

## 5.14 RISANKIZUMAB, Injection 150 mg in 1 mL pre-filled syringe Injection 150 mg in 1 mL pre-filled pen, Skyrizi<sup>®</sup>, AbbVie Pty Ltd.

### 1 Purpose of submission

- 1.1 The Category 2 submission requested a General Schedule, Authority Required (written) listing for risankizumab 150 mg for the treatment of patients with severe psoriatic arthritis (PsA).
- 1.2 Listing was requested on a cost minimisation basis versus guselkumab.

**Table 1: Key components of the clinical issue addressed in the submission**

Component	Description
Population	Patients with severe psoriatic arthritis unable to achieve an adequate response with at least 6 months of intensive treatment with csDMARDs, as per current criteria for PBS-listed advanced therapies
Intervention	Risankizumab 150 mg subcutaneous injection at week 0, week 4, and then every 12 weeks thereafter
Comparator	Guselkumab 100 mg subcutaneous injection at week 0, week 4, then every 8 weeks thereafter
Outcomes	Disease activity endpoints: ACR20, ACR50, Psoriatic Assessment Severity Index 75% response (PASI75) Patient reported outcome: Health Assessment Questionnaire disability index (HAQ-DI)
Clinical claim	In patients with severe psoriatic arthritis who have not achieved an adequate response with conventional therapies, risankizumab is non-inferior to guselkumab in terms of efficacy and safety

Source: Table 1-1, p17 of the submission.

Abbreviations: ACR20/50, American College of Rheumatology 20%/50% response; csDMARDs, conventional synthetic disease anti-rheumatic drugs.

### 2 Background

#### **Registration status**

- 2.1 TGA status at time of PBAC consideration: not registered. The submission was made under the TGA/PBAC Parallel Process. At the time of PBAC consideration, the draft Product Information, Clinical Evaluation Report and Delegate's overview were available.
- 2.2 Risankizumab has an approved TGA indication for the treatment of moderate to severe plaque psoriasis in adults who are candidates for phototherapy or systemic therapy.

### 3 Requested listing

- 3.1 An abbreviated version of the proposed restriction is presented below, for brevity purposes. For the recommended restriction, please see Section 8.

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
INITIAL RISANKIZUMAB, pre-filled syringe, 150 mg	1	2	\$5,400.51 (published)	Skyrizi® AbbVie Pty Ltd
INITIAL RISANKIZUMAB, pre-filled pen, 150 mg	1	2	\$5,400.51 (published)	Skyrizi® AbbVie Pty Ltd
CONTINUING RISANKIZUMAB, pre-filled syringe, 150 mg	1	1	\$5,400.51 (published)	Skyrizi® AbbVie Pty Ltd
CONTINUING RISANKIZUMAB, pre-filled pen, 150 mg	1	1	\$5,400.51 (published)	Skyrizi® AbbVie Pty Ltd
Category/Program:	General Schedule			
PBS indication:	Severe psoriatic arthritis			
Restriction:	Authority required – in Writing			
Treatment phase:	Initial treatment – initial 1 (new patient)			
Clinical criteria:	Patient must not have received PBS-subsidised treatment with a biological medicine for this condition, AND Patient must have failed to achieve an adequate response to methotrexate at a dose of at least 20 mg weekly for a minimum period of 3 months, AND Patient must have failed to achieve an adequate response to sulfasalazine at a dose of at least 2 g per day for a minimum period of 3 months; OR Patient must have failed to achieve an adequate response to leflunomide at a dose of up to 20 mg daily for a minimum period of 3 months, AND Patient must not receive more than 16 weeks of treatment under this restriction.			
Treatment phase:	Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 5 years)			
Clinical criteria:	Patient must have received prior PBS-subsidised treatment with a biological medicine 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 medicines for this condition within this treatment cycle, AND Patient must not have already failed, or ceased to respond to, PBS-subsidised treatment with this drug for this condition during the current treatment cycle, AND Patient must not receive more than 16 weeks of treatment under this restriction.			
Treatment phase:	Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years)			
Clinical criteria:	Patient must have previously received PBS-subsidised treatment with a biological medicine for this condition, AND Patient must have a break in treatment of 5 years or more from the most recently approved PBS-subsidised biological medicine for this condition, AND The condition must have an elevated erythrocyte sedimentation rate (ESR) greater than 25 mm per hour; OR The condition must have a C-reactive protein (CRP) level greater than 15 mg per L, AND The condition must have either (a) a total active joint count of at least 20 active (swollen and tender) joints; or (b) at least 4 active major joints, AND Patient must not receive more than 16 weeks of treatment under this restriction.			

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Treatment phase:	Transitioning from non-PBS to PBS-subsidised supply - 'Grandfather' arrangements
Clinical criteria:	<p>Patient must have received treatment with this drug for this PBS indication prior to [LISTING DATE]</p> <p>AND</p> <p>Patient must be receiving treatment with this drug for this condition at the time of application,</p> <p>AND</p> <p>Patient must have failed to achieve an adequate response to methotrexate at a dose of at least 20 mg weekly for a minimum period of 3 months prior to initiating non-PBS subsidised treatment with this drug for this condition,</p> <p>AND</p> <p>Patient must have failed to achieve an adequate response to sulfasalazine at a dose of at least 2 g per day for a minimum period of 3 months prior to initiating non-PBS subsidised treatment with this drug for this condition; OR</p> <p>Patient must have failed to achieve an adequate response to leflunomide at a dose of up to 20 mg daily for a minimum period of 3 months prior to initiating non-PBS subsidised treatment with this drug for this condition,</p> <p>AND</p> <p>Patient must have demonstrated an adequate response following at least 12 weeks of non-PBS-subsidised treatment with this drug for this condition,</p> <p>AND</p> <p>Patient must not receive more than 24 weeks of treatment under this restriction.</p>
Treatment phase:	Continuing treatment
Clinical criteria:	<p>Patient must have received this drug as their most recent course of PBS-subsidised biological medicine treatment for this condition,</p> <p>AND</p> <p>Patient must have demonstrated an adequate response to treatment with this drug,</p> <p>AND</p> <p>Patient must not receive more than 24 weeks of treatment under this restriction.</p>

- 3.2 The submission requested identical listings for both the 150 mg pre-filled syringe and pre-filled pen for subcutaneous injection. The requested maximum quantities permit up to 28 weeks of initial treatment (three doses) followed by 24 weeks of continuing therapy (two doses). The submission stated that this is in line with the PBS listing for ustekinumab for PsA, which has an equivalent dosing schedule to risankizumab.
- 3.3 A special pricing arrangement was requested for risankizumab, but the submission did not nominate an effective price. The submission advised that once the effective price for guselkumab is known, the effective price for risankizumab will be calculated.
- 3.4 The requested published DPMQ for risankizumab for severe PsA is the same as for the PBS listing for risankizumab for the treatment of psoriasis (\$5,400.51).
- 3.5 The requested restriction is the same as the PBS restrictions for guselkumab and other PBS-listed biologic disease-modifying anti-rheumatic drugs (bDMARDs) for severe PsA.
- 3.6 The requested restrictions are narrower than the proposed TGA indication, that specifies only the treatment of active PsA in adults. The proposed TGA indication also specifies that risankizumab may be used as monotherapy or in combination with conventional synthetic DMARDs (csDMARDs), while the requested restrictions do not mention co-administered therapies.

- 3.7 A grandfathering restriction was also requested to allow [REDACTED] patients enrolled in the long-term extension phases of the risankizumab clinical trials to transition to PBS-subsidised risankizumab treatment.

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

## 4 Population and disease

- 4.1 PsA is a common, chronic systemic inflammatory disease classified as a subtype of spondyloarthritis, characterised by features of arthritis and psoriasis. It is a clinically heterogeneous and progressive condition with flares and remission, with a prevalence estimated to be between 0.02% to 0.17% across regions (Li et al, 2012; Scottie et al, 2018). No Australian-specific prevalence estimates are available. PsA can develop at any age but appears in most patients between 30 and 50 years of age, affecting men and women equally (Duarte et al 2012). Varying combinations of disease manifestations occur, such as axial joint inflammation, enthesitis (inflammation of the sites where tendons or ligaments insert into the bone), dactylitis (severe inflammation of finger or toe joints), and anterior uveitis (inflammation of the middle layer of the eye).
- 4.2 Risankizumab is a humanised monoclonal antibody that inhibits IL-23. IL-23 is a key upstream regulator of multiple cytokines, including TNF and IL-17, that drive the induction and maintenance of psoriatic arthritis pathogenesis. IL-23 inhibitors encompass a broader inflammatory pathway than TNF inhibitors (e.g. adalimumab) or IL-17 inhibitors (e.g. ixekizumab, secukinumab). Risankizumab was listed on the PBS for the treatment of severe chronic plaque psoriasis on 1 December 2019.
- 4.3 The submission positioned risankizumab as an alternative to other bDMARDs as second-line (or subsequent-line) therapy in patients who have failed to achieve or maintain an adequate response to at least two csDMARDs (methotrexate and either leflunomide or sulfasalazine).

## 5 Comparator

- 5.1 The submission nominated guselkumab as the main comparator. The main arguments provided in support of this nomination were that guselkumab is an IL-23 inhibitor, a pharmacological analogue to risankizumab; and is currently the only IL-23 inhibitor listed on the PBS for patients with severe PsA.
- 5.2 Currently, there are eleven bDMARDs listed on the PBS for the treatment of severe PsA across five classes of medicines with different mechanisms of action:
- TNF inhibitors: adalimumab, etanercept, golimumab, infliximab, certolizumab pegol;
  - IL-17 inhibitors: secukinumab, ixekizumab;
  - IL-12/23 inhibitors: ustekinumab;
  - IL-23 inhibitors: guselkumab; and

- JAK inhibitors: tofacitinib, upadacitinib.
- 5.3 Although the nomination of guselkumab as the main comparator was considered reasonable, risankizumab could replace any of the current PBS-listed bDMARDs. The submission's financial estimates were based on an assumption that risankizumab would take a proportion of market share from all of the current PBS-listed bDMARDs for PsA. This is consistent with the PBAC's consideration of guselkumab for the treatment of PsA, whereby guselkumab could replace any of the current PBS-listed bDMARDs for severe PsA (para 5.1, guselkumab Public Summary Document (PSD), November 2020 PBAC meeting).
- 5.4 In the context of the cost-minimisation approach taken by the submission, a further consideration for PBAC is that, under Section 101(3B) of the *National Health Act 1953*, when the proposed medicine is substantially more costly than an alternative therapy, the committee cannot make a positive recommendation unless it is satisfied that, for some patients, the proposed medicine provides a significant improvement in efficacy and/or reduction of toxicity over the alternative therapy. If the committee is so satisfied, it must make a statement to this effect.
- 5.5 The PBAC has previously considered that ustekinumab, secukinumab, certolizumab pegol and tofacitinib were 'lower tier' medicines and etanercept, adalimumab, infliximab, ixekizumab and golimumab were 'higher tier' medicines for the treatment of PsA (para 5.2, guselkumab PSD, November 2020 PBAC meeting). The PBAC recommended listing guselkumab on a cost minimisation basis with the least costly bDMARD for severe PsA. The PBAC considered that guselkumab must be less expensive than the 'higher tier' bDMARDs to account for the lack of evidence to support non-inferiority to the higher tier medicines, and could not be any more costly than any of the 'lower tier' bDMARDs currently listed on the PBS for this condition (para 7.1, guselkumab PSD, November 2020 PBAC meeting).

