as outlined in the restriction for continuing treatment (face, hand, foot), AND The treatment must be as systemic monotherapy (other than methotrexate), AND Patient must not receive more than 24 weeks of treatment under this restriction. AND Must be treated by a dermatologist.</p>
Population criteria	Patients must be aged 18 years or older
Prescribing instructions:	<p>The authority application must be made in writing and must include:</p> <p>(a) a completed authority prescription form; and (b) a completed Severe Chronic Plaque Psoriasis PBS Authority Application - Supporting Information Form which includes the following:</p>

	<p>(i) 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 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]; and</p> <p>(iii) the signed patient and prescriber acknowledgements.</p> <p>The most recent PASI assessment must be no more than 1 month old at the time of application.</p> <p>The PASI assessment must be performed on the same affected area as assessed at baseline or prior to initiation of treatment with this drug.</p> <p>A patient may qualify for PBS-subsidised treatment under this restriction once only</p>
<p>Administrative Advice:</p>	<p>A PASI assessment of the patient's response to this initial PBS-subsidised course of therapy must be conducted within 4 weeks prior to completion of this course of treatment. This assessment, which will be used to determine eligibility for continuing treatment, must be submitted to the Department of Human Services no later than 1 month from the date of completion of this initial course of treatment. Where a response assessment is not undertaken and submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with this drug.</p> <p>In circumstances where it is not possible to submit a response assessment within these timeframes, please call the Department of Human Services on 1800 700 270 to discuss.</p> <p>It is recommended that an application is posted to the Department of Human Services no later than 2 weeks prior to the patient completing their current treatment course to ensure continuity of treatment for those patients who meet the continuation criterion for PBS-subsidised treatment with this drug.</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p> <p>No increase in the maximum number of repeats may be authorised No increase in the maximum number of units may be authorised. Special Pricing Arrangements apply.</p>

13 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

14 Sponsor's Comment

The sponsor had no comment.