5.03 BIMEKIZUMAB, Injection 160 mg in 1 mL single use pre-filled syringe, Injection 160 mg in 1 mL single use pre-filled pen, Bimzelx®, UCB Australia Proprietary Limited.

1 Purpose of submission

1.1 The Category 2 submission requested Authority Required listings for two presentations of bimekizumab (BKZ) subcutaneous injection, a 160 mg/1 mL pre-filled pen (PFP) and a 160 mg/1 mL pre-filled syringe (PFS), for the treatment of severe active psoriatic arthritis (PsA) in adult patients without an adequate response to conventional disease modifying anti-rheumatic drugs (cDMARDs).

1.2 If listed, BKZ would be the twelfth biologic or targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs), but the first interleukin (IL) 17A/F inhibitor, available on the PBS for PsA. The eleven b/tsDMARDs currently listed for PsA include treatments with five different mechanisms of action:

- tumour necrosis factor-α (TNF-α) inhibitors: adalimumab (ADA), certolizumab pegol (CZP), etanercept (ETN), golimumab (GOL), infliximab (IFX);
- Interleukin (IL) 12/13 inhibitor: ustekinumab (UST);
- IL 17A inhibitors: secukinumab (SEC) and ixekizumab (IXE);
- IL 23 inhibitor: guselkumab (GUS);
- Janus kinase (JAK) inhibitor: tofacitinib (TOF) and upadacitinib (UPA).

The PBAC recommended listing of risankizumab (an IL-23 inhibitor) for the treatment of PsA at the March 2022 PBAC meeting, but it was not available on the PBS at the time of the submission.

1.3 Listing was requested on a cost-minimisation basis versus IXE.

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

Component	Description
Population	Adult patients with active severe PsA in whom an adequate response has not been achieved with at least 6 months of intensive treatment with cDMARDs.
Intervention	BKZ 160 mg (1x 160 mg injection) subcutaneously every 4 weeks*
Comparator	IXE 160 mg (2x 80 mg injections) subcutaneously at Week 0, then 80 mg every 4 weeks*
Outcomes	ACR50, ACR20, PASI90, PASI75, HAQ-DI, safety
Clinical claim	In patients with severe PsA, BKZ (1x 160 mg injection every 4 weeks) is equivalent to IXE (2x 80 mg injection at Week 0, then 1x 80 mg injection every 4 weeks) in efficacy and safety.

Source: Table 1-1, p19 of the submission.

ACR=American College of Rheumatology; ACR20/50=≥20/50% improvement in tender and swollen joint counts and ≥20/50% improvement in 3 of 5 remaining ACR core set measures; BKZ=bimekizumab; cDMARD=conventional disease modifying anti-rheumatic drugs; IXE=ixekizumab; PASI=Psoriasis Area and Severity Index; PASI75/90=≥75/90% improvement from baseline; PsA=psoriatic arthritis.

* For patients with PsA and coexistent moderate-severe chronic plaque psoriasis (CPP), the dosing regimen for CPP is recommended.

2 Background

Registration status

2.1 The submission was made under the TGA and PBS Parallel Process. TGA status at time of PBAC consideration: not registered. The TGA Delegate's Overview was provided during the evaluation. The Delegate was inclined to approve the registration of bimekizumab for AS.

2.2 BKZ is TGA approved for the treatment of adult patients with plaque psoriasis (March 2022) and currently undergoing TGA evaluation for three new indications including non-radiographic axial spondyloarthritis, ankylosing spondylitis (radiographic axial spondyloarthritis) and PsA.

Previous PBAC consideration

2.3 This was the first submission to the PBAC for BKZ for adult patients with PsA. The sponsor has also lodged separate submissions to the PBAC for consideration at the March 2024 PBAC meeting, for the treatment of non-radiographic axial spondyloarthritis and ankylosing spondylitis. BKZ is currently listed on the PBS for the treatment of plaque psoriasis, following a positive recommendation by the PBAC at the March 2023 PBAC meeting.

3 Requested listing

3.1 The table below presents an abbreviated version of the requested restriction for initial and continuing treatment.

MEDICINAL PRODUCT medicinal product pack	Dispensed Price for Max. Qty	Max. qty packs	Max. qty units	№.of Rpts	Available brands
BIMEKIZUMAB					
[Initial treatment] 160 mg/1mL pre-filled syringe	$3,422.13 published price $TBC effective price	1	2	2	Bimzelx
[Initial treatment] 160 mg/1mL pre-filled pen	$3,422.13 published price $TBC effective price	1	2	2	Bimzelx
[Continuing treatment] 160 mg/1mL pre-filled syringe	$3,422.13 published price $TBC effective price	1	2	2	Bimzelx
[Continuing treatment] 160 mg/1mL pre-filled pen	$3,422.13 published price $TBC effective price	1	2	2	Bimzelx

Category / Program: General Schedule
Prescriber type: ☒Medical Practitioners
Treatment criteria:
Must be treated by a rheumatologist; or
Must be treated by a clinical immunologist with expertise in the management of psoriatic arthritis
Population criteria:
Patient must be aged 18 years or older
Indication: Severe psoriatic arthritis
Treatment Phase: Initial
Restriction type: ☒Authority Required (in writing only via post/HPOS upload)
Clinical criteria:
As for that of currently PBS listed b/tsDMARDs for psoriatic arthritis (e.g. patient must have failed to achieve an adequate response to methotrexate and sulfasalazine or leflunomide)
Patient must not receive more than 28 weeks of treatment under this restriction
Prescribing Instructions:
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.
Treatment Phase: Continuing
Restriction type: ☒Authority Required (in writing only via post/HPOS upload)
Clinical criteria:
As for that of currently PBS listed b/tsDMARDs for psoriatic arthritis (e.g. patient must have received this drug as their most recent course of PBS-subsidised treatment and must have demonstrated an adequate response to treatment)
Patient must not receive more than 24 weeks of treatment under this restriction
Prescribing Instructions:

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).

Source: p39, Table 1-9, p50, Table 1-10, pp51-61 of the submission.
b/tsDMARDs=biological and targeted synthetic disease-modifying, anti-rheumatic drugs; TBC=to be confirmed.

3.2 The sponsor requested General Schedule, Authority Required (in writing) PBS listing of the BKZ 160 mg/1 mL PFP and 160 mg/1 mL PFS for initial and continuing treatment of severe active PsA. The submission also requested a grandfather clause to allow patients enrolled in a planned patient familiarisation program to transition to PBS-subsidised treatment.

3.3 The requested restriction was generally consistent with the PBS criteria of other b/tsDMARDs, with minor differences related to the assessment period for treatment. The sponsor noted that there would also be flow-on changes to the administrative notes and prescriber instructions of other b/tsDMARDs, accounting for the availability of BKZ.

3.4 At the recommended dose of BKZ for PsA (160 mg every 4 weeks), the requested quantities including repeats would provide up to 24 weeks of initial treatment and 24 weeks of continuing treatment. For patients with PsA and coexisting moderate to severe plaque psoriasis, the recommended dose is the same as for plaque psoriasis (360 mg at Weeks 0, 4, 8, 12, 16 and every 8 weeks thereafter) and the same quantities would only permit 12 weeks of initial treatment and 24 weeks of continuing treatment. However, the sponsor anticipates that patients with PsA and coexisting moderate to severe plaque psoriasis would access BKZ through the current PBS listing for plaque psoriasis. The PBAC had previously noted that under current PBS criteria, patients are able to swap disease categories, thus patients with PsA and more severe psoriasis can receive treatment under the psoriasis restriction (paragraph 7.6, IXE Public Summary Document (PSD), July 2018 PBAC Meeting). However, patients with moderate psoriasis (PASI<15) would not be eligible to receive treatment under the psoriasis restriction.

3.5 There were a number of discrepancies related to the maximum duration of the initial treatment period allowed by the requested restriction. The clinical criteria states patients must not receive more than 28 weeks of initial treatment; the administrative advice states an application for initial treatment will be limited to provide a maximum of 16 weeks of therapy; the requested quantities and repeats permit up to 24 weeks of initial treatment; and the financial estimates assume a maximum of 16 weeks of initial treatment (see Estimated PBS usage & financial implications). The Pre-Sub-

Committee Response clarified that the intended initial treatment duration for bimekizumab for PsA was 16 weeks and the repeats should reflect this.

3.6 The sponsor requested a Special Pricing Arrangement (SPA) to be implemented, that would maintain the published AEMP for BKZ ($3,260 per pack) consistent with the current PBS listing for chronic plaque psoriasis and an effective AEMP that satisfies the non-inferiority claim to IXE. The submission stated that the effective AEMP is to be confirmed (TBC) because IXE is subject to a SPA and the effective price was unknown to the sponsor.

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

4 Population and disease

4.1 PsA is a chronic, immune-mediated, inflammatory disease mainly affecting the peripheral joints and skin, with multiple manifestations and comorbidities. The primary pathologic sites are the entheses (the sites of bony insertion of ligaments and tendons), the axial skeleton (including the sacroiliac joints of the pelvis), the peripheral joints, and some non-articular structures (soft tissue sites rather than joints) such as the gut, skin, eye, and aortic valve. Patients experience pain, swelling, joint tenderness and joint deformity, which results in a loss of function and limited movement, impacting productivity and quality of life.

4.2 The ultimate goal of treatment is to achieve the lowest possible level of disease activity in all domains, optimise functional status, improve quality of life and prevent structural damage as much as possible. Australian clinical practice is guided by the PBS eligibility criteria for b/tsDMARDs, which requires patients to have failed prior treatment with cDMARDs and meet other eligibility criteria before becoming eligible for treatment with b/tsDMARDs. Under the requested restriction, BKZ would provide patients with an alternative b/tsDMARD in the current treatment pathway.