*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 consumer organisation Creaky Joints Australia via the Consumer Comments facility on the PBS website. The comments outlined the benefit of an additional treatment option for patients with severe psoriatic arthritis.

### ***Clinical trials***

- 6.3 The submission was based on an indirect comparison of two randomised trials of risankizumab, and two randomised trials of guselkumab, with placebo as common reference:
- Risankizumab versus placebo: one trial (KEEPSAKE 1, N=964) in PsA patients with an inadequate response to csDMARDs (referred to as csDMARD-IR in the submission); and one trial (KEEPSAKE 2, N=443) in a mixed population of patients with an inadequate response to either csDMARDs or bDMARDs (bDMARD-IR and csDMARD-IR);
  - Guselkumab versus placebo: one trial (DISCOVER 2, N=739) in a csDMARD-IR PsA patient population; and one trial (DISCOVER 1, N=381) in a mixed population (bDMARD-IR and csDMARD-IR).
- 6.4 Details of the trials presented in the submission are provided in the table below.

**Table 2: Trials and associated reports presented in the submission**

Trial ID	Protocol title/ Publication title	Publication citation
<b>Risankizumab trials</b>		
KEEPSAKE 1	A Phase 3, Randomized, Double-Blind, Study Comparing Risankizumab to Placebo in Subjects with Active Psoriatic Arthritis (PsA) Who Have a History of Inadequate Response to or Intolerance to at Least One Disease Modifying Anti-Rheumatic Drug (DMARD) Therapy (KEEPSAKE 1) (NCT03675308)	Clinical Study Report, February 2021
KEEPSAKE 2	A Phase 3, Randomized, Double-Blind Study comparing Risankizumab to Placebo in Subjects with Active Psoriatic Arthritis Including Those Who Have a history of Inadequate response or Intolerance to Biologic Therapy(ies) (KEEPSAKE 2) (NCT03671148)	Clinical Study Report, February 2021
<b>Guselkumab trials</b>		
DISCOVER 2	Mease PJ, Rahman P, Gottlieb AB, et al. Guselkumab in biologic-naive patients with active psoriatic arthritis (DISCOVER-2): a double-blind, randomised, placebo-controlled phase 3 trial.	<i>Lancet</i> 2020; 395(10230):1126-1136
	McInnes I, Rahman P, Gottlieb AB, et al. Efficacy and safety of guselkumab, a monoclonal antibody specific to the P19-subunit of interleukin-23, through week 52 of a phase 3, randomized, double-blind, placebo-controlled study conducted in biologic-naive patients with active psoriatic arthritis.	<i>Arthritis and Rheumatology</i> 2021; 73(4):604-616
DISCOVER 1	Deodhar A, Helliwell PS, Boehncke WH, et al. Guselkumab in patients with active psoriatic arthritis who were biologic-naive or had previously received TNF $\alpha$ inhibitor treatment (DISCOVER-1): a double-blind, randomised, placebo-controlled phase 3 trial.	<i>Lancet</i> 2020; 395(10230):1115-1125.
	Ritchlin CT, Helliwell PS, Boehncke WH, et al. Guselkumab, an inhibitor of the IL-23p19 subunit, provides sustained improvement in signs and symptoms of active psoriatic arthritis: 1 year results of a phase III randomised study of patients who were biologic-naive or TNF $\alpha$ inhibitor-experienced.	<i>RMD Open</i> 2021 Feb;7(1): e001457
DISCOVER 1 and 2	Mease PJ Helliwell PS Gladman DD et al. Efficacy of guselkumab on axial involvement in patients with active psoriatic arthritis and sacroiliitis: a post-hoc analysis of the phase 3 DISCOVER-1 and DISCOVER-2 studies.	<i>Lancet Rheumatology</i> 2021; 3(10): E715-E723
	Sweet K., Song Q, Loza MJ et al. Guselkumab induces robust reduction in acute phase proteins and type 17 effector cytokines in active psoriatic arthritis: Results from phase 3 trials.	<i>RMD Open</i> 2021; 7(2): e001679
	Rahman P, Mease PJ, Helliwell PS et al. Guselkumab demonstrated an independent treatment effect in reducing fatigue after adjustment for clinical response-results from two phase 3 clinical trials of 1120 patients with active psoriatic arthritis.	<i>Arthritis Research and Therapy</i> 2021; 23(1): Article 190
	McGonagle D, McInnes IB, Deodhar A, et al. Resolution of Enthesitis by Guselkumab and Relationships to Disease Burden: 1-Year Results of Two Phase-3 Psoriatic Arthritis Studies.	<i>Rheumatology</i> 2021; 60(11): 5337–5350

Source: Table 2-4, pp36-39; Table 2-5, pp40-41 of the submission.

Note: Abstracts of studies with full publications are not presented.

6.5 The key features of the randomised trials are summarised in the table below.

**Table 3: Key features of the included evidence**

Trial	N	Design/ duration	Risk of bias	Treatments	Patient population	Outcomes
<b>Risankizumab versus placebo</b>						
KEEPSAKE 1	964	R, MC, DB 24 weeks; OL 184 weeks <sup>a</sup>	Low	<ul style="list-style-type: none"> <li>• SC risankizumab 150 mg at Week 0, 4, and every 12 weeks thereafter</li> <li>• PBO at Week 0, 4 and every 12 weeks thereafter</li> <li>• From Week 24, all patients received open label risankizumab 150 mg every 12 weeks</li> </ul>	Adults with active PsA with inadequate response to csDMARDs. Naïve to bDMARD treatment.	ACR20, ACR50, PASI75 and HAQ-DI improvement at Week 24 Safety
KEEPSAKE 2	443	R, MC, DB 24 weeks; OL 184 weeks <sup>a</sup>	Low		Adults with active PsA with inadequate response to csDMARDs. ~50% of enrolled patients could have previous history of one or two bDMARDs	
Meta-analysis	1407	Included KEEPSAKE 2 and KEEPSAKE 1; assessed efficacy and safety outcomes				
<b>Guselkumab versus placebo</b>						
DISCOVER 2	494 <sup>b</sup>	R, MC, DB 24 weeks; OL 76 weeks	Low	<ul style="list-style-type: none"> <li>• SC guselkumab 100 mg at Week 0, 4, and:                             <ul style="list-style-type: none"> <li>- every 4 weeks thereafter, or</li> <li>- every 8 weeks thereafter</li> </ul> </li> <li>• PBO at Week 0, 4 and every 4 weeks thereafter</li> <li>• At Week 24, PBO-treated patients crossed over to receive guselkumab 100 mg every 4 weeks.</li> </ul>	Adults with active PsA with inadequate response to csDMARDs. Naïve to bDMARD treatment.	ACR20, ACR50, PASI75 and HAQ-DI improvement at Week 24 Safety
DISCOVER 1	253 <sup>b</sup>	R, MC, DB 24 weeks; OL 52 weeks	Low		Adults with active PsA with inadequate response to csDMARDs. ~30% of enrolled patients could have previous history of one or two TNF-inhibitors	
Meta-analysis	747 <sup>b</sup>	Included DISCOVER 2 and DISCOVER 1; assessed efficacy and safety outcomes.				

Source: Table 2-7, pp49-50; Table 2-10, pp58-59 of the submission.

Abbreviations: ACR, American College of Rheumatology; bDMARDs, biological disease-modifying anti-rheumatic drugs; csDMARDs; conventional synthetic disease-modifying anti-rheumatic drugs; DB, double blind; MC, multi-centre; OL, open label; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; R, randomised.

<sup>a</sup> open-label phase of the KEEPSAKE trials is ongoing.

<sup>b</sup> excluding patients randomised to guselkumab 4-weekly arms which were not relevant to the indirect comparison in the submission

6.6 The eligibility criteria for the included trials allowed for less severe disease symptoms than the requested restriction of severe PsA (e.g. at least 3 or 5 swollen joints and 3 or 5 tender joints at screening and baseline in the trials, compared to at least 20 active swollen and tender joints in the requested restriction). However, baseline patient characteristics for active PsA were more comparable to the requested restrictions, with mean number of tender joints ranging from 17 to 23 across the trials.

6.7 The risankizumab and guselkumab trials included bDMARD-naïve and experienced patients, which aligns with the proposed PBS listing that does not preclude prior bDMARD therapy.

### **Comparative effectiveness**

6.8 The primary outcome for all trials was the proportion of patients who achieved 20% improvement on the American College of Rheumatology measure (ACR20) at Week 24, with the proportion of patients who achieved 50% improvement (ACR50) at

Week 24 a key secondary outcome. The PBAC has previously considered that ACR50 was more relevant than ACR20 because it better reflected the current PBS criteria for response to initial therapy. However, ACR20 has also been used to support non-inferiority (para 6.8, tofacitinib PSD, November 2018 PBAC meeting, and also noted in para 6.9, guselkumab PSD, November 2020 PBAC meeting).

- 6.9 The submission's non-inferiority margins nominated for ACR50 and ACR20 were consistent with the PBAC's previous considerations of biologics in PsA. As outlined in the tofacitinib PSD, "For non-inferiority to be demonstrated, the submission stated that the lower bound of the 95% confidence interval (CI) around the relative risk (RR) must exceed 0.29 for ACR50 and 0.46 for ACR20" (para 6.9, tofacitinib PSD November 2018; see also guselkumab PSD, November 2020 PBAC meeting; upadacitinib PSD, March 2021 PBAC meeting).
- 6.10 Secondary outcomes included the Psoriasis Area and Severity Index (PASI), a widely used tool to measure psoriasis severity, and the Health Assessment Questionnaire-Disability Index (HAQ-DI), a patient-reported measure of fine movements and locomotor activities of the upper and lower extremities.

### **Risankizumab versus placebo**

- 6.11 Individual trial results for the two risankizumab trials KEEPSAKE 1 and KEEPSAKE 2 are presented below, as well as the meta-analysed results of both trials for each outcome conducted for the submission. Despite the differences in the patient populations in terms of the level of treatment experience in both KEEPSAKE trials, the submission noted that the heterogeneity across the two trials when meta-analysed was low ( $I^2$  between 0% and 27%) and not statistically significant across any of the efficacy outcomes. Therefore, it was considered appropriate to meta-analyse the KEEPSAKE 1 and KEEPSAKE 2 trial data for each outcome using the full analysis set.

