

5.07 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 General Schedule Authority Required (in writing) listing for bimekizumab (BKZ) for the treatment of severe chronic plaque psoriasis (CPP).
- 1.2 Listing was requested on the basis of a cost-effectiveness analysis versus all PBS-listed biologic disease-modifying anti-rheumatic drug (bDMARDs) for CPP: adalimumab (ADA), guselkumab (GUS), ixekizumab (IXE), risankizumab (RIS), secukinumab (SEC), ustekinumab (UST), tildrakizumab (TIL), etanercept (ETN) and infliximab (IFX).

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

Component	Description
Population	Adult patients with severe chronic plaque psoriasis (CPP)
Intervention	Bimekizumab 320 mg (given as 2 SC injections of 160 mg) at Week 0, 4, 8, 12, 16 and every 8 weeks thereafter
Comparator	All current PBS-listed bDMARDs for CPP. ADA, UST and SEC are excluded for the purposes of a cost-minimisation approach to the least costly bDMARD, in view of the direct evidence demonstrating superiority of BKZ.
Outcomes	Primary: PASI 90 Other: PASI 100, PASI 75 ^a , safety. The submission's clinical claim was based on three direct randomised controlled trials of bimekizumab versus adalimumab, ustekinumab and secukinumab respectively; and a network meta-analysis of bimekizumab versus all bDMARDs listed on the PBS.
Clinical claim	In adults with severe CPP, bimekizumab is more effective than all currently PBS-listed bDMARDs, at achieving PASI 75 ^a , PASI 90 and PASI 100. Bimekizumab is similar in safety compared to the currently-PBS listed bDMARDs.

Blue shading indicates data previously seen by the PBAC.

Source: Table 1-1, p35 of the current submission.

: ADA = adalimumab; BKZ = bimekizumab; bDMARD = biologic disease-modifying anti-rheumatic drug; CPP = chronic plaque psoriasis; NMA = network meta-analysis; PASI=psoriasis area and severity index; SEC = secukinumab; SC = subcutaneous; UST = ustekinumab.

^a The March 2022 submission included PASI 75 as one of the other outcomes, but this current submission stated that PASI 90 and PASI 100 had replaced PASI 75 as the key treatment goals.

2 Background

Registration status

- 2.1 BKZ was TGA registered on 24 March 2022 for treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

*Public Summary Document - March 2023 PBAC Meeting***Previous PBAC consideration**

- 2.2 The March 2022 submission requested listing of BKZ for the treatment of CPP on the basis of cost effectiveness versus all PBS listed bDMARDs. The PBAC considered that, given the claim of superior effectiveness was not accepted, the economic model was largely uninformative for decision-making. Instead, the PBAC recommended listing of BKZ for the treatment of CPP on the basis of cost-minimisation to the least costly of alternative bDMARDs. The PBAC had considered that BKZ was likely superior to ADA, TIL and UST and non-inferior to GUS, IXE, SEC and RIS in terms of achieving PASI 75 and PASI 90 responses at Week 12/16 (paragraph 7.1, BKZ Public Summary Document (PSD), March 2022 PBAC meeting).
- 2.3 The PBAC considered that, whilst there was some evidence to suggest BKZ is associated with a statistically significantly higher proportion of patients achieving a PASI 90 score compared to GUS, IXE, SEC and RIS at Week 12/16, the differences were relatively small (paragraph 7.6, BKZ PSD, March 2022 PBAC Meeting). The ESC questioned whether the difference in PASI 90 response rates was clinically meaningful and noted that the most recent Cochrane Review by Sbidian 2021 found the clinical effectiveness of BKZ was similar to GUS, IXE, SEC and RIS (paragraph 6.38, BKZ PSD, March 2022 PBAC meeting).
- 2.4 The PBAC recalled that GUS, IXE and RIS were listed for CPP on the basis of cost-minimisation to the least costly alternative bDMARD and given the PBAC considered BKZ was likely to be non-inferior to these medicines, it was appropriate to list BKZ on the same basis. Following the March 2022 PBAC meeting, the Department of Health and Ageing advised the sponsor that the least costly bDMARD was ADA.
- 2.5 The current submission stated that the sponsor attempted to progress the PBAC's recommendation but was unable to accept a price based on cost minimisation to ADA, which it considered was incongruent with the PBAC's advice that BKZ was superior to ADA.
- 2.6 Therefore, the purpose of the current submission was to request that the PBAC reconsider the appropriate pricing for BKZ. The current submission approached this issue in two different ways, depending on the PBAC's interpretation of the clinical evidence.
- The current submission disagreed with the PBAC's interpretation of the clinical evidence and maintained that the premise of the original submission, that PASI 90 and PASI 100 are both clinically relevant outcomes and that the clinical evidence demonstrated that BKZ was superior to all PBS-listed bDMARDs in terms of PASI 90 and PASI 100. Hence, the model presented in the original submission was informative for decision making and a respecified base case supported a price premium over all PBS-listed bDMARDs.
 - The current submission also argued that ADA, TIL and UST should be excluded as comparators when interpreting the PBAC's advice to list BKZ on the basis of a cost-

Public Summary Document - March 2023 PBAC Meeting

minimisation approach to the least costly bDMARD given that the PBAC had considered that BKZ had superior effectiveness to ADA, TIL and UST.

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

3 Requested listing

Name, restriction, manner of administration, form	Maximum quantity (packs)	Maximum quantity (units)	No. of repeats	Dispensed price for maximum quantity	Proprietary name and manufacturer
BIMEKIZUMAB 160 mg in 1mL pre-filled syringe (initial and continuing)	1	2	Initial: 5 Continuing: 2	\$3,908.94 ¹ published price \$ effective price	Bimzelx®, UCB Australia
BIMEKIZUMAB 160 mg in 1mL pre-filled pen (initial and continuing)	1	2	Initial: 5 Continuing: 2	\$3,908.94 ¹ published price \$ effective price	Bimzelx®, UCB Australia

Blue shading indicates data previously seen by the PBAC.

Source: Table 1-9, p57 of the current submission.

1 The current submission requested the same published AEMP (\$3747.66) as the original submission, but a slight change in the pharmacy mark ups resulted in a slightly different published DMPQ.

- 3.1 The current submission requested a Special Pricing Arrangement, with a published AEMP of \$3,747.66 (DPMQ of \$3,908.94) and an effective AEMP of \$ (DMPQ of \$).
- 3.2 The current submission referred to restrictions in the March 2022 PSD which were not reproduced for the sake of brevity.
- 3.3 The current submission stated that the initial treatment period requested is 24 weeks and the maintenance period requested is 24 weeks. It was noted that for patients with body weight ≥ 120 kg, more frequent dosing of BKZ after Week 16 may be considered (i.e., dosing every 4 weeks rather than every 8 weeks), requiring 3 additional doses of BKZ during maintenance (i.e., total 6 doses rather than the 3 requested).
- 3.4 The current submission acknowledged that the 'PBAC considered the number of initial repeats should be reduced from 5 to 4, such that the first continuing dose is given in week 24, after the response to treatment has been assessed following the dose in week 16' (paragraph 7.4, BKZ PSD, March 2022 PBAC meeting), and stated that these amendments had been considered. However, the requested number of repeats for initial treatment in the current submission remain unchanged, providing up to 32 weeks of initial treatment with BKZ. The PBAC reiterated its previous consideration that the number of initial repeats be reduced to 4.

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

4 Population and disease

- 4.1 Psoriasis manifests as chronic inflammation of the skin, characterised by disfiguring, scaling and erythematous plaques that may be painful and severely pruritic and may cause significant reductions in quality of life (QoL). There are no universally accepted

Public Summary Document - March 2023 PBAC Meeting

definitions of mild, moderate and severe disease, and severity can be measured by several indicators, including the Psoriasis Area Severity Index (PASI), the extent of body surface affected (BSA) and the impact of the condition on patients' QoL, commonly measured by the Dermatology Life Quality Index (DLQI).

- 4.2 The proposed population for BKZ is the same as that for other PBS-listed bDMARDs for this condition: patients with severe CPP who have failed to achieve an adequate response with at least two therapies including methotrexate, cyclosporine, acitretin, apremilast or phototherapy (either UVB or PUVA).
- (i) For whole body disease, patients must have a PASI score > 15 for an initial course of bDMARD treatment. Continuing treatment is conditional on patients achieving and maintaining a 75% reduction in the PASI score at baseline (i.e., PASI 75 response).
 - (ii) For CPP affecting the face, hand or foot, patients must have 2 of 3 PASI symptom sub-scores for erythema, thickness or scaling rated as 'severe' or 'very severe', or the skin affected is more than 30% of the face, palm of hand or sole of foot. Continuing treatment is conditional on patients achieving and maintain and adequate response, defined as all 3 PASI sub-scores for erythema, thickness or scaling rated as 'slight' or 'better', or a 75% reduction in the skin area affected compared to baseline.
- 4.3 Consistent with the original submission, the current submission argued that with the availability of newer treatments, the new 'gold standard' should be PASI 90 and claimed that this has been recommended in recent international guidelines. The current submission also cited literature reporting higher health related QoL, improved work productivity, reduced indirect costs and cost savings from reduced use of topical treatments, dose escalation and treatment switching for those who achieve PASI 90 or PASI 100.
- 4.4 In March 2022, the ESC considered that whilst it is appropriate for treatment goals to change over time, also considered PASI 75 remained a relevant outcome, particularly in the context of this outcome being the primary outcome considered for previous bDMARD submissions for CPP. Furthermore, the ESC in March 2022 noted PASI 75 remained a key clinical outcome when considering whether to continue treatment with a bDMARD. The literature suggested the QoL difference between PASI 75 and PASI 90 may not be clinically significant (paragraphs 6.5, 6.6, BKZ PSD, March 2022 PBAC meeting).
- 4.5 The current submission reiterated that the ultimate goal of therapy is clear skin and presented results from a sponsor-commissioned survey of Australian dermatologists asked about treatment targets (Elbow 2022). Nine of 47 invited dermatologists completed the survey, which indicated that the single most desired outcome is complete clearance and all respondents indicated they aimed for at least PASI 90 response.