4.3 BKZ is a humanised monoclonal antibody that selectively inhibits both IL 17F and IL 17A cytokines, which are key drivers of inflammation and bone formation in the pathogenesis of psoriatic arthritis. The recommended dose of BKZ for PsA in the draft product information is 160 mg every 4 weeks administered via subcutaneous injection. For patients with PsA and coexisting moderate to severe plaque psoriasis, the recommended dose of BKZ is the same as for plaque psoriasis, 360 mg at Weeks 0, 4, 8, 12, 16 and every 8 weeks thereafter.

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

5 Comparator

5.1 The submission nominated IXE subcutaneous injection as the main comparator, on the basis that it would be the treatment most likely to be replaced by BKZ. IXE (an IL 17A inhibitor) has a similar mechanism of action to BKZ (an IL 17A/F inhibitor) and both treatments are administered via subcutaneous injection.

5.2 The submission acknowledged that the PBAC might consider that BKZ could replace any b/tsDMARDs in principle, but requested that the PBAC exclude oral (TOF, UPA) and intravenous (IFX) therapies as relevant comparators. The submission argued that patients currently treated with an oral or intravenous therapy have chosen not to use a subcutaneous therapy, hence a new subcutaneous therapy would not substitute for an oral or intravenous therapy. Such assumptions around mode of administration may be implausible, as PBS restrictions allow patients to try three b/tsDMARDs before commencing a treatment break, and is highly unlikely that patients who use an IV or oral therapy will simply cease treatment once agents with a specific manner of administration have been exhausted, rather than use the maximum allowable treatments in a cycle. In addition, in its most recent consideration of a b/tsDMARD for PsA, the PBAC accepted that any of the currently listed b/tsDMARDs for severe PsA could be an alternative therapy to risankizumab (paragraph 7.1, risankizumab PSD, March 2022 PBAC meeting). The Pre-PBAC Response argued the submission took a pragmatic approach in nominating IXE as the main comparator (as the one with the most similar mechanism of action) and reiterated the argument BKZ would likely not replace IV or oral therapies. The PBAC noted that while a range of factors may impact the rate at which bimekizumab replaces some agents, considered all PBS listed b/tsDMARDs are alternative therapies as all could be replaced. Additionally, the PBAC noted the PBS listings for b/tsDMARDs for PsA were line agnostic, and therefore any treatment could be chosen in any line within a treatment cycle.

5.3 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. The submission noted that PBAC had previously considered some treatments (UST, SEC, CZP, GUS, UPA and TOF) as 'lower tier' or less effective therapies and other treatments (ETN, ADA, IFX, IXE and GOL) as 'higher tier' or more effective therapies.

5.4 Based on the claim of non-inferior effectiveness versus IXE, the submission argued that BKZ should be considered a higher tier treatment for the purposes of Section 101(3B) of the National Health Act 1953. The submission further requested that the PBAC recommend listing of BKZ at a higher price compared to the higher tier treatments IFX and ADA, because IFX is not a relevant comparator (see paragraph above) and BKZ may provide a significant improvement in efficacy and/or safety over ADA. The submission stated that a direct comparison between BKZ versus ADA, although not powered to show superiority, numerically favoured BKZ for one psoriasis outcome in the subpopulation of patients with PsA and coexisting plaque psoriasis. The PBAC had previously dismissed the relevance any advantage in terms of skin response for patients with PsA and coexisting plaque psoriasis under Section 101(3B),

given the availability of b/tsDMARDs for patients with plaque psoriasis (paragraph 7.4, IXE PSD, July 2018 PBAC meeting).

5.5 At the July 2018 PBAC meeting, the PBAC considered that IXE was non-inferior in terms of comparative effectiveness compared to SEC, CZP, UST and ADA (i.e. three lower tier treatments and one higher tier treatment) and recommended listing against the least costly b/tsDMARD. However, two years later the PBAC advised that IXE should be treated as interchangeable with ETN, ADA, IFX, and GOL (i.e. higher tier treatments) when reviewing its' advice on the interchangeability of TOF with other bDMARDs (November 2020 PBAC Outcomes – Other Matters). The submission assumed this also implied superiority of IXE versus lower tier treatments. The advice provided in November 2020 (outlined in the TOF PSD from that meeting) specifically relates to interchangeability under Section 101(3BA) of the National Health Act 1953. The PBAC acknowledged IXE had been described as a 'higher tier' agent in some public summary documents following the November 2020 advice, however noted the evidence for IXE had not supported superiority over any alternative b/tsDMARDs (paragraph 7.3, ixekizumab Public Summary Document, July 2018 PBAC). The PBAC noted some previous descriptions of IXE as a 'higher tier' agent may be incorrect.

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

6 Consideration of the evidence

Sponsor hearing

6.1 There was no hearing for this item.

Consumer comments

6.2 The PBAC noted and welcomed the input from individuals (3), health care professionals (3) and organisations (2) via the Consumer Comments facility on the PBS website. The comments from individuals described bimekizumab as effective for both their joint pain and psoriasis symptoms associated with PsA, and also outlined the favourable side effect profile compared to other agents. The comments from health professionals described bimekizumab as being highly effective with patients experiencing a rapid response to treatment with PsA, and described the therapy as well tolerated with acceptable safety. The PBAC noted the input from CreakyJoints Australia described the need for additional treatment options for the numerous conditions for which b/tsDMARDs are listed, as different treatments work best for individual patients and more options gives patients more flexibility to find the therapy that best works for them. The PBAC also noted the input from Ankylosing Spondylitis Victoria supported the listing of bimekizumab.

Clinical trials

6.3 The submission was based on three randomised controlled trials (RCTs) comparing BKZ to placebo (BE ACTIVE, BE OPTIMAL, BE COMPLETE) and two RCTs comparing IXE

to placebo (SPIRIT-P1, SPIRIT-P2). Two of the RCTs also included ADA as an active control (BE OPTIMAL, SPIRIT-P1), but the submission did not focus on the direct comparisons between BKZ and IXE versus ADA. The PBAC had previously considered evidence from SPIRIT-P1 and SPIRIT-P2, comparing IXE versus ADA and/or placebo, in the July 2018 submission for IXE.

6.4 Details of the trials included in the submission are provided in Table 2.

Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
BKZ vs PBO		
BE ACTIVE NCT02969525 EUCTR2016-001103-23-CZ	A Multicenter, Phase 2B, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Dose-Ranging Study to Evaluate the Efficacy and Safety of Bimekizumab in Subjects with Active Psoriatic Arthritis Ritchlin CT, Kavanaugh A, Merola JF et al. Bimekizumab in patients with active psoriatic arthritis: results from a 48-week, randomised, double-blind, placebo-controlled, dose-ranging phase 2b trial	Clinical Study Report 2019 *Lancet* 2020; 395(10222):427-440.
BE OPTIMAL NCT03895203 EUCTR2017-002322-20-CZ JPRN-JapicCTI-194875	A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Active-Reference Study Evaluating the Efficacy and Safety of Bimekizumab in Study Participants with Active Psoriatic Arthritis McInnes IB, Asahina A, Coates LC et al. Bimekizumab in patients with psoriatic arthritis, naive to biologic treatment: a randomised, double-blind, placebo-controlled, phase 3 trial (BE OPTIMAL)	Clinical Study Report 2022 *Lancet* 2023; 401(10370): 25-37.
BE COMPLETE NCT03896581 EUCTR2017-002804-29-DE JPRN-JapicCTI-194876	A Multicenter, Phase 3, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy and Safety of Bimekizumab in the Treatment of Subjects with Active Psoriatic Arthritis Merola JF, Landewé R, McInnes IB et al. Bimekizumab in patients with active psoriatic arthritis and previous inadequate response or intolerance to tumour necrosis factor-α inhibitors: a randomised, double-blind, placebo-controlled, phase 3 trial (BE COMPLETE)	Clinical Study Report 2022 *Lancet* 2023; 401(10370):38-48.
IXE vs PBO		
SPIRIT-P1 NCT01695239 JPRN-jRCT2080222087 EUCTR2011-002326-49-GB	Mease PJ, van der Heijde D, Ritchlin CT et al. Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naive patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1.	*Ann Rheum Dis* 2017; 76(1):79-87.
SPIRIT-P2 NCT02349295	Nash P, Kirkham B, Okada M et al. Ixekizumab for the treatment of patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors: results from the 24-week randomised, double-blind, placebo-controlled period of the SPIRIT-P2 phase 3 trial.	*Lancet* 2017; 389(10086): 2317-2327.

Source: Table 2-5, pp70-72 of the submission.