Table 4: Results of key efficacy outcomes across the risankizumab trials

Trial ID	Risankizumab n/N (%)	Placebo n/N (%)	Odds ratio (95% CI)	Relative risk (95% CI)	Risk difference (95% CI)
<b>ACR20 response at week 24</b>					
KEEPSAKE 1	277/483 (57.4)	161/481 (33.5)	<b>2.67 (2.06, 3.47)</b>	<b>1.71 (1.48, 1.99)</b>	<b>0.24 (0.18, 0.30)</b>
KEEPSAKE 2	115/224 (51.3)	58/219 (26.5)	<b>2.93 (1.97, 4.36)</b>	<b>1.94 (1.50, 2.50)</b>	<b>0.25 (0.16, 0.34)</b>
Meta-analysis	-	-	<b>2.75 (2.21, 3.42)</b>	<b>1.77 (1.56, 2.01)</b>	<b>0.24 (0.19, 0.29)</b>
Heterogeneity: I <sup>2</sup> (p-value)			0% (0.71)	0% (0.41)	0% (0.86)
<b>ACR50 response at week 24</b>					
KEEPSAKE 1	162/483 (33.5)	54/481 (11.2)	<b>3.99 (2.84, 5.61)</b>	<b>2.99 (2.26, 3.96)</b>	<b>0.22 (0.17, 0.27)</b>
KEEPSAKE 2	59/224 (26.3)	20/219 (9.1)	<b>3.56 (2.06, 6.15)</b>	<b>2.88 (1.80, 4.62)</b>	<b>0.17 (0.10, 0.24)</b>
Meta-analysis	-	-	<b>3.87 (2.89, 5.16)</b>	<b>2.96 (2.33, 3.77)</b>	<b>0.20 (0.15, 0.25)</b>
Heterogeneity: I <sup>2</sup> (p-value)			0% (0.73)	0% (0.90)	27% (0.24)
<b>PASI75 response at week 24<sup>a</sup></b>					
KEEPSAKE 1	185/273 (67.8)	45/272 (16.5)	<b>10.60 (7.05, 15.95)</b>	<b>4.10 (3.10, 5.42)</b>	<b>0.51 (0.44, 0.58)</b>
KEEPSAKE 2	87/123 (70.7)	19/119 (16.0)	<b>12.72 (6.80, 23.78)</b>	<b>4.43 (2.89, 6.79)</b>	<b>0.55 (0.44, 0.65)</b>
Meta-analysis	-	-	<b>11.20 (7.95, 15.76)</b>	<b>4.19 (3.32, 5.30)</b>	<b>0.52 (0.46, 0.58)</b>
Heterogeneity I <sup>2</sup> (p-value)			0% (0.63)	0% (0.76)	0% (0.58)
<b>HAQ-DI improvement ≥0.35 at week 24<sup>b</sup></b>					
KEEPSAKE 1	208/414 (50.3)	117/419 (27.9)	<b>2.61 (1.96, 3.47)</b>	<b>1.80 (1.50, 2.16)</b>	<b>0.22 (0.16, 0.29)</b>
KEEPSAKE 2	78/196 (39.9)	44/187 (23.6)	<b>2.15 (1.38, 3.34)</b>	<b>1.69 (1.24, 2.31)</b>	<b>0.16 (0.07, 0.25)</b>
Meta-analysis	-	-	<b>2.46 (1.93, 3.13)</b>	<b>1.77 (1.51, 2.07)</b>	<b>0.20 (0.15, 0.26)</b>
Heterogeneity I <sup>2</sup> (p-value)			0% (0.47)	0% (0.74)	0% (0.29)

Source: Table 2-19 p75; Table 2-20, p77; Table 2-21, p78; Table 2-22, p79 of the submission.

Abbreviations: ACR, American College of Rheumatology; CI, confidence interval; FAS, full analysis set; HAQ-DI, Health Assessment Questionnaire – Disability Index; PASI, Psoriasis Area and Severity Index

**Bold** indicates statistically significant results

<sup>a</sup> The PASI75 outcome was only measured in patients with at least 3% of their body surface area (BSA) affected by psoriasis at baseline.

<sup>b</sup> The analysis for HAQ-DI improvement at Week 24 is in patients with a HAQ-DI score of at least 0.35 at baseline. The clinically meaningful improvement in HAQ-DI is defined as change from baseline ≤ -0.35.

6.12 A statistically significantly greater proportion of risankizumab-treated patients compared to those treated with placebo achieved all key efficacy outcomes at Week 24 in both risankizumab trials. Meta-analysed results for each outcome were also statistically significantly different in favour of risankizumab, with low heterogeneity across the trials.

## Risankizumab versus guselkumab

6.13 The submission conducted an indirect comparison of efficacy and safety data from the meta-analysed risankizumab trials (KEEPSAKE 1 and KEEPSAKE 2), and the meta-analysed guselkumab trials (DISCOVER 2 and DISCOVER 1). The submission noted that the main concern with the included trial data was the potential for heterogeneity due to the different inclusion criteria in terms of patient treatment experience. The submission argued that the low heterogeneity observed across the trials for each treatment when meta-analysed indicated that the different trial populations did not cause any significant impact to the measure of comparative treatment effect for risankizumab versus guselkumab. Low heterogeneity within the risankizumab and guselkumab trials and between prior treatment subgroups in the KEEPSAKE 2 trial, and comparable event rates across placebo arms, suggest that it was reasonable to conduct an indirect comparison between the risankizumab and guselkumab trials.

6.14 Results of the indirect comparison of risankizumab and guselkumab for efficacy outcomes are presented in the table below.

**Table 5: Summary of results of the indirect comparison of risankizumab and guselkumab for efficacy outcomes**

Comparison	bDMARD n/N (%)	Placebo n/N (%)	Odds ratio (95% CI)	Relative risk (95% CI)	Risk difference (95% CI)
<b>ACR20 response at Week 24 (non-inferiority margin 0.46 for RR)</b>					
Risankizumab	392/707 (55.5)	219/700 (31.3)	2.75 (2.21, 3.42)	1.77 (1.56, 2.01)	0.24 (0.19, 0.29)
Guselkumab	225/375 (60.0)	109/372 (29.3)	3.69 (2.71, 5.01)	2.03 (1.70, 2.42)	0.31 (0.24, 0.37)
Indirect comparison	-	-	0.75 (0.51, 1.09)	0.87 (0.70, 1.08)	-0.07 (-0.15, 0.01)
<b>ACR50 response at Week 24 (non-inferiority margin 0.29 for RR)</b>					
Risankizumab	221/707 (31.3)	74/700 (10.6)	3.87 (2.89, 5.16)	2.96 (2.33, 3.77)	0.20 (0.15, 0.25)
Guselkumab	116/375 (30.9)	46/372 (12.4)	3.22 (2.08, 4.97)	2.55 (1.70, 3.81)	0.19 (0.13, 0.24)
Indirect comparison	-	-	1.20 (0.71, 2.03)	1.16 (0.73, 1.86)	0.01 (-0.06, 0.08)
<b>PASI75 response at Week 24</b>					
Risankizumab	272/396 (68.7)	64/391 (16.4)	11.20 (7.95,15.76)	4.19 (3.32, 5.30)	0.52 (0.46, 0.58)
Guselkumab	201/258 (77.9)	53/261 (20.3)	14.09 (9.20,21.57)	4.01 (2.64, 6.09)	0.58 (0.51, 0.65)
Indirect comparison	-	-	0.80 (0.46, 1.37)	1.05 (0.65, 1.69)	-0.06 (-0.15, 0.03)
<b>HAQ-DI improvement ≥ 0.35 at Week 24</b>					
Risankizumab	286/610 (46.9)	161/606 (26.6)	2.46 (1.93, 3.13)	1.77 (1.51, 2.07)	0.20 (0.15, 0.26)
Guselkumab	171/340 (50.3)	106/346 (30.6)	2.29 (1.68, 3.13)	1.64 (1.36, 1.99)	0.20 (0.12, 0.27)
Indirect comparison	-	-	1.07 (0.72, 1.59)	1.08 (0.84, 1.38)	0 (-0.09, 0.09)

Source: 2-31, p94 of the submission.

Abbreviations: ACR, American College of Rheumatology; bDMARD, biologic disease-modifying anti-rheumatic drug; CI, confidence interval; HAQ-DI, Health Assessment Questionnaire – Disability Index; OR, odds ratio; PASI, Psoriasis Area and Severity Index; PBO, placebo; RD, risk difference; RR, relative risk

6.15 The non-inferiority margins for ACR20 and ACR50 were met for the comparison of risankizumab and guselkumab, with the lower 95% confidence interval of the relative risk for ACR20 and ACR50 exceeding 0.46 and 0.29, respectively. There were no statistically significant differences between treatments noted for any of the measured efficacy outcomes. The lack of a statistically significant difference for the PASI75 and HAQ-DI outcomes may not be sufficient to establish non-inferiority for these variables.

### **Risankizumab versus other PBS-listed bDMARDs for PsA**

6.16 To inform the PBAC of the relative effectiveness of risankizumab versus other PBS-listed therapies for the treatment of PsA, a series of indirect comparisons across the induction phase were performed using the data from the indirect comparison reported in the guselkumab PSD from the November 2020 PBAC meeting. This indirect comparison compared ACR20 and ACR50 response rates after the induction phase of each trial (between Week 12, Week 16 and Week 24 across all treatments).

6.17 The submission’s indirect comparison of risankizumab with other PBS-listed bDMARDs included data from the guselkumab DISCOVER trials, and the following additional treatments and trials:

- Ustekinumab: PSUMMIT-1 (N=515) and PSUMMIT-2 (N=312)
- Adalimumab: ADEPT (N=313), Genovese (2007; N=100)
- Secukinumab: FUTURE 2 (N=397), FUTURE 3 (N=414) and FUTURE 5 (N=996)
- Certolizumab pegol: RAPID-PsA (N=409)
- Tofacitinib: OPAL Broaden (N=422).

6.18 The non-inferiority margins for ACR20 and ACR50 response rates were met in all comparisons except for risankizumab (week 24) versus adalimumab (week 12), as the lower RR 95% CI did not exceed 0.46 for ACR20 (RR = 0.717, 95%CI: 0.355, 1.448, p=0.3533) and did not exceed 0.29 for ACR50 (RR = 0.506, 95%CI 0.228, 1.125, p=0.2165). The submission noted that this result was consistent with the comparison of guselkumab with adalimumab in the November 2020 guselkumab submission, in which guselkumab did not meet non-inferiority versus adalimumab (para 5.2, guselkumab PSD, November 2020 PBAC submission).

### **Comparative harms**

- 6.19 In both KEEPSAKE trials, similar proportions of patients across treatment arms experienced any treatment emergent adverse event (TEAE), serious TEAEs, or discontinuations due to TEAE. Only one TEAE, upper respiratory tract infection, was reported at 5% or greater incidence (in KEEPSAKE 2 only), and occurred in both treatment arms (risankizumab 7.6%, placebo 5.5%). No deaths occurred during the double-blind treatment phase of either trial.
- 6.20 TEAEs of interest included major adverse cardiovascular events (MACE and extended MACE), serious infections, malignant tumours, and non-melanoma skin cancers. Similar proportions of risankizumab and placebo-treated patients for experienced these outcomes in both trials, and very few patients overall experienced these adverse events. The submission noted that active tuberculosis, opportunistic infections (excluding tuberculosis and herpes zoster), serious anaphylactic reactions, and adjudicated anaphylactic reactions did not occur in either treatment arm in KEEPSAKE 1 or KEEPSAKE 2.
- 6.21 An indirect comparison of risankizumab and guselkumab for safety outcomes compared the frequency of treatment-emergent adverse events, serious adverse events and those leading to treatment discontinuation. There were no statistically significant differences between risankizumab and guselkumab for any of the safety outcomes, however the lack of a statistically significant difference for the safety outcomes may not be sufficient to establish non-inferiority.