Public Summary Document - March 2023 PBAC Meeting

- 4.6 The current submission also presented results from three case studies that highlight the ‘life changing’ benefits of achieving complete skin clearance, and emphasised that patients with CPP in high impact areas (scalp, face, genitalia, palms of hands, soles of feet) experience the greatest improvement in quality of life with clear skin given these areas are of most concern to patients. The current submission stated that psoriasis affecting the scalp, nails, palms and soles can cause significant physical impairment and negatively impact quality of life, and clearance of disease in these areas is clinically important.

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

5 Comparator

- 5.1 The current submission nominated all current PBS-listed bDMARDs as the main comparators.
- 5.2 If treatment with BKZ is proposed to be substantially more costly than any of the alternative therapies, the PBAC could only recommend listing BKZ if it is satisfied that BKZ provides, for some patients, a significant improvement in efficacy or reduction of toxicity over the alternative therapies (Section 101(3B) of the *National Health Act 1953*). The PBAC noted alternative therapies included ADA, GUS, IXE, RIS, SEC, UST, TIL, ETN and IFX.
- 5.3 The ESC noted that the mechanism of action and mode of administration of BKZ was not unique and considered the clinical need for additional treatment options for severe CPP was low.

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

6 Consideration of the evidence

Sponsor hearing

- 6.1 The sponsor requested a hearing for this item. The clinician reiterated the treatment goal for CPP is now complete clearance of skin lesions and the importance of the availability of additional safe and effective treatment options. The clinician outlined their clinical experience with IFX as a treatment option, noting it is not used commonly because of its low effectiveness and risk of adverse events. The clinician described a positive patient experience with BKZ. The clinician noted the adverse events observed with BKZ (notably candida infections) are manageable.

Consumer comments

- 6.2 The PBAC noted and welcomed the input from individuals (9), health care professionals (4) and organisations (3) via the Consumer Comments facility on the PBS website. The comments described the impact of CPP on patients’ physical and mental

Public Summary Document - March 2023 PBAC Meeting

health, and the improvements BKZ treatment has on overall quality of life. The comments from individuals who have used BKZ described it as more efficacious than other treatment options, with complete clearance of plaques, as well as a reduction of pain, flaking, itchiness, and other associated symptoms. The comments noted that BKZ is well tolerated, easy to administer and the less frequent dosing was an advantage.

- 6.3 The PBAC noted input was received from The Australian College of Dermatologists, Psoriasis Australia and Hornsby Dermatology. The comments described the significant impact of chronic plaque psoriasis on patients' quality of life and emphasised the importance of additional treatment options being available.

Clinical trials

- 6.4 Compared to the March 2022 submission, the evaluation considered the key clinical evidence presented in the current submission was largely unchanged overall and was primarily based on three direct RCTs comparing BKZ to ADA, UST and SEC, and a Bayesian network meta-analysis (NMA) comparing BKZ to RIS, IXE, GUS, TIL and IFX, referenced as the 'UCB NMA' (see Table 2). The UCB NMA included data for IFX but the PBAC had noted this had not been presented in the March 2022 submission (paragraph 7.9, BKZ PSD, March 2022 PBAC meeting). The comparison between BKZ and IFX was presented in the current submission.
- 6.5 The results of the indirect treatment comparison (ITC) presented in the March 2022 submission was not presented with the current submission instead placing greater emphasis on the results of the UCB NMA (published as Armstrong 2022) for comparisons versus RIS, IXE, GUS, TIL and IFX. For consistency, the results of the ITC were reproduced below including results for the comparison versus IFX. Data for the bDMARDs included in the ITC (i.e., RIS, IXE, GUS and TIL) were extracted from PBAC Public Summary Documents (PSDs); no independent searches were conducted for these comparators. The PBAC noted the PSDs for these medicines were published between 2016 and 2019 and there may be additional, informative clinical data that was published after this time period (paragraph 6.16, BKZ PSD, March 2022 PBAC meeting).
- 6.6 New clinical evidence presented in the current submission included:
- Results from the updated Cochrane review (Sbidian 2022). The previous version of this review Sbidian 2021 was presented in the March 2022 submission but had only included data from one BKZ trial in the NMA (compared to five BKZ trials in Sbidian 2022).
 - Results from a 'long-term' NMA conducted by Armstrong 2022a, comparing PASI response at Week 48 to 56 for patients treated with BKZ and some of the nominated comparators (ADA, ETN, UST, SEC, IXE, GUS, RIS).
 - Longer-term follow-up data for BKZ to three years, for patients enrolled in BE SURE and BE RADIANT who received treatment in an open label extension study.

Public Summary Document - March 2023 PBAC Meeting

The data was sourced from three conference posters (Thaci 2022, Lebwohl 2022, and Kokolakis 2022).

- Clinical data for patients with CPP in one of three high impact areas (i.e., scalp, nail and palmoplantar). The post hoc analyses reported the proportion of patients with 'complete clearance' of the high impact area over time for patients enrolled in BE VIVID, BE SURE, BE RADIANT and received treatment in an open label extension study. The data was sourced from two conference posters (Warren 2022, Merola 2022)

6.7 Details of the full list of trials and reports presented in the current submission are provided in Table 2.

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

Trial ID	Protocol title/ Publication title	Publication citation
BE READY	Bimekizumab efficacy and safety in moderate to severe plaque psoriasis (BE READY): a multicentre, double-blind, placebo-controlled, randomised withdrawal phase 3 trial.	September 2020
	Gordon KB, Foley P, Krueger JG, Pinter A, Reich K, Vender R, et al. Bimekizumab efficacy and safety in moderate to severe plaque psoriasis (BE READY): a multicentre, double-blind, placebo-controlled, randomised withdrawal phase 3 trial.	Lancet 2021; 397: 475-486
BE SURE	Bimekizumab versus adalimumab efficacy and safety in moderate to severe plaque psoriasis (BE SURE): a multicentre, double-blind, randomised withdrawal phase 3 trial.	September 2020
	Warren, R. B. B., A. Bagel, J. Papp, K. A. Yamauchi, P. Armstrong, A. Langley, et al. Bimekizumab versus Adalimumab in Plaque Psoriasis.	NEJM 2021; 385: 130-141
BE VIVID	Bimekizumab versus ustekinumab and placebo efficacy and safety in moderate to severe plaque psoriasis (BE VIVID): a multicentre, double-blind, placebo-controlled, randomised withdrawal phase 3 trial.	August 2020
	Reich K, Papp KA, Blauvelt A, Langley RG, Armstrong A, Warren RB, et al. Bimekizumab versus ustekinumab for the treatment of moderate to severe plaque psoriasis (BE VIVID): efficacy and safety from a 52-week, multicentre, double-blind, active comparator and placebo controlled phase 3 trial.	Lancet. 2021; 397:487-498
BE RADIANT	Bimekizumab versus secukinumab efficacy and safety in moderate to severe plaque psoriasis (BE RADIANT): a multicentre, double-blind, placebo-controlled, randomised withdrawal phase 3 trial.	October 2020
	Reich K, Warren RB, Lebwohl M, Gooderham M, Strober B, Langley RG, et al. Bimekizumab versus Secukinumab in Plaque Psoriasis.	NEJM 2021; 385:142-152
BE ABLE 1	Papp KA, Merola JF, Gottlieb AB, Griffiths CEM, Cross N, Peterson L, et al. Dual neutralization of both interleukin 17A and interleukin 17F with bimekizumab in patients with psoriasis: Results from BE ABLE 1, a 12-week randomized, double-blinded, placebo-controlled phase 2b trial.	J Am Acad Dermatol. 2018;79: 277-286.e10
BE ABLE 2	Blauvelt A, Papp KA, Merola JF, Gottlieb AB, Cross N, Madden C, et al. Bimekizumab for patients with moderate to severe plaque psoriasis: 60-week results from BE ABLE 2, a randomized, double-blinded, placebo-controlled, phase 2b extension study.	Am Acad Dermatol. 2020; 83:1367-1374.