6.5 The key features of the randomised trials are summarised in Table 3.

Table 3: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)
BKZ vs PBO					
BE ACTIVE	206 (83[a])	Phase IIb, 5-arm, PC, MC, R, DB (12 wks); BKZ 16mg and PBO crossover at wk12; dose-blind from 13-48wks; rescue treatment from wk16.	*Low*[b]	Active PsA, TNF-α naïve & experienced	1°: ACR50 (wk12); 2°: ACR20/70, PASI75/90
BE OPTIMAL	852	Phase III, 3-arm, PC, AC (ADA), MC, R, DB (16 wks); PBO crossover at wk16; active treatment-blind from 17-53wks; rescue treatment from wk16.	*Low*	Active PsA, TNF-α naive	1°: ACR50 (wk16); 2°: ACR20/70, PASI90
BE COMPLETE	400	Phase III, 2-arm, PC, MC, R, DB (16 wks);	*Low*[b]	Active PsA, TNF-α experienced	1°: ACR50 (wk16); 2°: ACR20/70, PASI90
IXE vs PBO or ADA					
SPIRIT-P1	417 (314[c])	Phase III, 4-arm, MC, PC, AC (ADA), R, DB (24 wks); ADA and PBO crossover or active dose escalation at wk16 if 'non-responder'[d]; PBO crossover at wk24 for responders; dose-blind from 24-264wks; rescue treatment from wk16.	*Low*	Active PsA, TNF-α naive	1°: ACR20 (wk24); 2°: ACR50/70, PASI75/90/100
SPIRIT-P2	363 (240[c])	Phase III, 3-arm, PC, MC, R, DB (24 wks); PBO crossover at wk16 if 'non-responder'[d]; PBO crossover at wk24 for responders; dose-blind from 24-156wks; rescue treatment from wk16.	*Low*	Active PsA, TNF-α experienced	1°: ACR20 (wk24); 2°: ACR50/70, PASI75/90/100

Source: complied during the evaluation from the trial publications

AC=active control; ACR20/50/70=≥20/50/70% improvement in tender and swollen joint counts and ≥20/50/70% improvement in 3 of 5 remaining American College of Rheumatology Criteria core set measures; ADA=adalimumab; BKZ=bimekizumab; DB=double blind; IXE=ixekizumab; MC=multi-centre; OL=open label; OS=overall survival; PASI75/90/100=75/90/100% improvement in Psoriasis Area and Severity Index from baseline; PBO = placebo; PC=placebo control; PFS=progression-free survival; PsA=psoriatic arthritis; R=randomised; TNF-α=tumour necrosis factor alpha; 1°=primary outcome, 2°=secondary outcomes

[a] excluding patients from irrelevant treatment arms, BKZ 160mg Q4W, BKZ 320 mg Q4W, BKZ 320 mg loading then 160mg Q4W.

[b] staff preparing and administering (& recording in BE COMPLETE) the investigational medicinal product were unblinded

[c] excluding patients from irrelevant treatment arms, IXE 80mg Q2W

[d] patients on ADA or PBO with <20% improvement in swollen and tender joint count at week 16 from baseline were re-randomised to IXE 80mg q2w or q4w; In SPIRIT-P1, non-responders on IXE q4w at Wk16 commenced IXE q2w.

6.6 All of the RCTs were either Phase IIb or III, multicentre, placebo and/or active (ADA) controlled trials with a double-blind phase of at least 12 weeks and only permitted rescue therapy after Week 16. All trials enrolled adult patients with severe active PsA using similar diagnostic criteria but there were differences in the use of prior treatments at baseline. Two trials only enrolled patients without prior exposure to bDMARDs (BE OPTIMAL, SPIRIT-P1), two trials only enrolled patients with an inadequate response to prior TNF-a inhibitors (BE COMPLETE, SPIRIT-P2), and one trial enrolled patients with or without prior exposure to bDMARDs (BE ACTIVE).

Comparative effectiveness

6.7 Response to b/tsDMARDs on the PBS is assessed using a combination of the American College of Rheumatology 20% and 50% improvement criteria (ACR20 and ACR50, respectively). Assessment of response to initial therapy must be made no later than 4 weeks before the end of the initial course of treatment, which corresponds to about 12 weeks for BKZ and ADA, and 16 weeks for IXE. The PBAC had previously considered that ACR50 was more relevant than ACR20 because it better reflected the current PBS criteria for response to initial therapy, and generally considered therapeutic relativity

between treatments using Week 12 data including for IXE and ADA (paragraph 7.5, UST PSD, November 2014, paragraph 6.11, IXE PSD, July 2018).

6.8 The submission presented indirect comparisons comparing BKZ versus IXE using placebo as common reference for ACR50 and ACR20 at Week 12 to 16, summarised in Table 4 and Table 5 respectively. The submission presented results for the ITT population and by prior biologic treatment exposure (biologic naïve, biologic experienced).

Table 4: ACR50 response at Week 12-16, trial results and indirect treatment comparison

Trial	Drug n/N (%)	Control n/N (%)	RR (95%CI)	OR (95%CI)	RD (95%CI)
BKZ vs ADA					
BE OPTIMAL, W16, ITT (bNaive)	189/431 (43.9)	64/140 (45.7)	0.96 (0.78, 1.18)	0.93 (0.63, 1.36)	-0.02 (-0.11, 0.08)
BKZ vs PBO					
BE ACTIVE, W12, ITT (bNaive+TNFe)	17/41 (41.5)	3/42 (7.1)	**5.80 (1.84, 18.32)**	**9.21 (2.44, 34.77)**	**0.34 (0.17, 0.51)**
BE OPTIMAL, W16, ITT (bNaive)	189/431 (43.9)	28/281 (10.0)	**4.40 (3.05, 6.35)**	**7.06 (4.57, 10.89)**	**0.34 (0.28, 0.40)**
BE COMPLETE, W16, ITT (TNFe)	116/267 (43.4)	9/133 (6.8)	**6.42 (3.37, 12.24)**	**10.58 (5.16, 21.71)**	**0.37 (0.29, 0.44)**
Meta-analysis, W12-16, ITT	322/739 (43.6)	40/456 (8.8)	**4.89 (3.60, 6.65)**	**7.96 (5.56, 11.38)**	**0.35 (0.31, 0.39)**
Meta-analysis, W16, ITT	*305/698 (43.7)*	*37/414 (8.9)*	***4.83 (3.50, 6.67)***	***7.87 (5.42, 11.41)***	***0.35 (0.30, 0.40)***
IXE vs ADA					
SPIRIT 1, W12, ITT (bNaive)	36/107 (33.6)	30/101 (29.7)	1.13 (0.76, 1.69)	1.20 (0.67, 2.16)	0.04 (-0.09, 0.17)
IXE vs PBO					
SPIRIT 1, W12, ITT (bNative)	36/107 (33.6)	5/106 (4.7)	**7.13 (2.91, 17.47)**	**10.24 (3.83, 27.38)**	**0.29 (0.19, 0.39)**
SPIRIT 1, W16, ITT (bNative)	32/107 (29.9)*	13/106 (12.3)*	**2.44 (1.36, 4.38)**	**3.05 (1.50, 6.23)**	**0.18 (0.07, 0.28)**
SPIRIT 2, W12, ITT (TFNe)	38/122 (31.1)	4/118 (3.4)	**9.19 (3.38, 24.94)**	**12.89 (4.43, 37.52)**	**0.28 (0.19, 0.37)**
SPIRIT 2, W16, ITT (TFNe)	39/122 (32.0)*	7/118 (5.9)*	**5.39 (2.51, 11.57)**	**7.45 (3.17, 17.49)**	**0.26 (0.17, 0.35)**
Meta-analysis, W12, ITT	74/229 (32.3)	9/224 (4.0)	**7.99 (4.10, 15.56)**	**11.38 (5.52, 23.47)**	**0.28 (0.22, 0.35)**
Meta-analysis, W16, ITT	71/229 (31.0)	20/224 (8.9)	**3.49 (1.59, 7.64)**	**4.62 (1.92, 11.09)**	**0.22 (0.14, 0.30)**
Indirect comparisons, ITT					
BKZ (W12-16 meta-analysis) v IXE (W12 meta-analysis), via PBO			0.61 (0.29, 1.28)	0.70 (0.31, 1.57)	0.07 (-0.01, 0.15)
BKZ (W12-16 meta-analysis) v IXE (W16 meta-analysis), via PBO			1.40 (0.60, 3.25)	1.72 (0.67, 4.44)	**0.13 (0.04, 0.22)**
BKZ (W16 meta-analysis) v IXE (W16 meta-analysis), via PBO			*1.38 (0.59, 3.23)*	*1.70 (0.66, 4.42)*	***0.13 (0.04, 0.22)***
BKZ (W16 BE OPTIMAL) v IXE (W12 SPIRIT 1), via ADA			*0.85 (0.54, 1.33)*	*0.78 (0.39, 1.56)*	*-0.06 (-0.22, 0.10)*
Indirect comparisons, bNaive					
BKZ (W16 BE OPTIMAL) v IXE (W12 SPIRIT 1), via PBO			0.62 (0.23, 1.63)	0.69 (0.24, 2.02)	0.05 (-0.07, 0.17)
BKZ (W16 BE OPTIMAL) v IXE (W16 SPIRIT 1), via PBO			1.80 (0.90, 3.60)	**2.32 (1.01,5.33)**	**0.16 (0.04, 0.28)**
BKZ (W16 BE OPTIMAL) v IXE (W12 SPIRIT 1), via ADA			*0.85 (0.54, 1.33)*	*0.78 (0.39, 1.56)*	*-0.06 (-0.22, 0.10)*
Indirect comparisons, TNFe					
BKZ (W16 BE COMPLETE) v IXE (W12 SPIRIT 2), via PBO			0.70 (0.21, 2.30)	0.82 (0.23, 2.97)	0.09 (-0.03, 0.21)
BKZ (W16 BE COMPLETE) v IXE (W16 SPIRIT 2), via PBO			1.19 (*0.44*, 3.24)	1.42 (0.47, 4.34)	0.11 (-0.01, 0.23)

Italics indicate results extracted, estimated or corrected during the evaluation.