### **Clinical claim**

- 6.22 The submission described risankizumab as non-inferior in terms of effectiveness and non-inferior in terms of safety compared with guselkumab. Based on the evidence presented, this claim was adequately supported.

- 6.23 The submission did not make an explicit claim of non-inferiority of risankizumab compared to other PBS-listed bDMARDs for the treatment of severe psoriatic arthritis. The evidence presented in the submission supported non-inferiority of risankizumab to the other bDMARDs for ACR20 and ACR50 efficacy outcomes, with the exception of adalimumab.
- 6.24 The PBAC considered that the claim of non-inferior comparative effectiveness and safety to guselkumab (and by extension, to other lower tier bDMARDs for PsA) was reasonable.

### **Economic analysis**

- 6.25 The submission presented a cost-minimisation analysis of risankizumab versus guselkumab. Equi-effective doses were estimated based on trial-based regimens, which are the same as those proposed in the draft Product Information for risankizumab, and the Product Information for guselkumab.
- 6.26 The equi-effective doses for initial and continuing therapy are: Risankizumab 150 mg Week 0, 4 and then every 12 weeks; and guselkumab 100 mg at Week 0, 4 and then every 8 weeks.
- 6.27 To account for differences in loading doses and dose frequency in both products, the cost-minimisation was calculated over 24 months. The PBAC previously considered the equi-effective doses of guselkumab (100 mg at week 0 and 4 then every 8 weeks) and 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. The cost-minimisation analysis should be conducted over two years using approved ex-manufacturer prices consistent with methodology previously accepted by the PBAC for bDMARDs (para 7.3, guselkumab PSD, November 2020 PBAC meeting).
- 6.28 Results of the cost-minimisation analysis are presented in the table below. The analysis was based on the published price of guselkumab, with the submission noting that the effective price of risankizumab will be calculated once the effective price of guselkumab is known.

**Table 6: Results of the cost-minimisation analysis (Published ex-manufacturer price)**

Component	Risankizumab	Guselkumab
Total costs AEMP over 2 years	\$49,067.37	\$49,067.37
Total packs over 2 years	9.33	13.5
AEMP per pack	\$5,257.22 (\$5,239.29) <sup>a</sup>	\$3,634.62

Source: Table 3-4, p112 of the submission.

Abbreviations: AEMP, approved ex-manufacturer price

<sup>a</sup> Current published AEMP for risankizumab for chronic plaque psoriasis

- 6.29 The submission proposed that the published ex-manufacturer price for risankizumab for PsA be \$5,239.29, the same as the current published ex-manufacturer price for risankizumab for chronic plaque psoriasis.
- 6.30 In the estimation of financial impact the submission assumed 10 scripts over two years for risankizumab and 14 scripts over two years for ixekizumab, which has the same

dosing schedule as guselkumab (Dose at Week 0, 4 and every 8 weeks thereafter). Similarly, in the November 2020 submission for guselkumab, 14 scripts over two years were used for guselkumab, and 10 scripts over two years for ustekinumab (which has the same dosing schedule as risankizumab; para 6.32, guselkumab PSD, November 2020 PBAC meeting). Using the same assumptions as used in the financial estimates (10 scripts over two years for risankizumab and 14 scripts over two years for guselkumab) for the cost-minimisation analysis, resulted in total costs (AEMP) over two years of \$50,884.68, with a cost-minimised AEMP for risankizumab \$5,088.47.

### **Drug cost/patient/2-year period**

6.31 The costs per patient per 2-year period, incorporating loading doses, are summarised in the table below. Estimates in the economic evaluation and financial implications assumed full adherence and persistence. Note that guselkumab was not included in estimating the financial implications of listing risankizumab, as it was listed on the PBS in July 2021 and full year data were not available. Guselkumab estimates for financial implications were based on the dosing of ixekizumab in which has the same dosing schedule as guselkumab. This is consistent with estimates used in the November 2020 guselkumab submission (para 6.32, guselkumab PSD, November 2020 PBAC meeting).

**Table 7: Drug cost per patient over a two-year period for risankizumab and guselkumab**

	Risankizumab		Guselkumab	
	Economic evaluation	Financial implications	Economic evaluation	Financial implications
Dosing schedule	150 mg at Weeks 0 and 4, then every 12 weeks		100 mg at Weeks 0 and 4, then every 8 weeks	
Price per dose	Proposed published DPMQ \$5,400.51		Published DPMQ \$3,795.84	
Doses per 2-year period	9.333 (0.25 (=1/4) doses/week for 4 weeks + 0.0833 (=1/12) doses/week for 100 weeks)	10 (Weeks 0, 4, 16, 28, 40, 52, 64, 76, 88, 100)	13.5 (0.25 (=1/4) doses/week for 4 weeks + 0.125 (=1/8) doses/week for 100 weeks)	14 (Weeks 0, 4, 12, 20, 28, 36, 44, 52, 60, 68, 76, 84, 92, 100)
Cost per patient over 2 years	\$50,404.76	\$54,005.10	\$51,243.84	\$53,141.76

Source: constructed during the evaluation using 'Attachment 7.1 Section 3 Workbook – Cost min RISA vs GUS' and 'Attachment 8.1 UCM-Release-3-Workbook-v3' spreadsheets provided with the submission

### **Estimated PBS usage & financial implications**

- 6.32 This submission was not considered by DUSC.
- 6.33 The submission used a market share approach to estimate the extent of use and financial implications associated with listing risankizumab on the PBS for severe psoriatic arthritis (PsA).
- 6.34 The sources of data used in the financial estimates are presented in the table below.

**Table 8: Key inputs for financial estimates**

Parameter	Value applied and source	Comment
Eligible patients (existing market)	█ in Year 1, increasing to █ in Year 6. PBS script data for adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, ixekizumab, secukinumab, tofacitinib, ustekinumab for psoriatic arthritis from 2016-2020 were converted to patient numbers by dividing by the average number of scripts per year for each treatment. Annual market growth was based on a linear extrapolation (█ additional patients per year). It was assumed that the listing of risankizumab would not grow the market.	It is unclear whether the derivation of patient numbers was reasonable due to inconsistencies between the average number of scripts per year and the number of doses per script for a number of therapies.
Uptake rate	█% in Year 1, increasing to █% in Year 6. The submission stated that the source was a commercial-in-confidence sponsor forecast.	No further details were provided for uptake rates.
Substitution	2020 PBS script data for each therapy were inflated by market growth estimates (based on the percentage increase in patient numbers for each year). All therapies were assumed to have the same growth. Substitution with risankizumab was assumed to be the same from each therapy (█% in Year 1 to █% in Year 6).	There are likely to be differences in market growth between therapies and differential substitution with risankizumab. However, this may be a reasonable simplifying assumption.
Grandfathered patients	The submission estimated that █ patients would be eligible for the grandfathered restriction. It was assumed that these patients would otherwise be prescribed one of the alternative therapies available for PsA and would be captured in uptake from continuing patients.	This assumption does not appear reasonable, given the small uptake of risankizumab in the first year of listing, which would result in grandfathered patients representing more than █% of risankizumab patients in Year 1 (█ patients).
Drug costs	Drug costs were based on published DPMQs of existing therapies, and the proposed published DPMQ for risankizumab.	For some therapies, the drug cost applied to several PBS item numbers was not consistent with the item's DPMQ. The overall impact of these inconsistencies was uncertain.
Patient copayment	\$27.56. Based on the distribution of scripts by beneficiary type in the existing market in 2020 (average PBS copayment \$27.67 – 99.13% scripts; average RPBS copayment \$4.68 – 0.87% scripts).	This was appropriate.
MBS items	The submission stated that no changes are expected to the volume of MBS items due to the listing of risankizumab.	This was appropriate.

Source: Table 4-1, p114 of the submission and 'Attachment 8.1 UCM-Release-3-Workbook-v3'spreadsheet provided with the submission.

- 6.35 For a number of substituted therapies, there were inconsistencies between the number of scripts required over a 2 year period (used to derive the average annual number of scripts per treatment to inform patient numbers/substitution with risankizumab), the number of doses per script, and the costs applied to item numbers. The overall impact of these inconsistencies on the budget impact model was uncertain.
- 6.36 A number of errors were identified in the budget impact model which resulted in an underestimate of script numbers. These were corrected during the evaluation.

6.37 The table below provides a summary of the net financial implications of listing risankizumab on the PBS for PsA, based on published prices.

**Table 9: Estimated use and financial implications**

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
<b>Estimated use and financial implications of risankizumab</b>						
Projected number of patients using existing therapies	2	2	2	2	2	10
Uptake of risankizumab	%	%	%	%	%	%
Risankizumab patients (population × uptake)	3	3	5	5	5	5
Risankizumab scripts (patients × 5 scripts/year)	3	5	5	8	8	8
Cost of risankizumab (scripts × \$5,400.51) (\$)	4	6	7	7	9	9
Copayments (\$27.56/script) <sup>1</sup> (\$)	4	4	4	4	4	4
<b>Net cost to PBS/RPBS (\$)</b>	4	6	7	7	9	9
<b>Estimated changes in use and financial implications of other therapies</b>						
Changes in script numbers						
- Adalimumab	3	5	5	5	5	8
- Secukinumab	3	5	5	5	5	5
- Etanercept	3	5	5	5	5	5
- Golimumab	3	5	5	5	5	5
- Tofacitinib	3	3	5	5	5	5
- Certolizumab pegol	3	3	5	5	5	5
- Ixekizumab	3	3	3	3	3	5
- Ustekinumab	3	3	3	3	3	3
- Infliximab	3	3	3	3	3	3
PBS/RPBS cost offsets						
- Adalimumab (\$)	4	4	4	4	4	4
- Secukinumab (\$)	4	4	4	4	4	4
- Etanercept (\$)	4	4	4	4	4	4
- Golimumab (\$)	4	4	4	4	4	4
- Tofacitinib (\$)	4	4	4	4	4	4
- Certolizumab pegol (\$)	4	4	4	4	4	4
- Ixekizumab (\$)	4	4	4	4	4	4
- Ustekinumab (\$)	4	4	4	4	4	4
- Infliximab (\$)	4	4	4	4	4	4
Total PBS/RPBS cost (\$)	4	4	6	6	6	7
Copayments (\$27.56/script) <sup>1</sup> (\$)	4	4	4	4	4	4
<b>Net cost offsets to PBS/RPBS (\$)</b>	4	4	6	6	6	7
<b>Net financial implications to the PBS/RPBS (cost of risankizumab minus cost offsets)</b>						
<b>Net cost to the PBS/RPBS (\$)</b>	4	4	4	6	6	6

Source: 'Attachment 8.1 UCM-Release-3-Workbook-v3'spreadsheet provided with the submission.

<sup>1</sup> Based on an average PBS copayment of \$27.76 (99.13% of use) and an average RPBS of \$4.66 (0.87% of use); some differences by year due to rounding of RPBS patient numbers in the budget impact model spreadsheet.