Public Summary Document - March 2023 PBAC Meeting

Trial ID	Protocol title/ Publication title	Publication citation
BE BRIGHT	Bimekizumab extension study BE BRIGHT of efficacy and safety in moderate to severe plaque psoriasis	December 2020
EADV 2022 conference posters		
Thaci 2022 (BE SURE / BE BRIGHT)	Thaci D, Vender R, de Rie M, et al. Bimekizumab efficacy and safety through three years in patients with moderate to severe plaque psoriasis: Long-term results from the BE SURE randomised controlled trial and the BE BRIGHT open-label extension	EADV 2022: 7-10 September.
Lebwohl 2022 (BE RADIANT)	Lebwohl M, Brunner PM, Soung J et al. Bimekizumab versus secukinumab in plaque psoriasis: Cumulative clinical and health-related quality of life benefit through 2 years of the BE RADIANT phase 3b trial and open-label extension.	EADV 2022: 7-10 September.
Kokolakis 2022 (BE RADIANT)	Kokolakis G, Langley RG, Gottlieb AB et al. Bimekizumab efficacy through 96 weeks in patients with moderate to severe plaque psoriasis: Patient-reported outcomes from the BE RADIANT phase 3b trial.	EADV 2022: 7-10 September.
Warren 2022 (BE SURE/BE BRIGHT; BE VIVID/BE BRIGHT; BE RADIANT)	Warren RB, Strober B, Pinter A et al. Bimekizumab efficacy over two years in patients with moderate to severe plaque psoriasis with scalp and nail involvement who switched from adalimumab, ustekinumab, or secukinumab: Results from the BE SURE, BE VIVID, BE BRIGHT, and BE RADIANT phase 3/3b trials	EADV 2022: 7-10 September.
Merola 2022 (BE SURE/BE BRIGHT; BE RADIANT)	Merola JF, Gottlieb AB, Morita A et al. Bimekizumab efficacy in high-impact areas for patients with moderate to severe plaque psoriasis: Pooled results through two years from the BE SURE and BE RADIANT phase 3 trials.	EADV 2022: 7-10 September.
Network meta-analyses		
Armstrong 2022 (UCB NMA)	Armstrong A, Fahrbach K, Leonardi C, et al. Efficacy of bimekizumab and other biologics in moderate to severe plaque psoriasis: A systematic literature review and a network meta-analysis.	<i>Dermatol. Ther.</i> 2022; 12:1777-1792.
Sbidian 2022	Sbidian E, Chaimani A, Garcia-Doval I, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis (Review)	<i>Cochrane Database of Systematic Reviews</i> 2022; 5: 1465-1858.
Armstrong 2022a	Armstrong AW, Soliman AM, Betts KA, et al. Long-term benefit-risk profiles of treatments for moderate-to-severe plaque psoriasis: A network meta-analysis.	<i>Dermatol. Ther.</i> 2022; 12:167-184.

Blue shading indicates data previously seen by the PBAC.

Source: Table 2-6, pp72-73 of the current submission.

- 6.8 All BKZ trials were phase 3, multicentre, active comparator or placebo (PBO) controlled, double-blind RCTs, except for the two open label (OL) extension studies (BE ABLE2 and BE BRIGHT), and the phase 2 dose-escalation trial (BE ABLE1). Only data from patients receiving the relevant dose of BKZ 320 mg from BE ABLE1 were presented and included in the analysis. This was appropriate.
- 6.9 Overall, the risk of bias in the controlled phase of the trials was considered low. As most of the trials allowed patients to switch treatment beyond the initial active comparator/placebo-controlled phase (12/16 weeks), outcomes from subsequent periods would be subject to bias. However, appropriately, trial outcomes were assessed at the end of the placebo-controlled periods. Baseline disease characteristics were generally well balanced across the BKZ trials and reflective of a population with moderate to severe CPP.

Public Summary Document - March 2023 PBAC Meeting

- 6.10 The UCB NMA (now published as Armstrong 2022) included data from 86 RCTs (including 34,476 patients); reasons for excluding data from an additional 4 trials were not explicitly reported. The literature search and selection criteria identified English language peer-reviewed publications of RCTs to July 2020 comparing biologic or non-biologic treatments at approved EMA doses for adults with moderate to severe plaque psoriasis and reported short-term PASI response outcomes (Week 10 to 16). RCTs that focused primarily on treatment of psoriatic arthritis were excluded. Most of the trials in the UCB NMA were considered to have a low risk of bias. The NMA report indicated there was a high degree of heterogeneity across the included trials, particularly with respect to disease duration, exposure to prior biologic treatment, phototherapy, or non-biologic treatments. The current submission argued that the UCB NMA was the most appropriate NMA to inform decision making but provided no clear rationale to support this statement (other than the analysis was now published in a peer reviewed journal).
- 6.11 The updated Cochrane review (Sbidian 2022) presented results of a NMA using a frequentist framework including data from 167 studies (58,912 patients). The literature search and selection criteria identified published and unpublished RCTs (irrespective of language) to October 2021 comparing biologic and non-biologic treatments for adults with moderate to severe plaque psoriasis and reported clinical response outcomes following induction treatment (Week 8 to 24). One half of the included RCTs (87) had a low risk of bias, one third (57) had a high risk of bias and one sixth (23) had unclear risk of bias. The main analysis included all treatments and doses but sensitivity analyses were conducted that included only approved treatments and doses, RCTs with low risk of bias and short-term outcomes. Although the updated Cochrane review included data from a total of 167 trials, the analysis of PASI response was based on fewer trials (for example, PASI 90 response appeared to be based on data from 114 trials).
- 6.12 The long-term Bayesian NMA (Armstrong 2022a) included data from 14 studies comparing BKZ to several comparators for treatment response following induction and maintenance therapy (Weeks 48 to 56). Armstrong 2022a conducted a fixed effects Bayesian probit NMA to jointly model PASI 75, PASI 90 and PASI 100 response, and fixed effects Bayesian logit NMAs to model safety outcomes. The literature search and selection criteria identified publications of RCTs to May 2021 comparing bDMARDs at approved doses for adults with moderate-to-severe plaque psoriasis and reported PASI efficacy outcomes by the end of the maintenance period (48-56 weeks from baseline). RCTs in which cross-over occurred before weeks 48-56, or RCTs which were re-randomised based on induction phase efficacy, were excluded. This NMA did not include all relevant comparators i.e., trials of ADA, IFX and TIL were not included. A risk of bias assessment did not appear to be conducted for this NMA.
- 6.13 The current submission did not provide any meaningful methodological comparison between the UCB NMA (Armstrong 2022) and the updated Cochrane NMA (Sbidian 2022). Overall, the UCB NMA included a subset of RCTs included in the Cochrane

Public Summary Document - March 2023 PBAC Meeting

review due to the narrower selection criteria (e.g., exclusion of unapproved treatments/doses, without PASI response outcomes, unpublished RCTs, non-English publications) and earlier search date. For the PASI 90 outcome, the Cochrane review included data from approximately 10 additional trials compared to the UCB NMA investigating non-biologics only or unapproved bDMARDs (e.g., sonelokimab, netakimab). Although the Cochrane review did not report which trials were included in the various sensitivity analyses, there would likely be much more consistency in terms of included evidence between the UCB NMA and several of the sensitivity analyses conducted in the Cochrane review (e.g., approved treatments/doses only, RCTs with low risk of bias).

Comparative effectiveness**Short term response**

- 6.14 The PBAC had previously based recommendations for listing of biologics for the treatment of severe CPP on the proportion of patients: i) achieving and ii) maintaining a PASI 75 response ($\geq 75\%$ improvement from baseline in the Psoriasis Area and Severity Index score). This was also consistent with the PBS eligibility criteria for continued treatment with biologics. The main outcome presented in the current submission was PASI 90. Results of PASI 75 are also presented herein.
- 6.15 Table 3 presents the estimated treatment effects in terms of relative risk (95%CI) for BKZ versus the nominated comparators in terms of PASI 75 and PASI 90 response at Week 10-16, by different statistical approach. The results were prior to crossover or where the originally assigned treatment was maintained; this was appropriate as crossover would introduce significant bias to the trial results.

Public Summary Document - March 2023 PBAC Meeting

Table 3: Estimated treatment effects (relative risk, 95%CI) for BKZ versus the nominated comparators in terms of PASI 75 and PASI 90 response at Week 10-16, by different statistical approach

Treatment	PASI 75			PASI 90		
	Direct or indirect evidence ^f	UCB NMA ^f (Armstrong 2022)	Cochrane NMA (Sbidian 2022)	Direct / indirect evidence ^f	UCB NMA ^f (Armstrong 2022)	Cochrane NMA (Sbidian 2022)
BKZ vs comparators						
RIS	ITC: 1.87 (0.83, 4.18)	1.03 (0.98, 1.07)	1.00 (0.89, 1.11) ^a	ITC: 1.50 (0.39, 5.76)	1.15 (1.06, 1.24)	1.05 (0.95, 1.17)
IXE	ITC: 0.91 (0.37, 2.24)	1.04 (0.99, 1.08)	0.99 (0.86, 1.12) ^b	ITC: 0.47 (0.07, 3.04)	1.19 (1.09, 1.30)	1.00 (0.91, 1.11)
GUS	ITC: 1.48 (0.68, 3.19)	1.07 (1.02, 1.12)	1.09 (0.97, 1.22)	ITC: 1.11 (0.33, 3.76)	1.25 (1.14, 1.37)	1.26 (1.16, 1.36)
IFX	ITC: 0.96 (0.34, 2.72)	1.16 (1.09, 1.24)	0.76 (0.50, 1.16) ^c	ITC: 1.09 (0.29, 4.15)	1.55 (1.38, 1.75)	0.60 (0.25, 1.47) ^d
TIL (100)	ITC: 1.62 (0.73, 3.61)	1.46 (1.31, 1.66)	1.27 (1.04, 1.55)	ITC: 1.72 (0.47, 6.33)	2.24 (1.86, 2.76)	1.63 (1.26, 2.10) ^e
ADA	Direct: 1.34 (1.20, 1.49)	1.32 (1.24, 1.40)	1.33 (1.20, 1.48)	Direct: 1.83 (1.54, 2.17)	1.85 (1.67, 2.06)	1.75 (1.59, 1.91)
UST (45 or 90)	Direct: 1.26 (1.14, 1.39)	1.29 (1.22, 1.37)	1.21 (1.10, 1.32)	Direct: 1.71 (1.46, 2.01)	1.86 (1.68, 2.06)	1.60 (1.48, 1.73)
SEC	Direct: 1.02 (0.98, 1.07)	1.10 (1.06, 1.15)	1.05 (0.97, 1.15)	Direct: 1.15 (1.07, 1.24)	1.32 (1.22, 1.44)	1.15 (1.08, 1.23)
ETN	NA	1.81 (1.67, 1.96) ^g	1.69 (1.49, 1.90)	NA	3.58 (3.13, 4.10) ^g	2.84 (2.50, 3.22)

Blue shading indicates data previously seen by the PBAC.