Source: Table 2.25, 2.31, 2.61 and 2.65, pp109,123,153,173 of the submission; Figures 2.41,2.46,2.47, pp154,158,159 of the submission

ACR50=≥50% improvement in tender and swollen joint counts and ≥50% improvement in 3 of 5 remaining American College of Rheumatology Criteria core set measures; ADA=adalimumab; BKZ=bimekizumab; bNaive=biologic naive; CI=confidence interval; ITT=intention-to-treat; IXE=ixekizumab; OR=odds ratio; PBO=placebo; RD=risk difference; RR=risk ratio; TNFe=tumor necrosis factor inhibitor experienced

* Unable to confirm exact results from Figure 1B, Mease 2017 (SPIRIT 1) and Figure 2B, Nash 2017 (SPIRIT 2)

Table 5: ACR20 response at Week 12-16, trial results and indirect treatment comparison

Trial	Drug n/N (%)	Control n/N (%)	RR (95%CI)	OR (95%CI)	RD (95%CI)
BKZ vs ADA					
BE OPTIMAL, W16, ITT (bNaive)	*268/431 (62.2)*	*96/140 (68.6)*	*0.91 (0.79, 1.04)*	*0.75 (0.50, 1.13)*	*-0.06 (-0.15, 0.03)*
BKZ vs PBO					
BE ACTIVE, W12, ITT (bNaive+TNFe)	30/41 (73.2)	8/42 (19.0)	**3.84 (2.00, 7.36)**	**11.59 (4.12, 32.62)**	**0.54 (0.36, 0.72)**
BE OPTIMAL, W16, ITT (bNaive)	268/431 (62.2)	67/281 (23.8)	**2.61 (2.09, 3.25)**	**5.25 (3.75, 7.35)**	**0.38 (0.32, 0.45)**
BE COMPLETE, W16, ITT (TNFe)	179/267 (67.0)	21/133 (15.8)	**4.25 (2.84, 6.34)**	**10.85 (6.38, 18.46)**	**0.51 (0.43, 0.60)**
Meta-analysis, W12-16, ITT	477/739 (64.5)	96/456 (21.1)	**3.32 (2.31, 4.77)**	**7.98 (4.45, 14.32)**	**0.46 (0.36, 0.57)**
Meta-analysis, W16, ITT	*447/698 (64.0)*	*88/414 (21.3)*	***3.23 (2.00, 5.23)***	***7.32 (3.60, 14.88)***	***0.45 (0.32, 0.57)***
IXE vs ADA					
SPIRIT 1, W12 ITT (bNaive)	*61/107 (57.0)*	*52/101 (51.5)*	*1.11 (0.86, 1.42)*	*1.25 (0.72, 2.16)*	*0.06 (-0.08, 0.19)*
IXE vs PBO					
SPIRIT 1, W12 ITT (bNaive)	61/107 (57.0)	33/106 (31.1)	**1.83 (1.32, 2.54)**	**2.93 (1.67, 5.14)**	**0.26 (0.13, 0.39)**
SPIRIT 2, W12 ITT (TNFe)	61/122 (50.0)	26/118 (22.0)	**2.27 (1.55, 3.33)**	**3.54 (2.02, 6.20)**	**0.28 (0.16, 0.40)**
Meta-analysis, W12, ITT	122/229 (53.3)	59/224 (26.3)	**2.00 (1.56, 2.57)**	**3.22 (2.17, 4.79)**	**0.27 (0.18, 0.36)**
Indirect comparisons, ITT					
BKZ (W12-16 meta-analysis) v IXE (W12 meta-analysis), via PBO			**1.66 (1.07, 2.58)**	**2.48 (1.22, 5.02)**	**0.19 (0.05, 0.33)**
BKZ (W16 meta-analysis) v IXE (W12 meta-analysis), via PBO			*1.62 (0.94, 2.78)*	***2.27 (1.01, 5.12)***	***0.18 (0.03, 0.33)***
BKZ (W16 BE OPTIMAL) v IXE (W12 SPIRIT 1), via ADA			*0.82 (0.62, 1.09)*	*0.60 (0.30, 1.19)*	*-0.12 (-0.28, 0.04)*
Indirect comparisons, bNaive					
BKZ (W16 BE OPTIMAL) v IXE (W12 SPIRIT 1), via PBO			1.43 (0.96, 2.12)	1.79 (0.93, 3.45)	0.12 (-0.03, 0.27)
BKZ (W16 BE OPTIMAL) v IXE (W12 SPIRIT 1), via ADA			*0.82 (0.62, 1.09)*	*0.60 (0.30, 1.19)*	-0.12 (-0.28, 0.04)
Indirect comparisons, TNFe					
BKZ (W16 BE COMPLETE) v IXE (W12 SPIRIT 2), via PBO			**1.87 (1.08, 3.26)**	**3.07 (1.42, 6.64)**	**0.23 (0.08, 0.38)**

Italics indicate results extracted, estimated or corrected during the evaluation.

Source: Tables 2.27, 2.32, 2.61 and 2.65, pp113,126,153 of the submission; Figures 2.42 and 2.48, pp155, 160 of the submission;

ACR20=≥20% improvement in tender and swollen joint counts and ≥20% improvement in 3 of 5 remaining American College of Rheumatology Criteria core set measures; ADA=adalimumab; BKZ=bimekizumab; bNaive=biologic naive; CI=confidence interval; ITT=intention-to-treat; IXE=ixekizumab; OR=odds ratio; PBO=placebo; RD=risk difference; RR=risk ratio; TNFe=TNF inhibitor experienced

6.9 The submission nominated a non-inferiority margin of 0.29 for ACR50 and 0.46 for ACR20 using the relative risk statistic, where non-inferiority was concluded if the lower bound of the 95% CI was larger than the nominated margin. The PBAC had considered the same non-inferiority margins in past decisions (paragraph 6.14, IXE PSD, July 2018; paragraph 6.9, TOF PSD, November 2018; paragraph 6.11, UPA PSD, March 2021).

6.10 The trial results demonstrated that BKZ and IXE were both more effective than placebo in terms of ACR50 and ACR20 response rates at Week 12 to 16, irrespective of prior biologic exposure. The evaluation considered results of the indirect treatment comparison indicated that BKZ was generally at least non-inferior to IXE in terms of ACR50 and ACR20. In terms of ACR50 response, there were no statistically significant differences between BKZ and IXE, and the indirect comparisons met the nominated non-inferiority margin in the ITT population. In terms of ACR20 response, the indirect comparison statistically favoured BKZ in the ITT population and TNF experienced subgroup and showed no significant difference between BKZ and IXE in the biologic naïve subgroup.

6.11 For completeness, ACR50 and ACR20 response rates at Week 12 to 16 for the direct comparisons, between BKZ versus ADA in BE OPTIMAL and between IXE versus ADA in SPIRIT-1, were extracted and presented in the tables above. Although neither BE OPTIMAL or SPIRIT-1 were powered to show non-inferiority, equivalence or

superiority between BKZ or IXE versus ADA, the evaluation considered the results showed ACR50 and ACR20 response rates for ADA were similar to BKZ and IXE.

6.12 The submission presented indirect treatment comparisons between BKZ versus IXE across other outcomes at Week 12 to 16 including PASI90 and PASI75. The submission considered the PASI90 and PASI75 outcomes important because they are highly relevant to patients with skin manifestation of the disease. The results generally showed no statistically significant differences between BKZ and IXE using placebo as the common comparator, but statistically favoured IXE in terms of PASI 75 using ADA as the common comparator. The submission noted that the direct comparison between BKZ versus ADA in BE OPTIMAL statistically favoured BKZ in terms of PASI 90 but there was no difference between the two treatments in terms of PASI 75. The Pre-PBAC Response argued these results are clinically relevant in this patient population as both skin and joint manifestations are the predominant clinical features of PsA, and that in many cases psoriasis symptoms emerge before arthritis symptoms in PsA. The Response also noted the results of a recent switching study showed 67% of patients who had not responded to ADA (in terms of PASI 90 outcomes) achieved response after switching to BKZ[1]. The PBAC considered the available evidence overall did not support a conclusion there is a clinically meaningful difference between BKZ and IXE outcomes in terms of skin outcomes. Furthermore, the PBAC considered that as the listings for b/tsDMARDs in PsA were line agnostic, it was not reasonable to make claim of superiority based on when a therapy may be used within a treatment cycle under the current design of these listings.

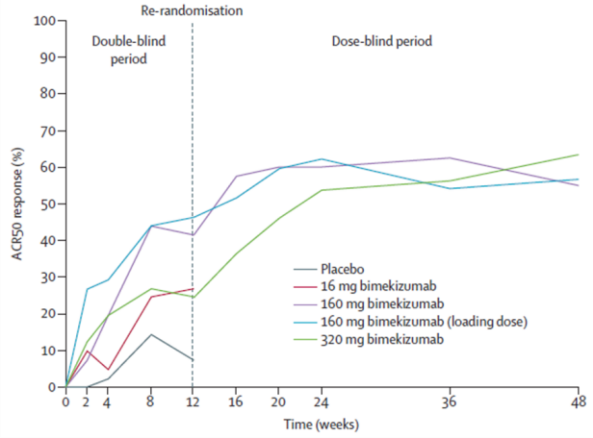
6.13 Figure 1 presents ACR50 and ACR20 response rates over the trial periods in BE ACTIVE (48 weeks) and BE OPTIMAL (52 weeks). The results illustrate response rates for BKZ plateau at approximately Week 16 and are generally maintained over the longer term. The results of BE OPTIMAL also illustrate that response rates with BKZ are similar to response rates with ADA at Week 52.