The redacted values correspond to the following ranges:

<sup>2</sup> 10,000 to < 20,000

<sup>3</sup> < 500

<sup>4</sup> \$0 to < \$10 million

<sup>5</sup> 500 to < 5,000

<sup>6</sup> \$10 million to < \$20 million

<sup>7</sup> \$20 million to < \$30 million

<sup>8</sup> 5,000 to < 10,000

<sup>9</sup> \$30 million to < \$40 million

<sup>10</sup> 20,000 to < 30,000

- 6.38 The estimated net cost to the PBS/RPBS of listing risankizumab was estimated to be \$0 to < \$10 million in Year 1 of listing, increasing to \$10 million to < \$20 million in Year 6, a total of \$50 million to < \$60 million over the first six years of listing, based on published prices.
- 6.39 The submission stated that the budget impact model, with a net increase in costs to the PBS/RPBS, does not represent the true impact of listing risankizumab, as it is based on published prices of all medicines in the analysis. The submission stated that risankizumab will be replacing existing treatments and is not expected to change or grow the established PsA market; and that listing is expected to be nil or cost-saving to the government.

### **Quality Use of Medicines**

- 6.40 The submission stated that the sponsor has a risk management plan, including an Australian-specific annex submitted to the TGA as part of the dossier. The sponsor will be extending the patient support program to provide support to prescribers and patients with regards to the use of risankizumab.

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

## **7 PBAC Outcome**

- 7.1 The PBAC recommended the General Schedule, Authority Required (in writing) listing of risankizumab (RIS) for the treatment of severe psoriatic arthritis (PsA), on a cost minimisation basis with the least costly biological disease modifying anti-rheumatic drug (bDMARD) for this condition. In making his recommendation, the PBAC accepted that any of the currently PBS listed bDMARDs for severe PsA could be an alternative therapy to RIS. The PBAC considered that RIS must be less expensive than the 'higher tier' bDMARDs to account for the lack of evidence to support non-inferiority to the higher tier medicines and could not be any more costly than any of the 'lower tier' bDMARDs currently listed on the PBS for this condition.
- 7.2 The PBAC noted that 11 alternative bDMARDs were listed on the PBS for the treatment of PsA at the time of consideration. The PBAC considered that while the clinical need for an additional treatment with a similar mechanism of action to another listed bDMARD was low (guselkumab/GUS), the addition of another option may be useful for some patients.
- 7.3 The PBAC considered the equi-effective doses of RIS, based on a dose of either 150 mg at week 0, 4 and then every 12 weeks for initial treatment could be derived with reference the relevant product information documents for the alternative bDMARDs.
- 7.4 The Committee considered the nominated primary comparator of GUS, as the therapy with the most similar mechanism of action, was reasonable; however also considered

- any of the bDMARDs currently listed on the PBS for PsA were relevant alternative therapies. The PBAC noted no evidence of superiority against any of the other alternative therapies was provided.
- 7.5 The PBAC noted non-inferiority margins were met for the indirect comparison of RIS and GUS (a lower tier medicine), with the lower 95% confidence interval of the relative risk for ACR20 and ACR50 exceeding 0.46 and 0.29, respectively. With regards to indirect comparisons with other bDMARDs, including ustekinumab (UST), adalimumab (ADA), secukinumab (SEC), certolizumab pegol (CZP) and tofacitinib (TOF), the PBAC noted the non-inferiority margins for ACR20 and ACR50 response rates were met in all comparisons except for RIS (week 24) versus ADA (week 12), as the lower RR 95% CI did not exceed 0.46 for ACR20 (RR = 0.355) and did not exceed 0.29 for ACR50 (RR = 0.228). The Committee noted this conclusion was similar to the GUS submission for PsA, in which GUS also did not meet non-inferiority versus ADA (para 5.2, guselkumab PSD, November 2020 PBAC submission).
- 7.6 Based on the evidence presented in the submission, the PBAC considered that, overall, the claim of non-inferior comparative effectiveness to GUS was adequately supported by the data. Based on the indirect comparisons presented versus the secondary nominated comparators, the PBAC was also satisfied that RIS is likely to be of non-inferior comparative effectiveness to UST, SEC and TOF. Given the non-inferiority margins were not met for the comparisons of RIS versus ADA (a higher tier medicine), the PBAC considered the evidence presented did not support a conclusion that RIS is of non-inferior comparative effectiveness to ADA.
- 7.7 The PBAC considered the claim of non-inferior comparative safety to GUS, and by extension to other bDMARDs for PsA, was adequately supported by the available data.
- 7.8 The PBAC considered it would be appropriate to align the listing of RIS with other written authority bDMARD listings for PsA. The Committee noted the flow-on changes to the administrative notes common to bDMARD listings to include RIS in the list of therapies in a PsA treatment cycle. The PBAC noted the submission requested a grandfather restriction for approximately 1 patients currently enrolled in clinical trials and considered this was reasonable and advised the grandfather restriction should be reviewed after 12 months, consistent with current practice.
- 7.9 As a claim of non-inferior comparative effectiveness and safety was adequately justified by the evidence provided in the submission, the PBAC considered a cost minimisation approach with costs over two years using effective prices, consistent with previous approaches for similar bDMARDs was the most appropriate approach to determine the cost-minimised effective price of RIS in the PsA indication.
- 7.10 The PBAC considered that, given its recommendation was on a cost minimisation basis to the least costly alternative bDMARD, the listing of RIS for PsA on this basis was likely to be cost neutral or modestly cost saving to the PBS, as it may also substitute for more costly bDMARDs.

- 7.11 The PBAC advised current arrangements for RIS with regards to Nurse Practitioner prescribing and the Early Supply Rule remained appropriate.
- 7.12 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because risankizumab is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over alternative bDMARDs for this indication or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met.
- 7.13 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

**Outcome:**

Recommended

## 8 Recommended listing

- 8.1 Add new item:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
RISANKIZUMAB					
risankizumab 150 mg/1 mL injection, 1 x 1 mL syringe	NEW	1	1	2	Skyrizi
<b>Base listing on Restriction Summary / ToC:</b>					
<b>Category / Program:</b> GENERAL – General Schedule (Code GE)					
<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners					
<b>Restriction type:</b> <input checked="" type="checkbox"/> Authority Required (in-writing only via post/HPOS upload)					
<p><b>Administrative Advice:</b>  <b>TREATMENT OF ADULT PATIENTS WITH SEVERE ACTIVE PSORIATIC ARTHRITIS</b>                      The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of the biological medicines adalimumab, certolizumab pegol, etanercept, golimumab, guselkumab, infliximab, ixekizumab, <i>risankizumab</i>, secukinumab, tofacitinib, upadacitinib and ustekinumab for adult patients with severe active psoriatic arthritis. Therefore, where the term 'biological medicine' appears in notes and restrictions, it refers to adalimumab, certolizumab pegol, etanercept, golimumab, guselkumab, infliximab, ixekizumab, <i>risankizumab</i>, secukinumab, tofacitinib, upadacitinib and ustekinumab only.                      A patient is eligible for PBS-subsidised treatment with only 1 of the above biological medicines at any 1 time.                      A patient receiving PBS-subsidised treatment for psoriatic arthritis is able to commence a treatment cycle where they may trial biological medicines without having to experience a disease flare when swapping to the alternate biological medicine. Under these arrangements, within a single cycle, a patient may receive long-term treatment with a biological medicine as long as they sustain a response to therapy.                      A patient who received PBS-subsidised adalimumab, certolizumab pegol, etanercept, golimumab, guselkumab, infliximab, ixekizumab, secukinumab, tofacitinib or ustekinumab treatment prior to 1 October 2021 is considered to start their first cycle as of 1 October 2021.</p>					