Source: constructed during the evaluation from data in Tables 2.5-6.1-2, Tables A2.5-6.1-2 in Attachment 2, Figure S2(a) and (b), p39 Armstrong 2022 ESM, Table 2-18, p97 of the current submission.

BKZ = bimekizumab; GUS = guselkumab; IFX = infliximab; IXE = ixekizumab; RIS = risankizumab; TIL = tildrakizumab; ITC = indirect treatment comparison; NA = not available; NMA = network meta-analysis.

a reported in publication as RISvBKZ: 1.00 (0.90, 1.12)

b reported in publication as IXEvBKZ: 1.01 (0.89, 1.16)

c reported in publication as IFXvBKZ: 1.32 (0.86, 2.01)

d reported in publication as IFXvBKZ: 1.66 (0.68, 4.03)

e appears to be TIL any dose (results from Papp 2015 included all TIL doses of 5 mg, 25 mg, 100 mg and 200 mg)

f re-expressed as a relative risk versus BKZ for this commentary to be consistent with results across different sources (results reported in Figure S2 of Armstrong 2022).

g Reported results are for ETN 50 mg sc only weekly regimen. Note dose for ETN is either 50mg once weekly or 25mg twice weekly, results were separately reported for these dosage regimens in the UCB NMA but were pooled in the Cochrane NMA.

6.16 The UCB NMA (multinomial model) found BKZ was statistically superior to all comparators for PASI 90 and for most comparators for PASI 75 except for RIS and IXE. In contrast, the updated Cochrane review (Sbidian 2022) found BKZ was statistically superior to ADA, TIL, UST, GUS, ETN and SEC for PASI 90 and statistically superior to ADA, TIL, UST and ETN for PASI 75. The Cochrane review found no difference between BKZ and RIS, IXE and IFX for PASI 90 or PASI 75 and no difference versus GUS and SEC for PASI 75 despite a difference for PASI 90. Overall, the findings of the main analysis in the updated Cochrane review were robust across the different sensitivities presented by the authors.

6.17 For the direct and indirect comparisons, the head-to-head trials showed statistically superior effectiveness of BKZ against ADA, UST and SEC for PASI 90 and against ADA and UST for PASI 75. For the ITCs, the interpretation of the results varied depending on the risk statistic, for PASI 90 although BKZ was statistically superior to RIS, IXE, GUS and TIL using the RD statistic, the differences versus these bDMARDs were no longer significant using the relative risk statistic (and only significant versus TIL on the odds ratio statistic). For PASI 75, although BKZ was statistically superior to RIS and TIL on

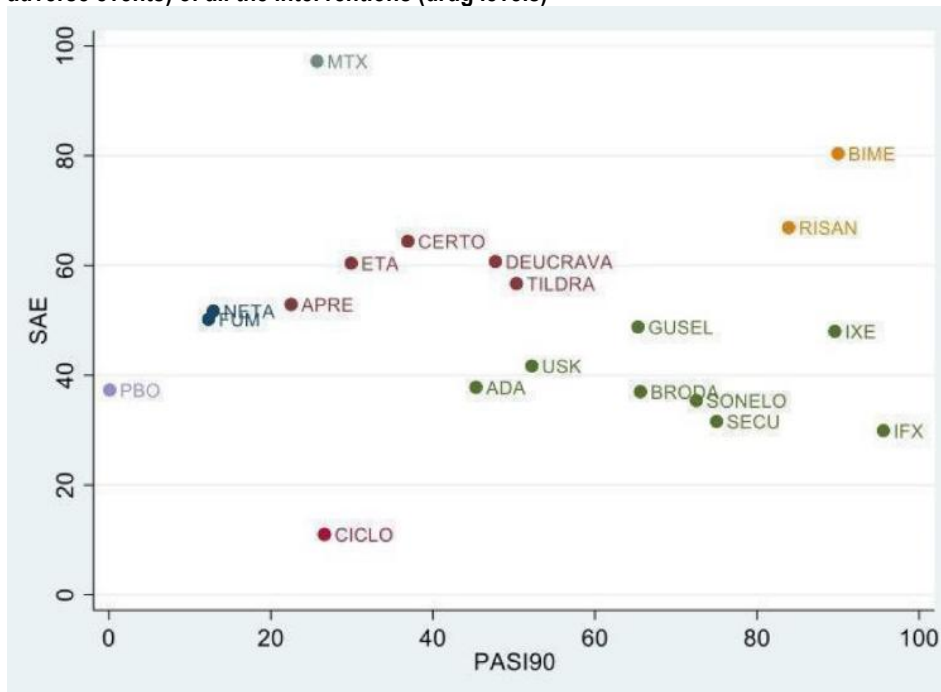
Public Summary Document - March 2023 PBAC Meeting

the OR and RD statistics, there were no significant differences versus any comparators on the RR statistic. The PBAC noted the previous conclusion that BKZ was superior to TIL was based on the odds ratio statistic but there was no significant difference based on the relative risk statistic presented in Table 3. The PBAC noted no direct or indirect comparison was conducted versus ETN; however, it was included in all three NMAs. The PBAC recalled the post market review of biologic medicines for CPP found ETN to have one of the lowest response rates (Figure 1, PMR PSD, April 2018 PBAC meeting).

- 6.18 As illustrated in Table 3, the results for BKZ versus each comparator varied across the comparisons. For example, the UCB NMA found that BKZ was significantly better than IFX for PASI 75 and PASI 90 response whereas the updated Cochrane review (Sbidian 2022) found IFX to be one of the most effective bDMARDs available. The PBAC noted IFX to be one of the more effective treatments for severe CPP; the post market review undertaken in 2018 also found that IXE and IFX were generally more effective than other PBS-listed bDMARDs (paragraphs 7.1 and 7.9, BKZ PSD, March 2022 PBAC meeting).
- 6.19 Compared to the Cochrane review presented in the March 2022 submission (Sbidian 2021), the addition of new BKZ trials in the updated review (Sbidian 2022) substantially tightened the estimated treatment effects for comparisons versus BKZ and several estimates reached statistical significance in favour of BKZ. Although the authors had identified seven biologics as being superior to other treatments for PASI 90 in Sbidian 2021 (BKZ, IFX, IXE, RIS, GUS, SEC and brodalumab), the updated review in 2022 narrowed that list down to four biologics with high degree of certainty (BKZ, IFX, IXE and RIS).
- 6.20 The Pre-Sub-Committee Response (PSCR) stated the Cochrane NMA is not the most suitable source of evidence for decision making in this situation as for all PBS listed molecules, “different dose groups were grouped together in one arm”. For example, infliximab 10 mg/kg is included which is inappropriate in an Australian context where 5 mg/kg is the recommended dose in CPP. The ESC noted only one study included infliximab at a dose of 10 mg/kg and it contributed results for the PASI 75 outcome, not the PASI 90 outcome. Additionally, the ESC noted the findings of the Cochrane NMA were robust across a number of sensitivity analyses, including the analysis that excluded unapproved doses of all treatments.
- 6.21 The PSCR acknowledged the Cochrane review found no difference between BKZ and RIS, IXE and IFX for PASI 90 but noted when both efficacy (PASI 90) and acceptability (SAEs) were combined together in a bivariate ranking plot (Figure 1), BKZ was considered the optimal treatment for chronic CPP (highest performance = best efficacy + best acceptability), appearing in the upper right corner of the plot. The PSCR contends this figure supports BZK having a superior safety profile to IXE and IFX. The ESC noted the authors of the Cochrane review stated that the analysis of safety outcomes was based on a very low number of events with low- to moderate-certainty for all the comparisons, and the findings should be interpreted with caution. The ESC noted in the longer term NMA (Armstrong 2022a) BKZ had (one of) the lowest surface

under the cumulative ranking curves (SUCRA) for safety outcomes (see Figure 2), thus a claim of superior safety was not supported.