[1] Kokolakis et al. Bimekizumab efficacy and safety in patients with moderate-to-severe plaque psoriasis who switched from adalimumab, ustekinumab or secukinumab: results from phase III/IIIb trials. British Journal of Dermatology, Volume 188, Issue 3, March 2023, Pages 330–340, https://doi.org/10.1093/bjd/ljac089

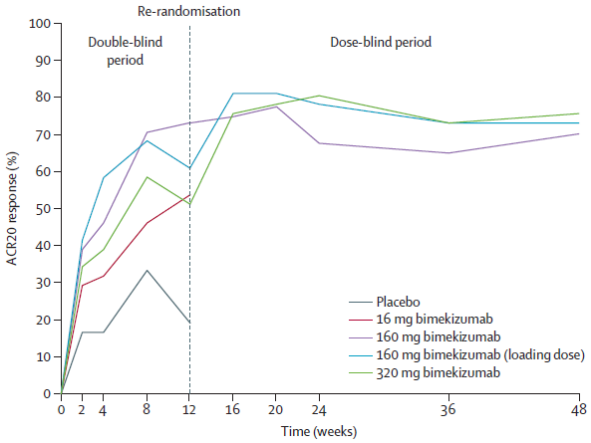
Figure 1: ACR50 and ACR20 response rates over time, bimekizumab trials

[A] ACR50 **[B] ACR20**

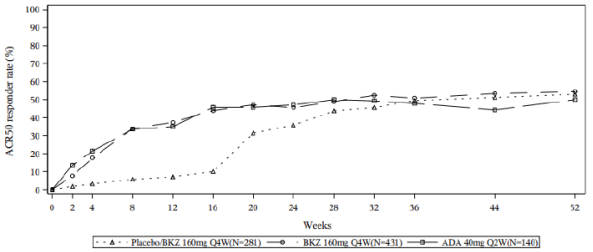
[A.1] BE ACTIVE



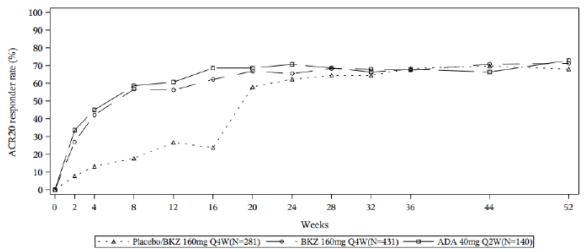
[B.1] BE ACTIVE



[A.2] BE OPTIMAL



[B.2] BE OPTIMAL



Source: Figures 2.11, 2.12, 2.15, and 2.16, pp112, 113, 115, 116 of the submission
ACR20/50=≥20/50% improvement in tender and swollen joint counts and ≥20/50% improvement in 3 of 5 remaining American College of Rheumatology Criteria core set measures

Comparative harms

6.14 Table 6 summarises treatment emergent adverse events (TEAEs) from the double-blind phase of BE ACTIVE, BE COMPLETE and BE OPTIMAL. Overall, the most frequently reported AEs with BKZ included nasopharyngitis, upper respiratory tract infection, and oral candidiasis which are consistent with the known safety profile of BKZ. The safety outcomes reported in the trials were consistent with the known safety profile of BKZ.

Table 6: Safety outcomes at Week 12-16, bimekizumab trials (double blind phase)

Outcomes	Drug n/N (%)	Control n/N (%)	RR (95%CI)	OR (95%CI)	RD (95%CI)
BKZ vs ADA					
Any TEAEs					
BE OPTIMAL, W16	257*/431 (59.6)	83/140 (59.3)	1.01 (0.86, 1.18)	1.01 (0.69, 1.50)	0.00 (-0.09, 0.10)
Serious TEAEs					
BE OPTIMAL, W16	8^/431 (1.9)	2/140 (1.4)	1.30 (0.28, 6.05)	1.30 (0.27, 6.22)	0.00 (-0.02, 0.03)
Disc. due to TEAEs					
BE OPTIMAL, W16	8/431 (1.9)	3/140 (2.1)	0.87 (0.23, 3.22)	0.86 (0.23, 3.30)	-0.00 (-0.03, 0.02)
BKZ vs PBO					
Any TEAEs					
BE ACTIVE, W12	19/43 (44.2)	24/42 (57.1)	0.77 (0.51, 1.18)	0.59 (0.25, 1.40)	-0.13 (-0.34, 0.08)
BE OPTIMAL, W16	257*/431 (59.6)	139/281 (49.5)	1.21 (1.05, 1.39)	1.51 (1.11, 2.04)	0.10 (0.03, 0.18)
BE COMPLETE, W16	108/267 (40.4)	44/132 (33.3)	1.21 (0.92, 1.61)	1.36 (0.88, 2.10)	0.07 (-0.03, 0.17)
Meta-analysis	384/741 (51.8)	207/455 (45.5)	1.12 (0.90, 1.38)	1.25 (0.85, 1.85)	0.05 (-0.04, 0.15)
Serious TEAEs					
BE ACTIVE, W12	1/43 (2.3)	1/42 (2.4)	0.98 (0.06, 15.11)	0.98 (0.06, 16.13)	-0.00 (-0.07, 0.06)
BE OPTIMAL, W16	8^/431 (1.9)	3/281 (1.1)	1.74 (0.47, 6.50)	1.75 (0.46, 6.66)	0.01 (-0.01, 0.03)
BE COMPLETE, W16	5/267 (1.9)	0/132 (0)	5.46 (0.30, 97.99)	5.55 (0.30, 101.17)	0.02 (-0.00, 0.04)
Meta-analysis	14/741 (1.9)	4/455 (0.9)	1.87 (0.62, 5.61)	1.89 (0.62, 5.77)	0.01 (-0.00, 0.02)
Disc. due to TEAEs					
BE ACTIVE, W12	1/43 (2.3)	2/42 (4.8)	0.49 (0.05, 5.19)	0.48 (0.04, 5.46)	-0.02 (-0.10, 0.05)
BE OPTIMAL, W16	8/431 (1.9)	3/281 (1.1)	1.74 (0.47, 6.50)	1.75 (0.46, 6.66)	0.01 (-0.01, 0.03)
BE COMPLETE, W16	2/267 (0.7)	0/132 (0)	2.48 (0.12, 51.32)	2.50 (0.12, 52.35)	0.01 (-0.01, 0.02)
Meta-analysis	11/741 (1.5)	5/455 (1.1)	1.40 (0.48, 4.10)	1.41 (0.47, 4.21)	0.01 (-0.00, 0.02)

Source: Table 2.36, p136 of the submission

ADA=adalimumab; BKZ=bimekizumab; CI=confidence interval; Disc=discontinued; OR=odds ratio; PBO=placebo; RD=risk difference; RR=risk ratio; TEAE=treatment-emergent adverse event

* McInnes 2023 reports n=258 (Table 3, p34); CSR reports n=257 (Table 11-5, p332)

^ McInnes 2023 reports n=7 (Table 3, p34); CSR reports n=8 (Table 11-5, p332)

6.15 The submission presented indirect comparisons of TEAEs, serious TEAEs and discontinuation due to TEAEs for BKZ and IXE, summarised in Table 7. The results showed no significant difference between BKZ and IXE in terms of safety outcomes. There were differences in the exposure periods across the trials, with safety outcomes reported at Week 12 (BE ACTIVE), Week 16 (BE COMPLETE and BE OPTIMAL) and Week 24 (SPIRIT-P1 and SPIRIT-P2).

Table 7: Safety outcomes at Week 12-24, indirect treatment comparison via placebo common reference

	RR (95%CI)	OR (95%CI)	RD (95%CI)
Any TEAEs			
BKZ vs IXE	0.93 (0.66, 1.33)	0.78 (0.38, 1.61)	-0.06 (-0.24, 0.12)
Serious TEAEs			
BKZ vs IXE	1.31 (0.22, 7.64)	1.30 (0.21, 7.96)	0.00 (-0.05, 0.05)
Disc. due to TEAEs			
BKZ vs IXE	1.65 (0.38, 7.15)	1.66 (0.37, 7.49)	0.01 (-0.02, 0.04)

Source: Figures 2.64, 2.65 and 2.66, pp179-181 of the submission

BKZ=bimekizumab; CI=confidence interval; Disc=discontinued; IXE=ixekizumab; OR=odds ratio; PBO=placebo; RD=risk difference; RR=risk ratio; TEAE=treatment-emergent adverse event

Benefits/harms

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

Clinical claim

6.17 The submission described BKZ as at least non-inferior in terms of effectiveness and non-inferior in terms of safety compared to IXE. The submission noted that response rates in terms of ACR 50 and ACR 20 were similar across the two treatments, and response rates in terms of PASI 90 and PASI 75 were numerically better for BKZ compared to IXE. This claim was adequately supported, although the clinical interpretation of the PASI outcomes was poorly justified given the point estimates did not always favour BKZ and varied depending on the risk statistic, outcome and common reference used for the indirect treatment comparison. The submission did not make any claim between BKZ versus other alternative b/tsDMARDs.

6.18 The PBAC considered that the claim of non-inferior comparative effectiveness and safety to ixekizumab was reasonable.

Economic analysis

6.19 The submission presented a cost-minimisation approach between BKZ and IXE. The proposed equi-effective doses were consistent with the recommended doses for PsA in the corresponding PIs:

- BKZ 160 mg subcutaneous injection every four weeks = IXE 160 mg subcutaneous injection at Week 0 then 80 mg subcutaneous injection every four weeks.