	<p>Within the same treatment cycle, a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised biological medicine more than once. Therefore, once a patient fails to meet the response criteria for a PBS-subsidised biological medicine, they must change to an alternate biological medicine if they wish to continue PBS-subsidised biological treatment.</p> <p>Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment, including serious infusion or injection related reactions, Steven's Johnson Syndrome, development of a demyelinating lesion, progressive multifocal leukoencephalopathy and malignancy related to treatment with the biological medicine, is not considered as a treatment failure.</p> <p>Once a patient has either failed or ceased to sustain a response to treatment 3 times, they are deemed to have completed a single cycle and they must have, at a minimum, a 5-year break in PBS-subsidised biological medicine therapy before they are eligible to commence another cycle [further details are under '(5) Recommencement of treatment after a 5-year break in PBS-subsidised therapy' below].</p> <p>The duration of the break in therapy will be measured from the date the last prescription for PBS-subsidised treatment was approved in the most recent cycle to the date of the first application for initial treatment with a biological medicine under the new cycle.</p> <p>A patient who has failed fewer than 3 biological medicines in a treatment cycle and who has a break in therapy of more than 5 years may commence a new treatment cycle under Initial 3 treatment restriction.</p> <p>A patient who has failed fewer than 3 biological medicines in a treatment cycle and who has a break in therapy of less than 5 years may commence a further course of treatment within the same treatment cycle under Initial 2 treatment restriction.</p> <p>There is no limit to the number of treatment cycles a patient may undertake in their lifetime.</p> <p>How to prescribe PBS-subsidised biological medicine treatment for severe active psoriatic arthritis.</p> <p>(1) Initial treatment.</p> <p>Applications for initial treatment should be made where:</p> <p>(i) a patient has not received prior PBS-subsidised biological medicine treatment and wishes to commence such therapy (Initial 1 - New patient); or</p> <p>(ii) a patient has received prior PBS-subsidised biological medicine therapy (initial or continuing) and wishes to trial an alternate medicine (Initial 2 - Change or Recommencement of treatment after a break in therapy of less than 5 years) [further details are under 'Swapping therapy' below]; or</p> <p>(iii) a patient wishes to recommence treatment with a specific biological medicine following a break in PBS-subsidised therapy of less than 5 years with the same medicine (Initial 2 - Change or Recommencement of treatment after a break in biological medicine of less than 5 years).</p> <p>(iv) a patient wishes to recommence treatment with a biological medicine following a break in PBS-subsidised therapy of more than 5 years (Initial 3 - Recommencement of treatment after a break in biological medicine of more than 5 years) or</p> <p>An application for initial treatment will be limited to provide for a maximum of 16 weeks of therapy for adalimumab, etanercept, golimumab, secukinumab, tofacitinib and upadacitinib, 18 to 20 weeks of therapy for certolizumab pegol (depending upon the dosing regimen), 20 weeks of therapy for guselkumab or ixekizumab, 22 weeks of therapy for infliximab, and 28 weeks of therapy for <i>risankizumab</i> or ustekinumab. It is recommended that a patient be reviewed in the 4 weeks prior to completing their course of initial treatment to ensure uninterrupted biological medicine supply.</p> <p>A patient must be assessed for response to a course of PBS-subsidised initial treatment following a minimum of 12 weeks of therapy and conducted no later than 4 weeks from the cessation of the treatment course. If the response assessment is not conducted within these timeframes, the patient will be deemed to have failed this course of treatment.</p> <p>(2) Continuing treatment.</p> <p>Following the completion of an initial treatment course with a specific biological medicine, a patient may qualify to receive up to 24 weeks of continuing treatment with that drug providing they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing biological medicine treatment with the same drug in courses of up to 24 weeks providing they continue to sustain the response. It is recommended that a patient be reviewed for response following a minimum of 12 weeks of therapy and no later than the 4 weeks from the completion of the most recent course of treatment.</p> <p>A patient must be assessed for response to a course of continuing therapy, and the assessment must be submitted to Services Australia where applicable. Where a response assessment is not submitted where applicable, the patient will be deemed to have failed to respond to treatment with that biological medicine,</p>
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	<p>unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.</p> <p>Infliximab, adalimumab and etanercept only:</p> <p>For the first continuing treatment course of PBS-subsidised biological medicine treatment, it is recommended that a patient is reviewed for response following a minimum of 12 weeks of therapy and no later than 4 weeks from the completion of the most recent course of treatment under the Initial 1, Initial 2 or Initial 3 treatment restrictions.</p> <p>For the second and subsequent continuing courses of PBS-subsidised biological medicine treatment, it is recommended that an assessment of a patient's response is conducted following a minimum of 12 weeks of therapy and no later than 4 weeks from the completion of the most recent course of treatment.</p> <p>(3) Swapping therapy.</p> <p>Once initial treatment with the first PBS-subsidised biological medicine is approved, a patient may swap to an alternate biological medicine without having to re-qualify with respect to either the indices of disease severity (i.e. erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) level, and active joint count) or the prior non-biological therapy requirements, except if the patient has had a break in therapy of more than 5 years who would need to requalify under the Initial 3 treatment restriction with respect to the indices of disease severity.</p> <p>A patient who is not able to complete a minimum of 12 weeks of an initial treatment course will be deemed to have failed treatment with that biological medicine unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.</p> <p>A patient may trial an alternate biological medicine at any time, regardless of whether they are receiving therapy (initial or continuing) with a biological medicine at the time of the application.</p> <p>However, they cannot swap to a particular biological medicine if they have failed to respond to prior treatment with that drug within the same treatment cycle.</p> <p>Within a treatment cycle a patient may alternate between therapy with any biological medicine of their choice (1 at a time) providing:</p> <ul style="list-style-type: none"> <li>(i) they have not received PBS-subsidised treatment with that particular biological medicine previously; or</li> <li>(ii) they have demonstrated an adequate response to that particular biological medicine if they have previously trialled it on the PBS; and</li> <li>(iii) they have not previously failed to respond to treatment 3 times in this treatment cycle with biological medicines.</li> </ul> <p>To ensure a patient receives the maximum treatment opportunities allowed under these arrangements, it is important that they are assessed for response to every course of treatment.</p> <p>(4) Baseline measurements to determine response.</p> <p>A response to treatment is to be determined by comparison of current disease activity measurements relative to the baseline measurements of the indices of disease severity submitted with the first authority application for a biological medicine. However, prescribers may provide new baseline measurements any time that an initial or change or recommencement treatment application is submitted within a treatment cycle and these revised baseline measurements will be used to assess response to the PBS-subsidised treatment.</p> <p>To ensure consistency in determining response, the same indices of disease severity used to establish baseline at the commencement of treatment with each initial treatment application must be used to determine response for all subsequent continuing treatments. Therefore, where only an ESR or CRP level is provided at baseline, an ESR or CRP level respectively must be used to determine response. Similarly, where the baseline active joint count is based on total active joints (i.e. 20 or more active joints), response will be determined according to a reduction in the total number of active joints.</p> <p>(5) Re-commencement of treatment after a 5-year break in PBS-subsidised therapy.</p> <p>A patient who wishes to trial a second or subsequent course of treatment following a break in PBS-subsidised biological therapy of at least 5 years, must qualify under Initial 3 treatment restriction according to the criteria of the relevant restriction and index of disease severity. The application must include a joint count and ESR and/or CRP measurement that is no more than 4 weeks old at the time of application.</p>
	<p><b>Administrative Advice:</b> No increase in the maximum quantity or number of units may be authorised.</p>
	<p><b>Administrative Advice:</b> No increase in the maximum number of repeats may be authorised.</p>
	<p><b>Administrative Advice:</b> Special Pricing Arrangements apply.</p>

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	<b>Indication:</b> Severe psoriatic arthritis
	<b>Treatment Phase:</b> Initial treatment - Initial 1 (New patient)
	<b>Treatment criteria:</b>
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of psoriatic arthritis
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must not have received PBS-subsidised treatment with a biological medicine for this condition
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must have failed to achieve an adequate response to methotrexate at a dose of at least 20 mg weekly for a minimum period of 3 months
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must have failed to achieve an adequate response to sulfasalazine at a dose of at least 2 g per day for a minimum period of 3 months; or
	Patient must have failed to achieve an adequate response to leflunomide at a dose of up to 20 mg daily for a minimum period of 3 months
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must not receive more than 28 weeks of treatment under this restriction
	<b>AND</b>
	<b>Population criteria:</b>
	Patient must be aged 18 years or older
	<b>Prescribing Instructions:</b>
	Where treatment with methotrexate, sulfasalazine or leflunomide is contraindicated according to the relevant TGA-approved Product Information, details must be provided at the time of application.
	<b>Prescribing Instructions:</b>
	Where intolerance to treatment with methotrexate, sulfasalazine or leflunomide 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.
	<b>Prescribing Instructions:</b>
	The following initiation criteria indicate failure to achieve an adequate response and must be demonstrated in all patients at the time of the initial application: an elevated erythrocyte sedimentation rate (ESR) greater than 25 mm per hour or a C-reactive protein (CRP) level greater than 15 mg per L; and either (a) an active joint count of at least 20 active (swollen and tender) joints; or (b) at least 4 active joints from the following list of major joints: (i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or (ii) shoulder and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth). If the above requirement to demonstrate an elevated ESR or CRP cannot be met, the application must state the reasons why this criterion cannot be satisfied.
	<b>Prescribing Instructions:</b> If the requirement to demonstrate an elevated ESR or CRP cannot be met, the application must state the reasons why this criterion cannot be satisfied. Treatment with prednisolone dosed at 7.5 mg or higher daily (or equivalent) or a parenteral steroid within the past month (intramuscular or intravenous methylprednisolone or equivalent) is an acceptable reason.

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	<b>Prescribing Instructions:</b>
	The authority application must be made in writing and must include: (a) a completed authority prescription form(s); and (b) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	<b>Administrative Advice:</b>
	The Services Australia website (www.servicesaustralia.gov.au) has details of the toxicities, including severity, which will be accepted where one is claimed.
	<b>Administrative Advice:</b>
	Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001
<b>Base listing on Restriction Summary / ToC:</b>	
	<b>Category / Program:</b> GENERAL – General Schedule (Code GE)
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners
	<b>Restriction type:</b> <input checked="" type="checkbox"/> Authority Required (in-writing only via post/HPOS upload)
	<b>Administrative Advice:</b> <b>TREATMENT OF ADULT PATIENTS WITH SEVERE ACTIVE PSORIATIC ARTHRITIS</b> <i>As above (not shown here in full for brevity reasons).</i>
	<b>Administrative Advice:</b> No increase in the maximum quantity or number of units may be authorised.
	<b>Administrative Advice:</b> No increase in the maximum number of repeats may be authorised.
	<b>Administrative Advice:</b> Special Pricing Arrangements apply.
	<b>Indication:</b> Severe psoriatic arthritis
	<b>Treatment Phase:</b> Initial treatment - Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 5 years)
	<b>Treatment criteria:</b>
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of psoriatic arthritis
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must have received prior PBS-subsidised treatment with a biological medicine for this condition in this treatment cycle
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must not have already failed, or ceased to respond to, PBS-subsidised treatment with 3 biological medicines for this condition within this treatment cycle
	<b>AND</b>
	<b>Clinical criteria:</b>

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	Patient must not have already failed, or ceased to respond to, PBS-subsidised treatment with this drug for this condition during the current treatment cycle
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must not receive more than 28 weeks of treatment under this restriction
	<b>AND</b>
	<b>Population criteria:</b>
	Patient must be aged 18 years or older
	<b>Prescribing Instructions:</b>
	The authority application must be made in writing and must include: (a) a completed authority prescription form(s); and (b) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	<b>Prescribing Instructions:</b>
	An application for a patient who has received PBS-subsidised biological medicine treatment for this condition who wishes to change or recommence therapy with this drug, must be accompanied by evidence of a response to the patient's most recent course of PBS-subsidised biological medicine treatment, within the timeframes specified below.
	<b>Prescribing Instructions:</b>
	Where the most recent course of PBS-subsidised biological medicine treatment was approved under either Initial 1, Initial 2, Initial 3 or continuing treatment restrictions, an assessment of a patient's response must have been conducted following a minimum of 12 weeks of therapy.
	<b>Prescribing Instructions:</b>
	Where an assessment is not conducted within these timeframes, the patient will be deemed to have failed to respond, or to have failed to sustain a response to treatment with this drug.
	<b>Prescribing Instructions:</b>
	If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition. Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.
	<b>Prescribing Instructions:</b>
	A patient may re-trial this drug after a minimum of 5 years have elapsed between the date the last prescription for a PBS-subsidised biological medicine was approved in this cycle and the date of the first application under a new cycle under the Initial 3 treatment restriction.
	<b>Administrative Advice:</b>
	Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at <a href="http://www.servicesaustralia.gov.au">www.servicesaustralia.gov.au</a> Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at <a href="http://www.servicesaustralia.gov.au/hpos">www.servicesaustralia.gov.au/hpos</a> Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001
<b>Base on Restriction Summary / ToC:</b>	
	<b>Category / Program:</b> GENERAL – General Schedule (Code GE)
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners
	<b>Restriction type:</b> <input checked="" type="checkbox"/> Authority Required (in-writing only via post/HPOS upload)

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	<p><b>Administrative Advice:</b>  <b>TREATMENT OF ADULT PATIENTS WITH SEVERE ACTIVE PSORIATIC ARTHRITIS</b></p> <p><i>As above (not shown here in full for brevity reasons).</i></p>
	<b>Administrative Advice:</b> No increase in the maximum quantity or number of units may be authorised.
	<b>Administrative Advice:</b> No increase in the maximum number of repeats may be authorised.
	<b>Administrative Advice:</b> Special Pricing Arrangements apply.
	<b>Indication:</b> Severe psoriatic arthritis
	<b>Treatment Phase:</b> Initial treatment - Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years)
	<b>Treatment criteria:</b>
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of psoriatic arthritis
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must have previously received PBS-subsidised treatment with a biological medicine for this condition
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must have a break in treatment of 5 years or more from the most recently approved PBS-subsidised biological medicine for this condition
	<b>AND</b>
	<b>Clinical criteria:</b>
	The condition must have an elevated erythrocyte sedimentation rate (ESR) greater than 25 mm per hour; or
	The condition must have a C-reactive protein (CRP) level greater than 15 mg per L
	<b>AND</b>
	<b>Clinical criteria:</b>
	The condition must have either (a) a total active joint count of at least 20 active (swollen and tender) joints; or (b) at least 4 active major joints
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must not receive more than 28 weeks of treatment under this restriction
	<b>AND</b>
	<b>Population criteria:</b>
	Patient must be aged 18 years or older
	<b>Prescribing Instructions:</b>
	Major joints are defined as (i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or (ii) shoulder and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth).
	<b>Prescribing Instructions:</b>
	All measures of joint count and ESR and/or CRP must be no more than one month old at the time of initial application.
	<b>Prescribing Instructions:</b>
	If the above requirement to demonstrate an elevated ESR or CRP cannot be met, the application must state the reasons why this criterion cannot be satisfied.
	<b>Prescribing Instructions:</b>