Figure 1: Ranking plot representing simultaneously the efficacy (x axis, PASI 90) and the acceptability (y axis, serious adverse events) of all the interventions (drug levels)



Source: Sbidian et al 2022

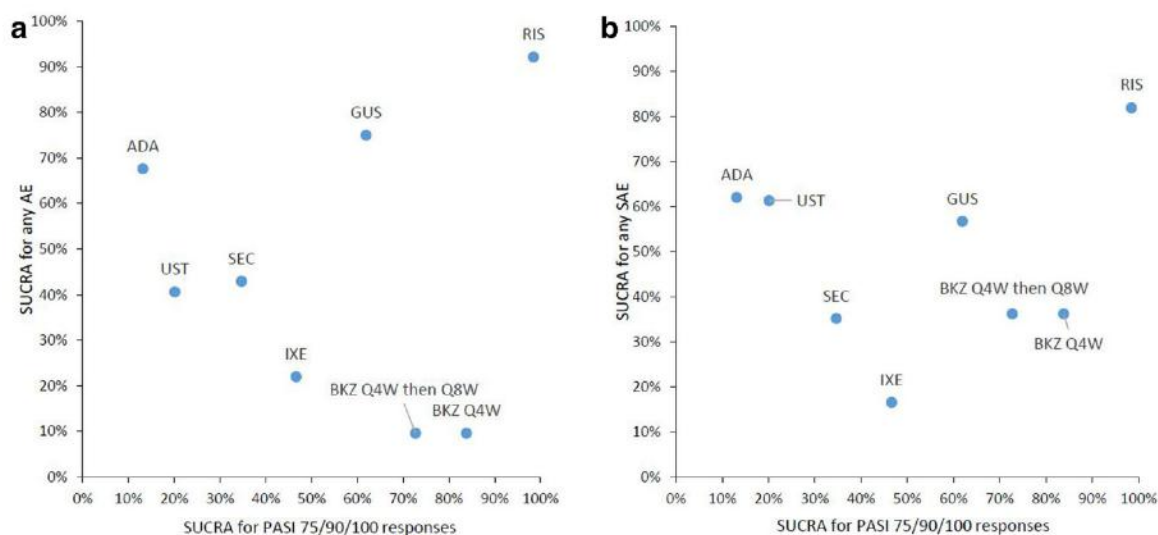
Longer term response

- 6.22 Figure 2 presents the results of the long-term NMA from Armstrong 2022a illustrated as bi-dimensional plots of SUCRA values for PASI response and safety outcomes to assess benefit-risk profiles of each treatment. Treatments with better efficacy and better safety appear in the top right-hand corner of the figure. The analysis found RIS and BKZ had the highest long-term PASI response rates and RIS had the lowest long-

term adverse event rates. Overall, the submission stated RIS was associated with the most favourable long-term benefit-risk profile (top right of figure).

Figure 2: Long-term benefit-risk profiles: Armstrong 2022a.

SUCRA for PASI 75/90/100 responses versus a. SUCRA for any AE. b. SUCRA for any SAE.



Source: Figure 3 of Armstrong 2022a publication.

SUCRA = surface under the cumulative ranking curves; ADA = adalimumab; BKZ = bimekizumab; GUS = guselkumab; IXE = ixekizumab; RIS = Risankizumab; SEC = secukinumab; UST = ustekinumab; QxW = every x weeks.

6.23 Results of pairwise comparison between active treatments in Armstrong 2022a found no statistically significant differences in terms of PASI 75 and PASI 90 between BKZ 'Q4W' versus RIS or GUS, or between BKZ 'Q4W then Q8W' versus RIS, GUS or IXE (Table 4). There was also no statistically significant difference between the two BKZ dose regimens (BKZ Q4W versus BKZ Q4W then Q8W). Given the recommended dose for patients weighing <120 kg is BKZ Q4W to Week 16 then Q8W thereafter, the pairwise comparisons versus BKZ Q4W then Q8W are more relevant for the majority of patients. The PBAC noted TIL and IFX were not included in the long term NMA.

Table 4: Pairwise odds ratio of achieving PASI 75 and PASI 90 (Week 48 to 56), posterior median (95% CrI)

BKZ versus	BKZ Q4W		BKZ Q4W then Q8W	
	PASI 75	PASI 90	PASI 75	PASI 90
RIS	0.75 (0.49, 1.13)	0.77 (0.53, 1.12)	0.66 (0.42, 1.04)	0.69 (0.46, 1.04)
GUS	1.31 (0.87, 1.96)	1.27 (0.88, 1.83)	1.15 (0.75, 1.78)	1.14 (0.77, 1.68)
IXE	1.79 (1.02, 3.09)	1.69 (1.01, 2.79)	1.57 (0.87, 2.82)	1.51 (0.88, 2.57)
SEC	2.39 (1.78, 3.26)	2.21 (1.69, 2.92)	2.10 (1.51, 2.98)	1.97 (1.46, 2.69)
UST	3.93 (2.90, 5.40)	3.54 (2.70, 4.70)	3.46 (2.42, 5.03)	3.15 (2.28, 4.41)
ADA	4.69 (2.93, 7.51)	4.20 (2.70, 6.56)	4.13 (2.53, 6.79)	3.75 (2.37, 5.98)
ETN	8.14 (5.44, 12.26)	7.26 (4.94, 10.74)	7.17 (4.66, 11.13)	6.47 (4.31, 9.82)

Source: Table 2 and Supplemental Table 2 of Armstrong et al 2022a publication.

CrI = credible interval; ADA = adalimumab; BKZ = bimekizumab; GUS = guselkumab; IXE = ixekizumab; RIS = Risankizumab; SEC = secukinumab; UST = ustekinumab; QxW = every x weeks.

6.24 Figure 3 presents new long-term efficacy data (proportion with PASI 90, PASI 100 and DLQI 0/1 response) for patients enrolled in BE SURE who continued treatment in the open-label extension trial BE BRIGHT (Thaci 2022). The results showed that patients

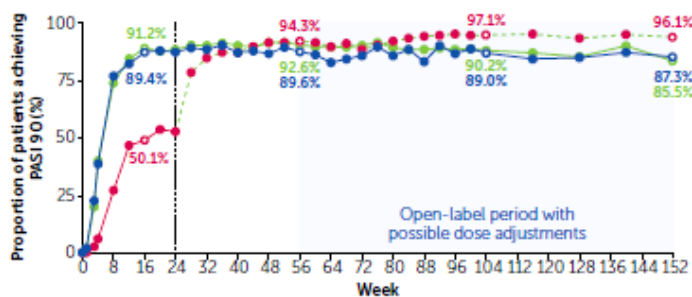
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treated with BKZ (irrespective of the dosing frequency) maintained high levels of treatment response over three years of treatment. Among ADA-randomised patients, there was an increase in proportion meeting the response criteria when patients switched to BKZ after Week 24.

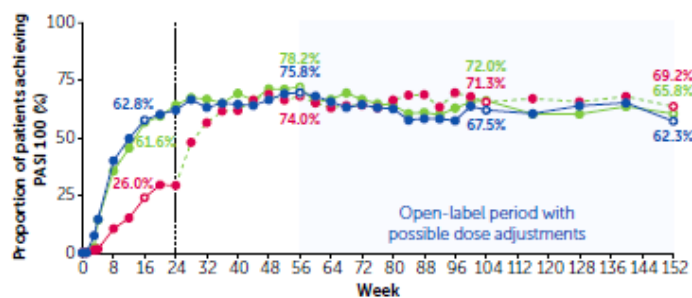
Figure 3: Efficacy responses by randomized treatment group through Week 152 in BE SURE / BE BRIGHT

— BKZ Q4W; N=158 — BKZ Q4W/Q8W; N=161 — ADA/BKZ Q4W; N=159

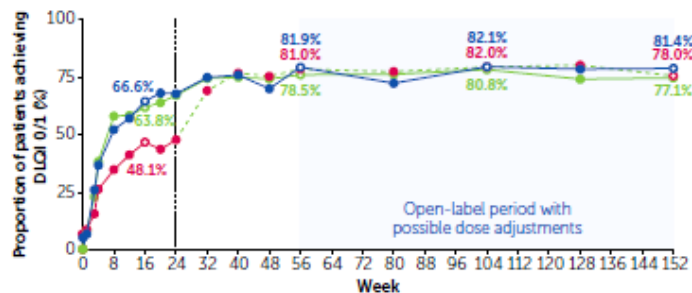
A) PASI 90



B) PASI 100



C) DLQI 0/1



Data are presented for the ITT population by initial randomisation group. The vertical line at Week 24 indicates when patients randomised to ADA switched to BKZ Q4W. Week 104 corresponds to OLE Week 48, and Week 152 to OLE Week 96.

Source: Figure 2-12, p104 of the current submission.

: ADA = adalimumab; BKZ = bimekizumab; DLQI = Dermatology Life Quality Index; Q4W = every 4 weeks; Q8W = every 8 weeks.

BKZ Q4W regimen: Baseline N = 158, Week 56 N = 140, Week 104 N = 129, Week 152 N = 123.

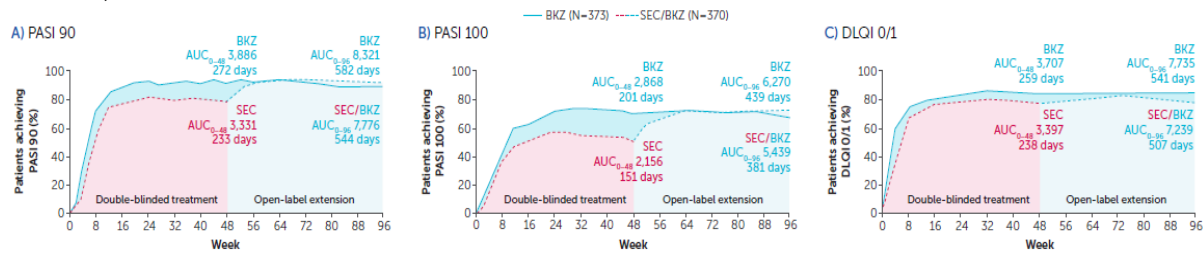
BKZ Q4W/Q8W regimen: Baseline N = 161, Week 56 N = 143, Week 104 N = 126; Week 152 N = 115.

ADA/BKZ Q4W/Q8W regimen: Baseline N = 159, Week 56 N = 133, Week 104 N = 123; Week 152 N = 114.

6.25 Figure 4 and Figure 5 presents new long-term efficacy data from the BE RADIANT open label extension study, reported by Lebwohl 2022 and Kokolakis 2022 respectively.