6.20 The cost-minimisation approach presented in the submission used the published AEMP of IXE and assumed equivalent costs (drug cost only) over the first two years. The submission requested a special pricing arrangement where the effective price of BKZ is derived from the effective price of IXE, but the effective AEMP of IXE was not available to the sponsor. The submission stated that the calculations can be updated with the effective AEMP of IXE to maintain equivalent costs following a positive PBAC recommendation.

6.21 Table 8 summarises the cost-minimisation approach presented in the submission.

Table 8: Results of the cost-minimisation approach

Component	Proposed medicine: BKZ	Comparator: IXE (11623R)
PBS item, max qty	160 mg injection x 2	80 mg injection x 2
DPMQ	$3,378.25[a]	$3,259.13
AEMP	$3,216.12[a]	$3,097.00
Dose	160 mg every four weeks	160 mg then 80mg every four weeks
Units / 104 weeks	26 units	27 units
Scripts / 104 weeks	13 scripts	13.5 scripts
Total medicine cost (AEMP) / 104 weeks	$41,809.50	$41,809.50
Difference in cost (AEMP) / 104 weeks	$0	$0

Source: Table 3.1, pp197-198 of the submission.

AEMP=approved ex-manufacturer price; BKZ=bimekizumab; DPMQ=dispensed price for maximum quantity; IXE=ixekizumab; PBS=Pharmaceutical Benefits Scheme

[a] The submission requested a special pricing arrangement with an effective price based on the cost-minimisation approach to the effective price of IXE and a published DPMQ of $3,422.13.

Drug cost/patient/year: $22,243.85

6.22 Assuming a DPMQ of $3,422.13 (the requested published price) and 6.5 scripts (13 injections) required for the first year of treatment at the recommended dose (160 mg subcutaneous injection every four weeks), the cost per patient per year is $22,243.85.

Estimated PBS usage & financial implications

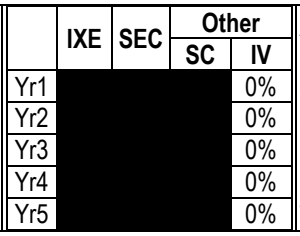
6.23 This submission was not considered by DUSC.

6.24 The submission estimated the financial impact of the proposed listing using a market share approach. Grandfathered patients were not estimated separately to avoid double counting, given the proposed restriction will not generate additional patients beyond the current market of eligible patients. The Pre-PBAC Response stated the Sponsor anticipated fewer than < 500 grandfather patients were expected for PsA.

6.25 For the market share approach, the submission assumed BKZ would substitute for all currently listed biologic treatments administered via subcutaneous injection (ADA, ETN, UST, SEC, IXE, CZP, GOL, GUS), but would not substitute for oral therapies (TOF and UPA) or intravenous infusions (IFX). The analysis used published DPMQs because the sponsor was not aware of the confidential effective prices of substituted treatments.

6.26 Table 9 summarises the key inputs used for the financial estimates.

Table 9: Data sources and parameter values applied in the utilisation and financial estimates

Data	Value	Source	Comment
Eligible population			
Current market of bDMARDs in PsA, scripts (excludes JAK inhibitors)	Yr0: 143,315 scripts (23,336 scripts for initial treatment, 119,980 scripts for continuing treatment)	Script dispensed for ADA, ETN, IFX IV, IFX SC, UST, SEC, IXE, CZP, GOL and GUS for PsA, July 2022-June 2023, Medicare Australia statistics. The submission excluded JAK inhibitors (TOF and UPA).	Potential underestimate. The submission estimated the size of the current market in calendar 2024 (Year 0) based on utilisation data for financial year 2023, and did not adequately justify why BKZ (an injection) would not substitute for TOF or UPA (oral tablets). There were also several errors with the item codes used in the analysis, with some items omitted (e.g. 9088H, 9087G, 10896L, 11326D) and an item for rheumatoid arthritis incorrectly included (e.g. 4284L).
Background market growth	Yr 0-6: 1.9%	Assumed equivalent to population growth (not cited), given the maturity of the market (e.g. 11 comparators).	Uncertain. Although reasonable for a stable market, the growth rate over the past three years was higher than population growth.
Treatment utilisation			
Uptake rate, BKZ (%)	 Yr1 0% Yr2 0% Yr3 0% Yr4 0% Yr5 0%	Assumption. Higher uptake assumed for IXE and SEC given the same mechanism of action (i.e. IL-17 inhibitors), and lower uptake assumed for other treatments, including 0%	Uncertain, although greater substitution of treatments with similar mechanism of action was reasonable. The submission also did not adequately justify why BKZ (an injection) would not substitute for IFX (an intravenous infusion, or subsequent subcutaneous injection after intravenous loading dose).

Data	Value	Source	Comment
	Yr6 [redacted] 0%	substitution with IFX IV (or subsequent IFX SC).	
Script equivalence, bDMARD:BKZ	<table><tr><th></th><th>Init.</th><th>Cont.</th></tr><tr><td>ADA</td><td>0.5</td><td>0.5</td></tr><tr><td>ETN</td><td>0.5</td><td>0.5</td></tr><tr><td>IFX IV</td><td>0.5 (0.1*)</td><td>0.75 (0.15*)</td></tr><tr><td>IFX SC</td><td>0.25</td><td>0.38</td></tr><tr><td>UST</td><td>1</td><td>1.5</td></tr><tr><td>SEC</td><td>0.5</td><td>0.5</td></tr><tr><td>IXE</td><td>0.67</td><td>1</td></tr><tr><td>CZP</td><td>0.5</td><td>0.5</td></tr><tr><td>GOL</td><td>0.5</td><td>0.54</td></tr><tr><td>GUS</td><td>0.67</td><td>1</td></tr></table> *assuming 5x100mg IV vials/script	Derived from recommended dose and corresponding number of scripts for initial treatment (16-20 weeks) and continuing treatment (52 weeks).	Generally reasonable. The submission overestimated the number of IFX SC scripts required for 52 weeks of maintenance treatment (17.33 vs 13), but this error did not impact results given the submission assumed 0% substitution rate with IFX SC.
Costs			
Proposed and comparator medicines, $/script	BKZ: published DPMQ ($3,422.13); Comparator treatments: published DPMQs by item number	Drug costs were based on the proposed DPMQ of BKZ and the published DPMQs of comparator treatments (by item code).	The published DPMQs may not provide an accurate estimate of unit cost given special pricing arrangements apply to several existing therapies in this market.
Patient copayment	PBS: $20.68 (SEC, IFX), $21.21 (ADA, IXE, UST, CZP, GOL, GUS, ETN) RPBS: $5.07 (SEC, IFX), $4.81 (ADA, IXE, UST, CZP, GOL, GUS, ETN)	Based on the distribution of scripts by beneficiary type in the current market (July 2022-June 2023).	This was appropriate, although a single copayment estimate across all treatments would also be appropriate.

Source: pp204-221 of the submission; 'Attachment 3.2_UCB PsA UCM 1.xlsx'; 'Attachment 3.2_UCB PsA UCM 2.xlsx'.
ADA=adalimumab; bDMARD=biologic disease-modifying antirheumatic drug; BKZ=bimekizumab; CZP=certolizumab pegol; DPMQ= dispensed price for maximum quantity; ETN=etanercept; GOL=golimumab; GUS=guselkumab; IFX=infliximab; IL=interleukin; IV=intravenous; IXE= ixekizumab; JAK=Janus kinase; PBS=Pharmaceutical Benefits Scheme; PsA=psoriatic arthritis; RPBS=Repatriation Pharmaceutical Benefits Scheme; SC=subcutaneous(ly); SEC=secukinumab; TOF=tofacitinib; UPA=upadacitinib; UST= ustekinumab.

6.27 Table 10 summarises the estimated net financial implications for the proposed listing of BKZ on the PBS/RPBS for PsA.

Table 10: Estimated net cost of BKZ to the PBS/RPBS

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimation of use and financial impact of the proposed medicine (BKZ)						
Scripts of BKZ	[1]	[1]	[2]	[2]	[2]	[2]
Initial treatment	[3]	[1]	[1]	[1]	[1]	[1]
Continuing treatment	[1]	[1]	[1]	[2]	[2]	[2]
BKZ net cost to PBS/RPBS	[4]	[5]	[5]	[6]	[6]	[6]
Estimation of changes in use and financial impact of other medicines						
Other b/tsDMARD scripts	[7]	[7]	[7]	[7]	[7]	[7]
Initial treatment	[7]	[7]	[7]	[7]	[7]	[7]
Continuing treatment	[7]	[7]	[7]	[7]	[7]	[7]
Net cost to PBS/RPBS	[7]	[7]	[7]	[7]	[7]	[7]
ADA	[7]	[7]	[7]	[7]	[7]	[7]
IXE	[7]	[7]	[7]	[7]	[7]	[7]
UST	[7]	[7]	[7]	[7]	[7]	[7]
CZP	[7]	[7]	[7]	[7]	[7]	[7]
GOL	[7]	[7]	[redacted][7]	[7]	[7]	[7]
GUS	[7]	[7]	[7]	[7]	[7]	[7]
ETN	[7]	[7]	[7]	[7]	[7]	[7]
SEC	[7]	[7]	[7]	[7]	[7]	[7]
IFX IV	[4]	[4]	[4]	[4]	[4]	[4]
IFX SC	[4]	[4]	[4]	[4]	[4]	[4]
TOF	[4]	[4]	[4]	[4]	[4]	[4]
UPA	[4]	[4]	[4]	[4]	[4]	[4]
Estimated financial implications for the PBS/RPBS						
Net cost to PBS/RPBS	[4]	[4]	[4]	[4]	[4]	[4]
Estimated financial implications for the health budget						
Net cost to health budget	[4]	[4]	[4]	[4]	[4]	[4]

Source: Tables 4.4, 4.5, 4.6, 4.9, 4.11, 4.13, pp208-223 of the submission.