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	Where the baseline active joint count is based on total active joints (i.e. more than 20 active joints), response will be determined according to the reduction in the total number of active joints. Where the baseline is determined on total number of major joints, the response must be demonstrated on the total number of major joints. If only an ESR or CRP level is provided with the initial application, the same marker will be used to determine response.
	<b>Prescribing Instructions:</b>
	The authority application must be made in writing and must include: (a) a completed authority prescription form(s); and (b) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	<b>Administrative Advice:</b>
	Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at <a href="http://www.servicesaustralia.gov.au">www.servicesaustralia.gov.au</a> Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at <a href="http://www.servicesaustralia.gov.au/hpos">www.servicesaustralia.gov.au/hpos</a> Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001
<b>Restriction Summary / ToC:</b>	
	<b>Category / Program:</b> GENERAL – General Schedule (Code GE)
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners
	<b>Restriction type:</b> <input checked="" type="checkbox"/> Authority Required ( <i>telephone/online PBS Authorities system</i> )
	<b>Administrative Advice:</b> <b>TREATMENT OF ADULT PATIENTS WITH SEVERE ACTIVE PSORIATIC ARTHRITIS</b> <i>As above (not shown here in full for brevity reasons).</i>
	<b>Administrative Advice:</b> No increase in the maximum quantity or number of units may be authorised.
	<b>Administrative Advice:</b> No increase in the maximum number of repeats may be authorised.
	<b>Administrative Advice:</b> Special Pricing Arrangements apply.
	<b>Indication:</b> Severe psoriatic arthritis
	<b>Treatment Phase:</b> Initial 1 (new patient) or Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 5 years) or Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years) - balance of supply
	<b>Treatment criteria:</b>
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of psoriatic arthritis
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must have received insufficient therapy with this drug for this condition under the Initial 1 (new patient) restriction to complete 28 weeks treatment; or
	Patient must have received insufficient therapy with this drug for this condition under the Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 5 years) restriction to complete 28 weeks treatment; or

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Patient must have received insufficient therapy with this drug for this condition under the Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years) restriction to complete 28 weeks treatment					
<b>AND</b>					
<b>Clinical criteria:</b>					
The treatment must provide no more than the balance of up to 28 weeks treatment available under the above restrictions					
<b>Administrative Advice:</b>					
Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see <a href="http://www.servicesaustralia.gov.au/HPOS">www.servicesaustralia.gov.au/HPOS</a> ) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).					
<b>MEDICINAL PRODUCT medicinal product pack</b>	<b>PBS item code</b>	<b>Max. qty packs</b>	<b>Max. qty units</b>	<b>No. of Rpts</b>	<b>Available brands</b>
<b>RISANKIZUMAB</b>					
risankizumab 150 mg/1 mL injection, 1 x 1 mL syringe	NEW	1	1	1	Skyrizi
<b>Restriction Summary / ToC:</b>					
<b>Category / Program:</b> GENERAL – General Schedule (Code GE)					
<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners					
<b>Restriction type:</b>					
<input checked="" type="checkbox"/> Authority Required (in-writing only via post/HPOS upload)					
<b>Administrative Advice:</b>					
<b>TREATMENT OF ADULT PATIENTS WITH SEVERE ACTIVE PSORIATIC ARTHRITIS</b>					
The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of the biological medicines adalimumab, certolizumab pegol, etanercept, golimumab, guselkumab, infliximab, ixekizumab, <i>risankizumab</i> , secukinumab, tofacitinib, upadacitinib and ustekinumab for adult patients with severe active psoriatic arthritis. Therefore, where the term 'biological medicine' appears in notes and restrictions, it refers to adalimumab, certolizumab pegol, etanercept, golimumab, guselkumab, infliximab, ixekizumab, <i>risankizumab</i> , secukinumab, tofacitinib, upadacitinib and ustekinumab only.					
A patient is eligible for PBS-subsidised treatment with only 1 of the above biological medicines at any 1 time.					
A patient receiving PBS-subsidised treatment for psoriatic arthritis is able to commence a treatment cycle where they may trial biological medicines without having to experience a disease flare when swapping to the alternate biological medicine. Under these arrangements, within a single cycle, a patient may receive long-term treatment with a biological medicine as long as they sustain a response to therapy.					
A patient who received PBS-subsidised adalimumab, certolizumab pegol, etanercept, golimumab, guselkumab, infliximab, ixekizumab, secukinumab, tofacitinib or ustekinumab treatment prior to 1 October 2021 is considered to start their first cycle as of 1 October 2021.					
Within the same treatment cycle, a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised biological medicine more than once. Therefore, once a patient fails to meet the response criteria for a PBS-subsidised biological medicine, they must change to an alternate biological medicine if they wish to continue PBS-subsidised biological treatment.					
Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment, including serious infusion or injection related reactions, Steven's Johnson Syndrome, development of a demyelinating lesion, progressive multifocal leukoencephalopathy and malignancy related to treatment with the biological medicine, is not considered as a treatment failure.					
Once a patient has either failed or ceased to sustain a response to treatment 3 times, they are deemed to have completed a single cycle and they must have, at a minimum, a 5-year break in PBS-subsidised biological medicine therapy before they are eligible to commence another cycle [further details are under (5) Recommencement of treatment after a 5-year break in PBS-subsidised therapy' below].					

	<p>The duration of the break in therapy will be measured from the date the last prescription for PBS-subsidised treatment was approved in the most recent cycle to the date of the first application for initial treatment with a biological medicine under the new cycle.</p> <p>A patient who has failed fewer than 3 biological medicines in a treatment cycle and who has a break in therapy of more than 5 years may commence a new treatment cycle under Initial 3 treatment restriction.</p> <p>A patient who has failed fewer than 3 biological medicines in a treatment cycle and who has a break in therapy of less than 5 years may commence a further course of treatment within the same treatment cycle under Initial 2 treatment restriction.</p> <p>There is no limit to the number of treatment cycles a patient may undertake in their lifetime.</p> <p>How to prescribe PBS-subsidised biological medicine treatment for severe active psoriatic arthritis.</p> <p>(1) Initial treatment.</p> <p>Applications for initial treatment should be made where:</p> <p>(i) a patient has not received prior PBS-subsidised biological medicine treatment and wishes to commence such therapy (Initial 1 - New patient); or</p> <p>(ii) a patient has received prior PBS-subsidised biological medicine therapy (initial or continuing) and wishes to trial an alternate medicine (Initial 2 - Change or Recommencement of treatment after a break in therapy of less than 5 years) [further details are under 'Swapping therapy' below]; or</p> <p>(iii) a patient wishes to recommence treatment with a specific biological medicine following a break in PBS-subsidised therapy of less than 5 years with the same medicine (Initial 2 - Change or Recommencement of treatment after a break in biological medicine of less than 5 years).</p> <p>(iv) a patient wishes to recommence treatment with a biological medicine following a break in PBS-subsidised therapy of more than 5 years (Initial 3 - Recommencement of treatment after a break in biological medicine of more than 5 years) or</p> <p>An application for initial treatment will be limited to provide for a maximum of 16 weeks of therapy for adalimumab, etanercept, golimumab, secukinumab, tofacitinib and upadacitinib, 18 to 20 weeks of therapy for certolizumab pegol (depending upon the dosing regimen), 20 weeks of therapy for guselkumab or ixekizumab, 22 weeks of therapy for infliximab, and 28 weeks of therapy for <i>risankizumab</i> or ustekinumab. It is recommended that a patient be reviewed in the 4 weeks prior to completing their course of initial treatment to ensure uninterrupted biological medicine supply.</p> <p>A patient must be assessed for response to a course of PBS-subsidised initial treatment following a minimum of 12 weeks of therapy and conducted no later than 4 weeks from the cessation of the treatment course. If the response assessment is not conducted within these timeframes, the patient will be deemed to have failed this course of treatment.</p> <p>(2) Continuing treatment.</p> <p>Following the completion of an initial treatment course with a specific biological medicine, a patient may qualify to receive up to 24 weeks of continuing treatment with that drug providing they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing biological medicine treatment with the same drug in courses of up to 24 weeks providing they continue to sustain the response. It is recommended that a patient be reviewed for response following a minimum of 12 weeks of therapy and no later than the 4 weeks from the completion of the most recent course of treatment.</p> <p>A patient must be assessed for response to a course of continuing therapy, and the assessment must be submitted to Services Australia where applicable. Where a response assessment is not submitted where applicable, the patient will be deemed to have failed to respond to treatment with that biological medicine, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.</p> <p>Infliximab, adalimumab and etanercept only:</p> <p>For the first continuing treatment course of PBS-subsidised biological medicine treatment, it is recommended that a patient is reviewed for response following a minimum of 12 weeks of therapy and no later than 4 weeks from the completion of the most recent course of treatment under the Initial 1, Initial 2 or Initial 3 treatment restrictions.</p> <p>For the second and subsequent continuing courses of PBS-subsidised biological medicine treatment, it is recommended that an assessment of a patient's response is conducted following a minimum of 12 weeks of therapy and no later than 4 weeks from the completion of the most recent course of treatment.</p> <p>(3) Swapping therapy.</p>
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	<p>Once initial treatment with the first PBS-subsidised biological medicine is approved, a patient may swap to an alternate biological medicine without having to re-qualify with respect to either the indices of disease severity (i.e. erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) level, and active joint count) or the prior non-biological therapy requirements, except if the patient has had a break in therapy of more than 5 years who would need to requalify under the Initial 3 treatment restriction with respect to the indices of disease severity.</p> <p>A patient who is not able to complete a minimum of 12 weeks of an initial treatment course will be deemed to have failed treatment with that biological medicine unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.</p> <p>A patient may trial an alternate biological medicine at any time, regardless of whether they are receiving therapy (initial or continuing) with a biological medicine at the time of the application.</p> <p>However, they cannot swap to a particular biological medicine if they have failed to respond to prior treatment with that drug within the same treatment cycle.</p> <p>Within a treatment cycle a patient may alternate between therapy with any biological medicine of their choice (1 at a time) providing:</p> <p>(i) they have not received PBS-subsidised treatment with that particular biological medicine previously; or  (ii) they have demonstrated an adequate response to that particular biological medicine if they have previously trialled it on the PBS; and  (iii) they have not previously failed to respond to treatment 3 times in this treatment cycle with biological medicines.</p> <p>To ensure a patient receives the maximum treatment opportunities allowed under these arrangements, it is important that they are assessed for response to every course of treatment.</p> <p>(4) Baseline measurements to determine response.</p> <p>A response to treatment is to be determined by comparison of current disease activity measurements relative to the baseline measurements of the indices of disease severity submitted with the first authority application for a biological medicine. However, prescribers may provide new baseline measurements any time that an initial or change or recommencement treatment application is submitted within a treatment cycle and these revised baseline measurements will be used to assess response to the PBS-subsidised treatment.</p> <p>To ensure consistency in determining response, the same indices of disease severity used to establish baseline at the commencement of treatment with each initial treatment application must be used to determine response for all subsequent continuing treatments. Therefore, where only an ESR or CRP level is provided at baseline, an ESR or CRP level respectively must be used to determine response. Similarly, where the baseline active joint count is based on total active joints (i.e. 20 or more active joints), response will be determined according to a reduction in the total number of active joints.</p> <p>(5) Re-commencement of treatment after a 5-year break in PBS-subsidised therapy.</p> <p>A patient who wishes to trial a second or subsequent course of treatment following a break in PBS-subsidised biological therapy of at least 5 years, must qualify under Initial 3 treatment restriction according to the criteria of the relevant restriction and index of disease severity. The application must include a joint count and ESR and/or CRP measurement that is no more than 4 weeks old at the time of application.</p>
	<p><b>Administrative Advice:</b> No increase in the maximum quantity or number of units may be authorised.</p>
	<p><b>Administrative Advice:</b> No increase in the maximum number of repeats may be authorised.</p>
	<p><b>Administrative Advice:</b> Special Pricing Arrangements apply.</p>
	<p><b>Indication:</b> Severe psoriatic arthritis</p>
	<p><b>Treatment Phase:</b> Continuing treatment</p>
	<p><b>Treatment criteria:</b></p>
	<p>Must be treated by a rheumatologist; or</p>
	<p>Must be treated by a clinical immunologist with expertise in the management of psoriatic arthritis</p>
	<p><b>AND</b></p>
	<p><b>Clinical criteria:</b></p>
	<p>Patient must have received this drug as their most recent course of PBS-subsidised biological medicine treatment for this condition</p>
	<p><b>AND</b></p>