Public Summary Document - March 2023 PBAC Meeting

Figure 4: Total AUC and cumulative benefit through 48 weeks and 96 weeks for clinical and HRQoL outcomes in BE RADIANT, mNRI[^]



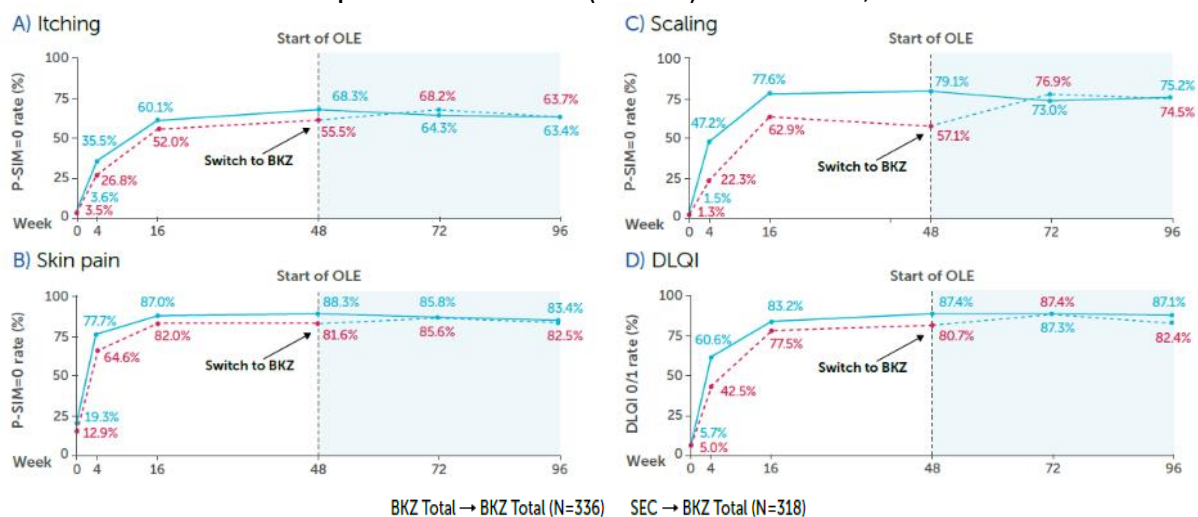
Source: Figure 2-13, p106 of the current submission.

AUC = area under the curve; BKZ = bimekizumab; DLQI = Dermatology Life Quality Index; HRQoL = health-related quality of life; SEC = secukinumab; mNRI=modified non-responder imputation

[^] patients who discontinued due to lack of efficacy were considered non-responders at subsequent timepoints; multiple imputation was used for all other missing data.

BKZ N (baseline) = 373; SEC N (baseline) = 370

Figure 5: Percentage of patients with no symptoms in the itching, skin pain and scaling items on the P-SIM (score 0), and no effect of skin disease on patients life in the DLQI (score 0/1) in BE RADIANT, mNRI[^]



Source: Figure 2-14, p108 of the current submission

OLE=open label extension; BKZ = bimekizumab; DLQI = Dermatology Life Quality Index; SEC = secukinumab; mNRI=modified non-responder imputation; P-SIM=Psoriasis Symptoms and Impacts Measure

[^] patients who discontinued due to lack of efficacy were considered non-responders at subsequent timepoints; multiple imputation was used for all other missing data.

BKZ regimen: Baseline N= 336; Week 48 N = 327; Week 72 N = 318; Week 96 N = 307.

SEC regimen: Baseline N= 318; Week 48 N = 313; Week 72 N = 297; Week 96 N = 287.

6.26 Figure 4 showed that for PASI 90, PASI 100 and DLQI 0/1 responses the estimated number of days with treatment response through to Week 48 was higher with BKZ versus SEC. Among patients randomised to SEC, there was an increase in the proportion of patients meeting the response criteria after Week 48 when patients switched to BKZ, but the cumulative benefit remained lower through to Week 96 compared to patients treated with BKZ straight through.

6.27 Figure 5 showed that a high proportion of patients treated with BKZ in BE RADIANT achieved a score of 0 for itching, skin pain and scaling items on the Psoriasis Symptoms

Public Summary Document - March 2023 PBAC Meeting

and Impacts Measure (P-SIM), or a score of 0/1 on the Dermatology Life Quality Index (DLQI). Patient response in patient reported outcomes was maintained to Week 96.

Subgroup analysis (psoriasis in high impact areas)

- 6.28 The current submission also presented additional follow up data for patients with psoriasis affecting high impact areas, reported in two separate *post-hoc* analyses of patients enrolled in the key head-to-head RCTs by Warren 2022 and Merola 2022. The analyses relied on three outcomes to define patients with regional involvement in high impact areas and complete clearance following treatment:
- modified Nail Psoriasis Severity Index (mNAPSI); The mNAPSI is one of several measures to assess nail involvement in psoriasis (pitting, onycholysis, and crumbling), the score for an individual nail ranging from 0 to 13 (maximum 130, the sum of all scores).
 - scalp Investigators Global Assessment (scalp IGA); A five point scale to assess scalp lesions in terms of redness, thickness and scaliness.
 - palmoplantar Investigators Global Assessment (palmoplantar IGA); A five point scale to assess palmoplantar disease in terms of redness, thickness and scaliness.
- 6.29 The first analysis by Warren 2022 focused on patients with regional involvement of the nails (mNAPSI ≥ 10) or scalp (scalp IGA ≥ 3) enrolled in BE SURE, BE VIVID and BE RADIANT, who were randomised to the active comparator arm and subsequently switched to BKZ. The analysis found that a high proportion of patients with regional involvement of the nails or scalp who did not achieve complete clearance with ADA, SEC or UST subsequently achieved complete clearance after switching to BKZ, and results were maintained over time.
- 6.30 The second analysis by Merola 2022 focused on patients with regional involvement of the nails (mNAPSI ≥ 10), scalp (scalp IGA ≥ 3) or soles/palms (palmoplantar IGA ≥ 3) enrolled in BE SURE and BE RADIANT, who were randomised to BKZ (specifically those treated with BKZ Q4W/Q4W/Q4W or BKZ Q4W/Q8W/Q8W over different trial phases). The analysis found a high proportion of patients achieved complete clearance of the scalp and palmoplantar regions, and complete clearance of the nails increased over the first year reflecting the longer time scales required for nail growth and repair.
- 6.31 Consistent with the follow-up data of the ITT population, the data presented for patients with CPP in a high impact area suggested that patients without an adequate response to other biologics (ADA, UST, SEC) would likely benefit from switching to BKZ and that the benefits would likely be maintained for at least one year. The current submission did not present any data comparing the effectiveness of BKZ versus other biologics at the same time point for patients with CPP in a high impact area. Although not the same population, the proportion with complete nail clearance and complete scalp clearance was similar after 48 weeks of SEC in Warren 2022 (59.3% and 80.5% respectively) and 48 weeks of BKZ in Merola 2022 (54-72%, and 88-89% respectively, depending on the regimen).

Comparative harms

- 6.32 The current submission presented additional safety data from the Periodic Safety Update Report (PSUR), which was unavailable for the March 2022 submission, and the results of a cohort study evaluating the 2 year safety profile of BKZ in patients with moderate to severe CPP (Gordon 2022). Gordon et al. included pooled safety data from phase 2 and phase 3 trials (BE ABLE 1, BE ABLE 2, PS0016, and PS0018, BE VIVID, BE READY, BE SURE, and BE BRIGHT) to include 2 years of study treatment. The PSUR found no new important identified risks for the use of BKZ and the important potential risks include serious hypersensitivity reactions, serious infections, inflammatory bowel disease, major adverse cardiac events and malignancy. The benefit-risk balance of BKZ remained favourable for the use in the psoriasis indication. Gordon et al found no increased risk of AEs with longer duration of BKZ exposure.
- 6.33 From the March 2022 PBAC consideration it was noted that the overall rates of serious and severe treatment emergent adverse events (TEAEs), and discontinuation rates due to TEAEs were low across trials and treatments following induction therapy, with no significant differences observed. The ITCs of BKZ versus RIS, IXE, GUS and TIL, with placebo as a common reference for the safety outcomes of serious adverse events (AEs), severe AEs, and discontinuation due to AEs also showed no significant differences between BKZ and these comparators regarding these outcomes. The NMA for safety outcomes presented in the March 2022 submission comparing BKZ versus RIS, IXE, GUS and TIL showed similar results. The PBAC considered a claim of non-inferior safety compared to all currently PBS-listed bDMARDs was reasonable (paragraph 7.8, BKZ PSD, March 2022 PBAC meeting). New evidence from Armstrong 2022a reported BKZ ranked poorly compared to alternative bDMARDs for any AEs evaluated between Weeks 48 and 56 after baseline (see Figure 1 above).
- 6.34 The PSCR stated that IFX has been associated with important adverse events including reactions (observed with both IV and SC formulations), serious infections and malignancy, including lymphoma. In addition, there can be challenges with IV administration and the development of anti-infliximab antibodies which may result in a lower response rate and dose escalation. The PSCR considered it likely that these safety concerns and administration challenges have contributed to the very low utilisation of IFX in Australia and globally for CPP. The PBAC considered the data presented in the current submission did not support BKZ being of superior safety to IFX.