ADA=adalimumab; BKZ=bimekizumab; CZP=certolizumab pegol; ETN=etanercept; GOL=golimumab; GUS=guselkumab; IFX=infliximab; IL=interleukin; IV=intravenous; IXE= ixekizumab; JAK=Janus kinase; PBS=Pharmaceutical Benefits Scheme; RPBS=Repatriation Pharmaceutical Benefits Scheme; SC=subcutaneous(ly); SEC=secukinumab; TOF=tofacitinib; UPA=upadacitinib; UST= ustekinumab.

The redacted values correspond to the following ranges:

[1] 500 to < 5,000

[2] 5,000 to < 10,000

[3] < 500

[4] $0 to < $10 million

[5] $10 million to < $20 million

[6] $20 million to < $30 million

[7] Net cost saving

6.28 Based on the published DPMQs, the submission estimated a net cost to the PBS/RPBS of approximately $30 million to < $40 million over the first six years. The estimate was likely an overestimate due to the use of published DPMQs rather than effective DPMQs. Assuming BKZ were to be listed on a cost-minimisation basis to the least costly alternative therapy and the current market growth was unchanged, then the requested listing would be expected to be approximately cost neutral to the PBS/RPBS.

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 bimekizumab for the treatment of severe psoriatic arthritis (PsA). The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost effectiveness of bimekizumab would be acceptable if it were cost minimised to the least costly alternative biologic or targeted synthetic disease modifying anti-rheumatic drug (b/tsDMARD) for the treatment of PsA. The PBAC noted the alternative therapies included adalimumab, certolizumab pegol, etanercept, golimumab, guselkumab, infliximab, ixekizumab, secukinumab, tofacitinib, upadacitinib and ustekinumab.

7.2 The PBAC considered the equi-effective doses of bimekizumab and the alternative b/tsDMARDs could be derived with reference to the relevant Product Information documents, noting the bimekizumab equi-effective dose component was 1 x 160 mg injection given at 4-weekly intervals. The PBAC agreed with the Sponsor and considered a separate dosing schedule for patients with co-existent chronic plaque psoriasis (as outlined in the draft Product Information) was not required, as patients who meet the criteria for treatment under the psoriasis restrictions will access the appropriate regimen as prescribed by their clinician.

7.3 The PBAC considered it was reasonable for the listing of bimekizumab to be consistent with other b/tsDMARDs for PsA, with prescribing limited to eligible medical practitioners, an initial treatment period of 16 weeks (as corrected during the evaluation), followed by maintenance therapy with re-assessment at 24-week intervals. The Committee noted the flow-on changes to other PsA b/tsDMARD listings to include bimekizumab in the list of eligible therapies.

7.4 The PBAC noted a grandfather restriction was requested for bimekizumab for PsA and considered this was reasonable, and the grandfather listing should remain in place for 12 months from the date of listing, per standard policy. The grandfather restriction will have similar eligibility criteria to the initial restriction. A grandfather patient would be required to have met these criteria prior to the non-PBS supply of bimekizumab.

7.5 The PBAC noted the only registered and marketed pack size for bimekizumab provides 2 x 160 mg injections per pack. The PBAC noted this pack size is currently PBS listed for psoriasis and provides 8 weeks of therapy at a dose of 320 mg (given as 2 x 160 mg injections) every 8 weeks. The PBAC noted a pack size of 2 injections would also provide 8 weeks of therapy for PsA patients at a dose of 160 mg (given as 1 x 160 mg injection) every 4 weeks. The PBAC noted it was of a mind to revise the PBS listings for other b/tsDMARDs if the listing of this pack size for bimekizumab creates inconsistencies across the listings for PsA.

7.6 The PBAC noted that 11 treatments were currently PBS listed for PsA and considered the clinical need for additional therapies for PsA that were of similar effectiveness and safety to other options was low. The Committee further noted two other IL-17

inhibitors (secukinumab and ixekizumab) were listed for PsA, but that bimekizumab has a different affinity for IL-17 subunits than secukinumab or ixekizumab.

7.7 The PBAC considered the nominated main comparator of ixekizumab was reasonable, given the similar mechanism of action of these two agents (noting secukinumab is also an IL-17A inhibitor like ixekizumab). However, the Committee considered that bimekizumab could substitute for any of the PBS listed b/tsDMARDs for PsA in practice.

7.8 The PBAC noted no direct trials comparing bimekizumab to ixekizumab were available, and the submission relied on an indirect treatment comparison (ITC) with placebo as the common comparator to support the claim of non-inferior effectiveness and safety. The PBAC noted there were no statistically significant differences between BKZ and IXE for the relative risk (RR) and odds ratio (OR) for ACR50 response and the ITC met the nominated non-inferiority margin in the intention-to-treat (ITT) population. The PBAC noted that for the ACR20 outcome, bimekizumab was statistically favoured in the ITT population for the indirect comparison presented in the submission but not in the supplementary indirect comparisons conducted by the evaluation. The PBAC considered that, overall, a claim of non-inferior effectiveness was supported by the evidence presented.

7.9 With respect to comparative safety, the PBAC noted the submission presented an ITC of relevant treatment-emergent adverse events (TEAEs) and noted no statistically significant differences were observed, although the 95% CIs were wide for these comparisons. The Committee considered the safety data in PsA to be consistent with the known safety profiles of these agents in other indications, and overall, the claim of non-inferior comparative safety to ixekizumab was reasonable.

7.10 The PBAC noted it had previously considered adalimumab a higher tier, more effective medicine for PsA (see paragraph 5.3). The PBAC also noted the limited direct comparative data versus adalimumab in a b/tsDMARD naïve population found no statistically significant differences between bimekizumab and adalimumab for ACR20 and ACR50 and considered it may be reasonable to conclude these two therapies also have comparable effectiveness in PsA.

7.11 Under Section 101(3B) of the National Health Act (1953), the PBAC cannot recommend listing a therapy that is substantially more costly than an alternative therapy unless it is satisfied that the therapy provides, for some patients, a significant improvement in efficacy and/or reduction in toxicity. The submission did not present any evidence that bimekizumab provided a significant improvement in efficacy and/or reduction in toxicity compared to any alternative for the treatment of PsA, and therefore there was no basis for bimekizumab to have a price advantage over any relevant alternative for an equivalent treatment period. The PBAC did not accept the submission argument that intravenous (IV) or oral therapies should be excluded as alternative therapies (paragraph 5.2 refers).

7.12 The PBAC considered that a listing based on a cost minimisation approach with costs over two years, consistent with the approach previously used for b/tsDMARDs, was appropriate to determine the cost minimised price of bimekizumab. The PBAC considered the cost of bimekizumab should be no greater than the alternative therapies.

7.13 The PBAC noted the utilisation and financial estimates as presented in the submission resulted in an incremental cost for the listing of bimekizumab, however also noted the estimates were based on a price of bimekizumab calculated from a cost minimisation approach using the published price of ixekizumab (rather than the least costly alternative). The PBAC considered the uptake and rate of replacement of specific b/tsDMARDs to be uncertain, however considered that if listed on a cost minimisation basis with the least costly alternative, the listing would most likely be cost neutral or modestly cost saving to the PBS as it will only replace therapies that are either of equivalent cost or more expensive.

7.14 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because bimekizumab is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over secukinumab (or the alternative b/tsDMARDs), or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.

7.15 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 indication to bimekizumab as follows:*

For brevity reasons, the large common administrative note (concept 27834) is presented once at the end of this section.

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Proprietary Name and Manufacturer	
Initial treatment						
BIMEKIZUMAB bimekizumab 160 mg/mL injection, 2 x 1 mL pen devices	New (initial) New (continuing + grandfather)	1	2	1/2*	Bimzlx®	UCB Australia Proprietary Limited
bimekizumab 160 mg/mL injection, 2 x 1 mL syringes	New (initial) New (continuing+ grandfather)	1	2	1/2*		

*Maximum repeats of 1 for initial therapy, 2 for continuing and grandfather therapy

Concept ID	**Category / Program:** GENERAL – General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners
	Restriction Level / Method: ☒Authority Required – In Writing
	Administrative Advice: Overarching administrative note, see below.
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Severity: Severe
	Condition: Psoriatic arthritis
	Indication: Severe psoriatic arthritis
	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
	Clinical criteria:
	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
	Clinical criteria:
	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
	Clinical criteria:
	Patient must not receive more than 16 weeks of treatment under this restriction
	AND
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of psoriatic arthritis
	AND

	Population criteria:
	Patient must be at least 18 years of age
	Prescribing Instructions: 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.
	Prescribing Instructions: 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.
	Prescribing Instructions: 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. 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.
	Prescribing Instructions: 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).
	Prescribing Instructions: An assessment of a patient's response to this initial course of treatment must be conducted following a minimum of 12 weeks of therapy and no later than 4 weeks prior the completion of this course of treatment.
	Prescribing Instructions: Where a response assessment is not conducted within the required timeframe, the patient will be deemed to have failed to respond to treatment with this drug, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.
	Prescribing Instructions: If a patient 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.
	Administrative Advice: The Services Australia website (www.servicesaustralia.gov.au) has details of the toxicities, including severity, which will be accepted where one is claimed.
	Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au, Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos, Or mailed to: Services Australia,

	Complex Drugs, Reply Paid 9826, HOBART TAS 7001
	Treatment Phase: Initial treatment - Initial 2 (change or recommencement of treatment after a break in 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
	Clinical criteria:
	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
	Clinical criteria:
	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
	Clinical criteria:
	Patient must not receive more than 16 weeks of treatment under this restriction
	AND
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of psoriatic arthritis
	AND
	Population criteria:
	Patient must be at least 18 years of age
	Prescribing Instructions: 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).
	Prescribing Instructions: 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).
	Prescribing Instructions: An application for a patient who has received PBS-subsidised treatment with this drug and who wishes to re-commence therapy with this drug, must be accompanied by evidence of a response to the patient's most recent course of PBS-subsidised treatment with this drug, within the timeframes specified below.
	Prescribing Instructions: To demonstrate a response to treatment the application must be accompanied with the assessment of response, conducted following a minimum of 12 weeks of therapy and no later than 4 weeks from cessation of the most recent course of biological medicine. It is recommended that an application for the continuing treatment be submitted no later than 4 weeks from the date of completion of the most recent course of treatment. This is to ensure treatment continuity for those who meet the continuing restriction.