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	<b>Clinical criteria:</b>
	Patient must have demonstrated an adequate response to treatment with this drug
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must not receive more than 24 weeks of treatment under this restriction
	<b>AND</b>
	<b>Population criteria:</b>
	Patient must be aged 18 years or older
	<b>Prescribing Instructions:</b>
	An adequate response to treatment is defined as: an erythrocyte sedimentation rate (ESR) no greater than 25 mm per hour or a C-reactive protein (CRP) level no greater than 15 mg per L or either marker reduced by at least 20% from baseline; and either of the following: (a) a reduction in the total active (swollen and tender) joint count by at least 50% from baseline, where baseline is at least 20 active joints; or (b) a reduction in the number of the following major active joints, from at least 4, by at least 50%: (i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or (ii) shoulder and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth).
	<b>Prescribing Instructions:</b>
	The same indices of disease severity used to establish baseline at the commencement of treatment with each initial treatment application must be used to determine response for all subsequent continuing treatments.
	<b>Prescribing Instructions:</b>
	The authority application must be made in writing and must include: (a) a completed authority prescription form(s); and (b) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	<b>Prescribing Instructions:</b>
	Where the most recent course of PBS-subsidised biological medicine treatment was approved under either Initial 1, Initial 2, Initial 3 or continuing treatment restrictions, an assessment of a patient's response must have been conducted following a minimum of 12 weeks of therapy.
	<b>Prescribing Instructions:</b>
	Where an assessment is not conducted within these timeframes, the patient will be deemed to have failed to respond, or to have failed to sustain a response to treatment with this drug.
	<b>Prescribing Instructions:</b>
	If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition. Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.
	<b>Prescribing Instructions:</b>
	A patient may re-trial this drug after a minimum of 5 years have elapsed between the date the last prescription for a PBS-subsidised biological medicine was approved in this cycle and the date of the first application under a new cycle under the Initial 3 treatment restriction.
	<b>Administrative Advice:</b>
	Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at <a href="http://www.servicesaustralia.gov.au">www.servicesaustralia.gov.au</a> Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at <a href="http://www.servicesaustralia.gov.au/hpos">www.servicesaustralia.gov.au/hpos</a>

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	Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001
<b>Base on Restriction Summary / ToC:</b>	
	<b>Category / Program:</b> GENERAL – General Schedule (Code GE)
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners
	<b>Restriction type:</b> <input checked="" type="checkbox"/> Authority Required ( in-writing only via post/HPOS upload)
	<b>Administrative Advice:</b> <b>TREATMENT OF ADULT PATIENTS WITH SEVERE ACTIVE PSORIATIC ARTHRITIS</b> <i>As above (not shown here in full for brevity reasons).</i>
	<b>Administrative Advice:</b> No increase in the maximum quantity or number of units may be authorised.
	<b>Administrative Advice:</b> No increase in the maximum number of repeats may be authorised.
	<b>Administrative Advice:</b> Special Pricing Arrangements apply.
	<b>Indication:</b> Severe psoriatic arthritis
	<b>Treatment Phase:</b> Transitioning from non-PBS to PBS-subsidised supply - Grandfather arrangements
	<b>Treatment criteria:</b>
	<i>Must be treated by a rheumatologist; or</i>
	<i>Must be treated by a clinical immunologist with expertise in the management of psoriatic arthritis</i>
	<b>AND</b>
	<b>Clinical criteria:</b>
	<i>Patient must have received treatment with this drug for this PBS indication prior to [DD-MM-YYYY]</i>
	<b>AND</b>
	<b>Clinical criteria:</b>
	<i>Patient must be receiving treatment with this drug for this condition at the time of application</i>
	<b>AND</b>
	<b>Clinical criteria:</b>
	<i>Patient must have failed to achieve an adequate response to methotrexate at a dose of at least 20 mg weekly for a minimum period of 3 months prior to initiating non-PBS subsidised treatment with this drug for this condition</i>
	<b>AND</b>
	<b>Clinical criteria:</b>
	<i>Patient must have failed to achieve an adequate response to sulfasalazine at a dose of at least 2 g per day for a minimum period of 3 months prior to initiating non-PBS subsidised treatment with this drug for this condition; or</i>
	<i>Patient must have failed to achieve an adequate response to leflunomide at a dose of up to 20 mg daily for a minimum period of 3 months prior to initiating non-PBS subsidised treatment with this drug for this condition</i>
	<b>AND</b>
	<b>Clinical criteria:</b>
	<i>Patient must have demonstrated an adequate response following at least 12 weeks of non-PBS-subsidised treatment with this drug for this condition</i>
	<b>AND</b>
	<b>Clinical criteria:</b>
	<i>Patient must not receive more than 24 weeks of treatment under this restriction</i>

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	<b>AND</b>
	<b>Population criteria:</b>
	<i>Patient must be aged 18 years or older</i>
	<p><b>Prescribing Instructions:</b>  <i>The following initiation criteria indicate failure to achieve an adequate response and must be demonstrated in all patients at the time of the initial application:</i>  <i>an elevated erythrocyte sedimentation rate (ESR) greater than 25 mm per hour or a C-reactive protein (CRP) level greater than 15 mg per L; and</i>  <i>either</i>  <i>(a) an active joint count of at least 20 active (swollen and tender) joints; or</i>  <i>(b) at least 4 active joints from the following list of major joints:</i>  <i>(i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or</i>  <i>(ii) shoulder and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth).</i>  <i>If the above requirement to demonstrate an elevated ESR or CRP cannot be met, the application must state the reasons why this criterion cannot be satisfied.</i></p>
	<p><b>Prescribing Instructions:</b>  <i>An adequate response to treatment is defined as:</i>  <i>an erythrocyte sedimentation rate (ESR) no greater than 25 mm per hour or a C-reactive protein (CRP) level no greater than 15 mg per L or either marker reduced by at least 20% from baseline; and</i>  <i>either of the following:</i>  <i>(a) a reduction in the total active (swollen and tender) joint count by at least 50% from baseline, where baseline is at least 20 active joints; or</i>  <i>(b) a reduction in the number of the following major active joints, from at least 4, by at least 50%:</i>  <i>(i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or</i>  <i>(ii) shoulder and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth).</i></p>
	<p><b>Prescribing Instructions:</b>  <i>The same indices of disease severity used to establish baseline at the commencement of treatment with each initial treatment application must be used to determine response for all subsequent continuing treatments.</i></p>
	<p><b>Prescribing Instructions:</b>  <i>The assessment of the patient's response to this PBS-subsidised course of therapy must be conducted no later than 4 weeks from the cessation of the treatment course.</i></p>
	<p><b>Prescribing Instructions:</b>  <i>If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition within this treatment cycle. Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.</i></p>
	<p><b>Prescribing Instructions:</b>  <i>A Grandfathered patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the continuing treatment criteria.</i></p>
	<p><b>Prescribing Instructions:</b>  <i>The authority application must be made in writing and must include:</i>  <i>(1) a completed authority prescription form; and</i>  <i>(2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice); and</i>  <i>(3) the date of commencement of this drug; and</i>  <i>(4) results of the baseline patient assessment prior to initiation of non-PBS subsidised therapy with this drug.</i></p>

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	<p><b>Administrative Advice:</b> This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.</p>
	<p><b>Administrative Advice:</b> Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at <a href="http://www.servicesaustralia.gov.au">www.servicesaustralia.gov.au</a> Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at <a href="http://www.servicesaustralia.gov.au/hpos">www.servicesaustralia.gov.au/hpos</a> Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
<b>Restriction Summary / ToC:</b>	
	<b>Category / Program:</b> GENERAL – General Schedule (Code GE)
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners
	<b>Restriction type:</b> <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)
	<p><b>Administrative Advice:</b> <b>TREATMENT OF ADULT PATIENTS WITH SEVERE ACTIVE PSORIATIC ARTHRITIS</b> <i>As above (not shown here in full for brevity reasons).</i></p>
	<b>Administrative Advice:</b> No increase in the maximum quantity or number of units may be authorised.
	<b>Administrative Advice:</b> No increase in the maximum number of repeats may be authorised.
	<b>Administrative Advice:</b> Special Pricing Arrangements apply.
	<b>Indication:</b> Severe psoriatic arthritis
	<b>Treatment Phase:</b> Continuing treatment - balance of supply
	<b>Treatment criteria:</b>
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of psoriatic arthritis
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must have received insufficient therapy with this drug for this condition under the continuing treatment restriction to complete 24 weeks treatment
	<b>AND</b>
	<b>Clinical criteria:</b>
	The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restriction
	<b>Administrative Advice:</b>
	Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see <a href="http://www.servicesaustralia.gov.au/HPOS">www.servicesaustralia.gov.au/HPOS</a> ) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

### Flow on changes

Add the following Prescribing instruction to the initial 1 listings for certolizumab, etanercept, golimumab, guselkumab, infliximab, ixekizumab, secukinumab tofacitinib, upadacitinib, and ustekinumab, for this indication

	<p><b>Prescribing Instructions:</b> If the requirement to demonstrate an elevated ESR or CRP cannot be met, the application must state the reasons why this criterion cannot be satisfied. Treatment with prednisolone dosed at 7.5 mg or higher daily (or equivalent) or a parenteral steroid within the past month (intramuscular or intravenous methylprednisolone or equivalent) is an acceptable reason.</p>
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***This restriction may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.***

## 9 Context for Decision

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

## 10 Sponsor's Comment

The sponsor had no comment.