Benefits/harms

- 6.35 Based on the included direct evidence, BKZ is superior to ADA and UST for PASI 75 and PASI 90, and superior to SEC for PASI 90. For the indirect comparisons including NMAs, the differences in outcomes varied in effect size and interpretation depending on the statistic and analysis and some analyses also did not report absolute differences. The current submission also did not present any new evidence on harms or safety outcomes. For these reasons, the benefits and harms table below is only presented

Public Summary Document - March 2023 PBAC Meeting

for benefits based on the direct evidence. A summary of relative benefits of BKZ versus all comparators from all analyses is presented in Table 3.

Table 5: Summary of comparative benefits (PASI 75, PASI 90) for BKZ versus proposed comparators

Comparison (Trial)	BKZ n/N	Comparator n/N	RR (95% CI)	Event rate/100 patients		RD (95% CI)
				BKZ	Comparator	
PASI 75 at 16 weeks – direct comparisons						
BKZ v ADA (BE SURE)	295/319	110/159	1.34 (1.20, 1.49)	92.5	69.2	0.23 (0.16, 0.31)
BKZ v UST (BE VIVID)	296/321	119/163	1.26 (1.14, 1.39)	92.2	73.0	0.19 (0.12, 0.27)
BKZ v SEC (BE RADIANT)	348/373	337/370	1.02 (0.98, 1.07)	93.3	91.1	0.02 (-0.02, 0.06)
PASI 90 at 16 weeks – direct comparisons						
BKZ v ADA (BE SURE)	275/319	75/159	1.83 (1.54, 2.17)	86.2	47.2	0.39 (0.31, 0.48)
BKZ v UST (BE VIVID)	273/321	81/163	1.71 (1.46, 2.01)	85.0	49.7	0.35 (0.27, 0.43)
BKZ v SEC (BE RADIANT)	319/373	275/370	1.15 (1.07, 1.24)	85.5	74.3	0.11 (0.05, 0.17)

Bold=statistically significant.

Source: Tables 2.5-6.1-2 of the Commentary.

ADA=adalimumab, BKZ=bimekizumab, CI=confidence interval, MA=meta-analysis, OR=odds ratio, PASI=psoriasis area and severity index, PBO=placebo; RD=risk difference; SEC=secukinumab, UST=ustekinumab.

6.36 On the basis of direct evidence presented by the current submission, for every 100 patients treated with BKZ over the initial 16 weeks of treatment in comparison with:

- ADA – Approximately 23 additional patients would achieve PASI 75, and 39 additional patients would achieve PASI 90.
- UST – Approximately 19 additional patients would achieve PASI 75, and 35 additional patients would achieve PASI 90.
- SEC – There were no significant differences in the number of patients achieving PASI 75, and approximately 11 additional patients would achieve PASI 90.

Clinical claim

6.37 Consistent with the March 2022 submission, the current submission described BKZ as superior in terms of effectiveness and non-inferior in terms of safety compared with all current PBS-listed bDMARDs. The PBAC had accepted the claim of non-inferior safety versus all comparators and the claim of superior effectiveness versus ADA, TIL and UST (as measured by PASI 75 and PASI 90). Based on the direct and indirect evidence, the PBAC had considered that the claim of superior effectiveness versus IXE, GUS, SEC and RIS was not supported but a claim of non-inferior effectiveness was reasonably supported (paragraphs 7.1 and 7.8, BKZ PSD, March 2022).

6.38 The current submission argued that the clinical evidence does support the claim of superior effectiveness of BKZ versus all PBS-listed bDMARDs and new evidence presented in the current submission further strengthened this claim:

- Expert opinion presented in the current submission validated the clinical relevance of the PASI 90 (and the PASI 100 outcome in patients with high impact disease).

Public Summary Document - March 2023 PBAC Meeting

- The head-to-head evidence (versus ADA, UST and SEC) and UCB NMA (versus all other comparators) demonstrated that significantly more patients achieved PASI 90 response following BKZ compared to all other PBS-listed bDMARDs.
 - The updated Cochrane review (Sbidian 2022) found that BKZ is positioned as one of the best overall treatments considering both efficacy and tolerability.
 - The new clinical evidence from the open label extension studies demonstrated that the clinical benefit of BKZ was maintained up to 3 years after initial treatment.
 - New clinical evidence for patients with CPP in high impact demonstrated the additional value of BKZ in patients with high impact disease areas.
- 6.39 Overall, the evaluation considered the clinical evidence presented in the March 2022 submission and current submission did not conclusively demonstrate that BKZ is more effective than all other PBS-listed bDMARDs in terms of PASI 75 and PASI 90 response. Although results from three direct trials (versus ADA, UST and SEC) and the UCB NMA (Armstrong 2022) statistically favoured BKZ versus all PBS-listed bDMARDs in terms of PASI 90, this excluded main findings from the new NMAs presented in the current submission as well as results of the ITCs presented in the March 2022 submission but omitted in the current submission. For example, the updated Cochrane review by Sbidian 2022 found no difference in short-term PASI 90 response at Week 10 to 16 between BKZ, IFX, IXE and RIS and the new NMA by Armstrong 2022a found no difference in long-term PASI 90 response at Week 48 to 56 between BKZ, RIS, GUS and IXE (for at least one dose of BKZ). The claim also ignored results for PASI 75, for which the UCB NMA found no difference between BKZ, RIS and IXE, and the updated Cochrane review found no difference between BKZ, GUS, IXE, SEC, RIS, IFX.
- 6.40 The current submission did not discuss the inconsistent conclusions across the different NMAs or provide any clear justification for why the UCB NMA would provide more reliable estimates than the updated Cochrane review. Although the Cochrane review included more trials and comparators for its main analysis than the UCB NMA, the findings of the Cochrane review were also robust across multiple sensitivity analyses (which likely included similar trials to the UCB NMA, as discussed above). This suggests that the differences in findings between the two NMAs may also be due to differences in methodologies (i.e., Bayesian versus frequentist frameworks) rather than the included evidence. Without further information, the inconsistent findings across different approaches results in uncertainty around the interpretation of the indirect evidence, in particular where efficacy conclusions were based on small statistical differences.
- 6.41 Based on the results for PASI 90, the evaluation considered there may be sufficient evidence across the totality of the clinical evidence to support the claim of superior effectiveness between BKZ and some treatments (e.g., ADA, TIL, UST, SEC and potentially GUS) but not all treatments (e.g., RIS, IXE and IFX). Based on results for PASI 75, the clinical evidence presented in the current submission generally supports

Public Summary Document - March 2023 PBAC Meeting

the claim of superior effectiveness for BKZ versus ADA, TIL and UST (consistent with the PBAC's conclusion in March 2022).

- 6.42 The ESC considered that BKZ was likely non-inferior to at least RIS, IXE, IFX at 10-16 week and non-inferior to RIS, IXE and GUS (no data for IFX) at 48-56 weeks.
- 6.43 The pre-PBAC response stated the sponsor does not accept the proposition that BKZ is equivalent to IFX on either an efficacy or safety basis. The pre-PBAC response outlined some of the shortcomings with the Cochrane NMA that may impact its reliability in terms of conclusions regarding the comparative effectiveness and safety of IFX. The PBAC acknowledged the pre-PBAC response but considered that, overall, the totality of clinical evidence did not support a claim of superior effectiveness or safety for BKZ versus IFX.
- 6.44 The PBAC considered that, overall, the clinical evidence presented supported the claim that BKZ is superior in terms of effectiveness to ADA, UST and ETN. The PBAC considered a claim of non-inferior effectiveness for BKZ vs IXE, TIL, GUS, SEC, IFX and RIS was reasonably supported. Consistent with its previous consideration, the PBAC considered the claim of non-inferiority in terms of safety compared with all current PBS-listed bDMARDs was reasonable.

Economic analysis

- 6.45 The ESC considered the updated cost-utility analysis presented in the current submission was not informative given the clinical evidence presented in the current submission did not support the clinical claim that BKZ was superior to all PBS-listed bDMARDs.
- 6.46 The current submission presented an updated cost-utility analysis using the individual patient level simulation model presented in the March 2022 submission. The structure of the model remained unchanged but key model parameters were updated in line with the March 2022 ESC advice. Although the PBAC had subsequently considered the economic model was largely uninformative for decision making because the clinical claim of superior effectiveness versus all PBS-listed bDMARDs had not been accepted, the ESC had recommended a respecified base case. This included using (i) effect estimates from the UCB NMA, (ii) no difference in time to quality of life benefit between treatments, (iii) utilities sourced from the BKZ trials, and (iv) a specific sequence of treatments in the comparator arm (paragraphs 6.78, 6.80 and 7.9, BKZ PSD, March 2022 PBAC meeting). Table 6 summarises the key model parameters and assumptions in the March 2022 submission and current submission. The updated analysis in the current submission included all of the model parameters recommended by ESC as well as updated drug costs (estimated effective rather than published prices) and updated health care resource costs (inflated from 2021 to 2023 values).