	Prescribing Instructions: Where a response assessment is not conducted within the required timeframe, the patient will be deemed to have failed to respond to treatment with this drug, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.
	Prescribing Instructions: If a patient 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.
	Prescribing Instructions: A patient may re-trial this drug after a minimum of 5 years have elapsed between the date the last prescription for a PBS-subsidised biological medicine was approved in this cycle and the date of the first application under a new cycle under the Initial 3 treatment restriction.
	Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au, Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos, Or mailed to: Services Australia, Complex Drugs, Reply Paid 9826, HOBART TAS 7001
	Treatment Phase: Initial treatment - 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
	Clinical criteria:
	Patient must have had a break in treatment of 5 years or more from the most recently approved PBS-subsidised biological medicine for this condition
	AND
	Clinical criteria:
	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
	Clinical criteria:
	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
	Clinical criteria:
	Patient must not receive more than 16 weeks of treatment under this restriction
	AND
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of psoriatic arthritis
	AND

	Population criteria:
	Patient must be at least 18 years of age
	Prescribing Instructions: 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).
	Prescribing Instructions: All measures of joint count and ESR and/or CRP must be no more than 4 weeks old at the time of initial application.
	Prescribing Instructions: 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.
	Prescribing Instructions: 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.
	Prescribing Instructions: 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).
	Prescribing Instructions: An application for a patient who has received PBS-subsidised biological medicine treatment for this condition who wishes to 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.
	Prescribing Instructions: To demonstrate a response to treatment the application must be accompanied with the assessment of response, conducted following a minimum of 12 weeks of therapy and no later than 4 weeks from cessation of the most recent course of biological medicine. It is recommended that an application for the continuing treatment be submitted no later than 4 weeks from the date of completion of the most recent course of treatment. This is to ensure treatment continuity for those who meet the continuing restriction.
	Prescribing Instructions: Where a response assessment is not conducted within the required timeframe, the patient will be deemed to have failed to respond to treatment with this drug, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.
	Prescribing Instructions: If a patient 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.
	Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au, Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos, Or mailed to: Services Australia,

	Complex Drugs, Reply Paid 9826, HOBART TAS 7001
	Treatment Phase: 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
	Clinical criteria:
	Patient must have received insufficient therapy with this drug for this condition under the Initial 1 (new patient) restriction to complete 16 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 16 weeks treatment; or
	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 16 weeks treatment
	AND
	Clinical criteria:
	The treatment must provide no more than the balance of up to 16 weeks treatment available under the above restrictions
	AND
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of psoriatic arthritis
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

Concept ID	**Category / Program:** GENERAL – General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners
	Restriction Level / Method: ☒Authority Required – In Writing
	Severity: Severe
	Condition: Psoriatic arthritis
	Indication: Severe psoriatic arthritis
	Treatment Phase: Continuing treatment
	Clinical criteria:
	Patient must have received this drug as their most recent course of PBS-subsidised biological medicine treatment for this condition
	AND
	Clinical criteria:
	Patient must have demonstrated an adequate response to treatment with this drug
	AND
	Clinical criteria:
	Patient must not receive more than 24 weeks of treatment under this restriction
	AND
	Treatment criteria:
	Must be treated by a rheumatologist; or

	Must be treated by a clinical immunologist with expertise in the management of psoriatic arthritis
	AND
	Population criteria:
	Patient must be at least 18 years of age
	Prescribing Instructions: 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).
	Prescribing Instructions: 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.
	Prescribing Instructions: 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).
	Prescribing Instructions: An application for the continuing treatment must be accompanied with the assessment of response conducted following a minimum of 12 weeks of therapy and no later than 4 weeks from cessation of the most recent course of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment.
	Prescribing Instructions: Where a response assessment is not conducted within the required timeframe, the patient will be deemed to have failed to respond to treatment with this drug, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.
	Prescribing Instructions: If a patient 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.
	Prescribing Instructions: A patient may re-trial this drug after a minimum of 5 years have elapsed between the date the last prescription for a PBS-subsidised biological medicine was approved in this cycle and the date of the first application under a new cycle under the Initial 3 treatment restriction.
	Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au, Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos, Or mailed to: Services Australia, Complex Drugs, Reply Paid 9826, HOBART TAS 7001
	Treatment Phase: Continuing treatment - balance of supply

	Clinical criteria:
	Patient must have received insufficient therapy with this drug for this condition under the continuing treatment restriction to complete 24 weeks treatment
	AND
	Clinical criteria:
	The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restriction
	AND
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of psoriatic arthritis
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).
	Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply – Grandfather arrangements
	Indication: Severe psoriatic arthritis
	Clinical criteria:
	Patient must have received treatment with this drug for this PBS indication prior to listing date
	AND
	Clinical criteria:
	Patient must be receiving treatment with this drug for this condition at the time of application
	AND
	Clinical criteria:
	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
	AND
	Clinical criteria:
	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
	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
	AND
	Clinical criteria:
	Patient must have demonstrated an adequate response to treatment with this drug for this condition if the patient has received non-PBS-subsidised treatment for at least 12 weeks
	Clinical criteria:
	Patient must not receive more than 24 weeks of treatment under this restriction
	AND
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of psoriatic arthritis
	AND
	Population criteria:
	Patient must be at least 18 years of age
	Prescribing Instructions:

	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.
	Prescribing Instructions: 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.
	Prescribing Instructions: 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. 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.
	Prescribing Instructions: 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).
	Prescribing Instructions: The authority application must be made in writing and must include: (a) a completed authority prescription form; 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). (c) the date of commencement of this drug; and (d) results of the baseline patient assessment prior to initiation of non-PBS subsidised therapy with this drug
	Prescribing Instructions: 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.
	Prescribing Instructions: 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.
	Prescribing Instructions: An assessment of a patient's response to this initial course of treatment must be conducted following a minimum of 12 weeks of therapy and no later than 4 weeks prior the completion of this course of treatment.
	Prescribing Instructions: Where a response assessment is not conducted within the required timeframe, the patient will be deemed to have failed to respond to treatment with this drug, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.

	Prescribing Instructions: If a patient 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.
	Prescribing Instructions: Patients 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.
	Administrative Advice: The Services Australia website (www.servicesaustralia.gov.au) has details of the toxicities, including severity, which will be accepted where one is claimed.
	Administrative Advice: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.
	Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au, Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos, Or mailed to: Services Australia, Complex Drugs, Reply Paid 9826, HOBART TAS 7001

Administrative Advice	**TREATMENT OF ADULT PATIENTS WITH SEVERE PSORIATIC ARTHRITIS,** The following information applies to Pharmaceutical Benefits Scheme (PBS) listed for adult patients with severe psoriatic arthritis. Where the term 'biological medicine' appears in notes and restrictions, it refers to any PBS benefit where the PBS indication specifies: Severe Psoriatic Arthritis. Some benefits are not biological medicines, but are small molecules. However, for administrative purposes, these benefits are included within the term 'biological medicine'. A patient is eligible for PBS-subsidised treatment with only 1 of the above biological medicines at any one time. Under these arrangements, within a single treatment 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. 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.

	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. There is no limit to the number of treatment cycles a patient may undertake in their lifetime. How to prescribe PBS-subsidised biological medicine treatment for severe psoriatic arthritis. (1) Initial treatment. Applications for initial treatment should be made where: (i) a patient has not received prior PBS-subsidised biological medicine treatment and wishes to commence such therapy (Initial 1 - New patient); or, (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, (iii) a patient wishes to recommence treatment with a specific biological medicine following a break in PBS-subsidised therapy of less than 5 years with the same medicine (Initial 2 - Change or Recommencement of treatment after a break in biological medicine of less than 5 years). (iv) a patient wishes to recommence treatment with a biological medicine following a break in PBS-subsidised therapy of more than 5 years (Initial 3 - Recommencement of treatment after a break in biological medicine of more than 5 years) or, 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. (2) Continuing treatment. 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. 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. (3) Swapping therapy. 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. An authority application must be made under the 'Initial 2' treatment phase. 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. A patient may trial an alternate biological medicine at any time, regardless of whether they are receiving therapy (initial or continuing) with a biological medicine at the time of the application. However, they cannot swap to a particular biological medicine if they have failed to respond to prior treatment with that drug within the same treatment cycle. (4) Baseline measurements to determine response. 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., 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. (5) Re-commencement of treatment after a 5-year break in PBS-subsidised therapy. 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.

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.