Public Summary Document - March 2023 PBAC Meeting

Table 6: Summary of model structure, key inputs and rationale

Table 6. Summary of model structure, key inputs and rationale				
Component	March 2022 submission and ESC/PBAC comments		March 2023 current submission	
Treatments	Scenario with PBS listing of BKZ vs scenario without PBS listing of BKZ			
Time horizon	7 years in the model base case versus 16 weeks of comparative data in the initial treatment period in the key trials			
Outcomes	Quality-adjusted life years (QALYs)			
Methods used to generate results	Microsimulation model (simulating individual patient outcomes) which enabled the model to: (i) remember the number of bDMARDs a patient had used in the treatment cycle; (ii) memory of prior treatments, which bDMARD had been used (to avoid re-use of same bDMARD); and (iii) count the 5-year bDMARD free period mandated in the PBS criteria.			
Health states	6 states based on PASI response: Baseline, < PASI 50, 50 ≤ PASI < 75, 75 ≤ PASI < 90, 90 ≤ PASI < 100, PASI 100. Patients can also move to the death state during any cycle based on background mortality.			
Cycle length	2 weeks			
Baseline characteristics	Pooled BKZ phase 3 trials (DLQI ≥ 10)			
	Starting age	44.3 years		
	% females	36.3%		
Transition probabilities	<u>PASI Response</u> • BKZ based on BE VIVID (base case), BE SURE, BE RADIANT and NMA in sensitivity. • ADA (BE SURE), SEC (BE RADIANT) and UST (BE VIVID) in base case, and NMA in sensitivity analyses. • Other bDMARDs: NMA. Source data for BKZ were from trial subgroups with baseline DLQI≥10 and the Bayesian NMA was for patients with moderate to severe CPP, but the requested PBS population was severe CPP (PASI≥15). The model also assumed bDMARD treatments to be equally efficacious regardless of the order administered or a patient's prior biologic experience. The ESC noted the effect estimates used in the economic model were the most favourable to BKZ across all of the available data sources and considered this was likely to bias in favour of BKZ. Overall, the ESC considered it would be appropriate to use the results from the NMA as the primary source of PASI response estimates for the model, as it was likely to provide the most consistent effect estimates across all bDMARDs (paragraph 6.55, BKZ PSD, March 2022 PBAC meeting).		PASI response based on NMA for BKZ and comparators. (ESC's respecified base case)	
	Discontinuation during maintenance therapy: NostraData 2021. While data were provided by the sponsor during evaluation, there were no explanations accompanying the data so it remained unclear how discontinuation rates were derived and why it was preferred over PBS data. Discontinuation due to lack of efficacy: Assumption.			
	Probability of all cause death: Australian life tables			
	Time to response: 8-24 weeks; based on when the maximum proportion of PASI 75 responders were reported in the direct RCTs (BKZ, ADA, UST, SEC), trials for other bDMARDs, and NMA for BSC. The assumption that BKZ patients were assumed to experience a QoL benefit earlier at Week 8, compared to those treated with other bDMARDs, based on PASI 75 response, likely favoured BKZ (paragraph 6.56, BKZ PSD, March 2022 PBAC Meeting). The ESC considered that, in the absence of an appropriate methodology, it was appropriate to assume no difference in time to response in the base case (paragraph 6.59, BKZ PSD, March 2022 PBAC meeting).		Time to QoL benefit was assumed to be the same for all bDMARDs at 16 weeks. (ESC's respecified base case)	

Public Summary Document - March 2023 PBAC Meeting

Component	March 2022 submission and ESC/PBAC comments	March 2023 current submission																																										
	bDMARD sequence: Treatment selection was based on a random number between 0 and 1. The ESC noted sensitivity analyses found the ICER to be sensitive to the assumed market share and the resulting order in which bDMARDs are used on the PBS, and recommended user-defined order of treatment (RIS, UST, SEC, ADA) should be considered (paragraphs 6.64 and 6.78, BKZ PSD, March 2022 PBAC meeting). Timing of PBS continuation criteria: 16-24 weeks, based on PBS continuation criteria.	User-defined order of treatment (RIS, UST, SEC, ADA). Assumed RIS will be used first (fast growth on PBS) and then trying a different mechanism of action when treatment fails. (ESC's respecified base case)																																										
Extrapolation method	The model assumed no waning of response to any bDMARDs in second or third-line use. In the base case, it was assumed that half of the discontinuations in maintenance were due to treatment failure (the rest were assumed to due to intolerance).																																											
Health related quality of life	Health state utility was based on EQ-5D-3L values from BKZ and certolizumab data. <table><thead><tr><th>Health state</th><th>Utility weight</th></tr></thead><tbody><tr><td>Baseline</td><td>0.7235</td></tr><tr><td>PASI < 50</td><td>0.7486</td></tr><tr><td>50 ≤ PASI < 75</td><td>0.8436</td></tr><tr><td>75 ≤ PASI < 90</td><td>0.872</td></tr><tr><td>90 ≤ PASI < 100</td><td>0.8996</td></tr><tr><td>PASI 100</td><td>0.9192</td></tr></tbody></table> The ESC noted the ICER was sensitive to alternative utility values and that the utility values in the PASI 90 and PASI 100 health states appeared to be higher than that of the general population and was therefore unsure if the values in these health states were plausible. The ESC recommended the BKZ trials as the source of utilities (paragraphs 6.67, 6.68 and 6.78, BKZ PSD, March 2022 PBAC meeting).	Health state	Utility weight	Baseline	0.7235	PASI < 50	0.7486	50 ≤ PASI < 75	0.8436	75 ≤ PASI < 90	0.872	90 ≤ PASI < 100	0.8996	PASI 100	0.9192	Health state utility was based on EQ-5D-3L values from BKZ data. <table><thead><tr><th>Health state</th><th>Utility weight</th></tr></thead><tbody><tr><td>Baseline</td><td>0.7826</td></tr><tr><td>PASI < 50</td><td>0.7865</td></tr><tr><td>50 ≤ PASI < 75</td><td>0.8807</td></tr><tr><td>75 ≤ PASI < 90</td><td>0.8953</td></tr><tr><td>90 ≤ PASI < 100</td><td>0.9128</td></tr><tr><td>PASI 100</td><td>0.9318</td></tr></tbody></table> (ESC's respecified base case)	Health state	Utility weight	Baseline	0.7826	PASI < 50	0.7865	50 ≤ PASI < 75	0.8807	75 ≤ PASI < 90	0.8953	90 ≤ PASI < 100	0.9128	PASI 100	0.9318														
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Costs	Prices of bDMARDs: Requested published price for BKZ of \$3,908.88 DPMQ. Published prices used for other bDMARDs. <table><thead><tr><th></th><th>DPMQ</th></tr></thead><tbody><tr><td>UST</td><td>\$3,943.23</td></tr><tr><td>SEC</td><td>\$1,403.68</td></tr><tr><td>IXE</td><td>\$3,421.22</td></tr><tr><td>GUS</td><td>\$3,795.84</td></tr><tr><td>TIL</td><td>\$3,271.27</td></tr><tr><td>RIS</td><td>\$5,400.51</td></tr><tr><td>ADA</td><td>\$885.50</td></tr><tr><td>ETN</td><td>\$1,050.14</td></tr><tr><td>IFX IV</td><td>\$320.71</td></tr></tbody></table>		DPMQ	UST	\$3,943.23	SEC	\$1,403.68	IXE	\$3,421.22	GUS	\$3,795.84	TIL	\$3,271.27	RIS	\$5,400.51	ADA	\$885.50	ETN	\$1,050.14	IFX IV	\$320.71	Prices of bDMARDs: Requested effective price for BKZ of \$ [REDACTED] DPMQ. 'Estimated' effective prices used for other bDMARDs. <table><thead><tr><th></th><th>DPMQ^a(\$)</th></tr></thead><tbody><tr><td>UST</td><td>[REDACTED]</td></tr><tr><td>SEC</td><td>[REDACTED]</td></tr><tr><td>IXE</td><td>[REDACTED]</td></tr><tr><td>GUS</td><td>[REDACTED]</td></tr><tr><td>TIL</td><td>[REDACTED]</td></tr><tr><td>RIS</td><td>[REDACTED]</td></tr><tr><td>ADA</td><td>[REDACTED]</td></tr><tr><td>ETN</td><td>[REDACTED]</td></tr><tr><td>IFX IV</td><td>[REDACTED]</td></tr><tr><td>IFX SC</td><td>[REDACTED]</td></tr></tbody></table>		DPMQ ^a (\$)	UST	[REDACTED]	SEC	[REDACTED]	IXE	[REDACTED]	GUS	[REDACTED]	TIL	[REDACTED]	RIS	[REDACTED]	ADA	[REDACTED]	ETN	[REDACTED]	IFX IV	[REDACTED]	IFX SC	[REDACTED]
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ETN	[REDACTED]																																											
IFX IV	[REDACTED]																																											
IFX SC	[REDACTED]																																											
Healthcare resource use: Dupilumab March 2020 model for severe atopic dermatitis The ESC recalled it had considered some elements of this cost may not be plausible (paragraph 6.45, dupilumab PSD, March 2020) and, in particular, the magnitude of phototherapy costs was not reasonable (paragraph 7.15, dupilumab PSD, March 2020 PBAC meeting). Additionally, the ESC considered it was highly uncertain whether health care resource use and costs would be the same for CPP as for atopic dermatitis and noted that while the same range of services are likely to be needed for both sets of patients, the frequency of use may differ (paraqraph 6.76, BKZ PSD, March 2022 PBAC meeting).																																												

Public Summary Document - March 2023 PBAC Meeting

Component	March 2022 submission and ESC/PBAC comments	March 2023 current submission
	Healthcare costs inflated to 2021 prices.	Healthcare costs inflated to 2023 prices.

Blue shading indicates data previously seen by the PBAC.

Source: adapted during the evaluation based on Table 3-1, pp266-267 of the March 2022 submission.

ADA = adalimumab; BKZ = bimekizumab; RIS = risankizumab; SEC = secukinumab; UST = ustekinumab; bDMARD = biologic disease-modifying anti-rheumatic drug; CPP = chronic plaque psoriasis; DLQI = Dermatology Life Quality Index; NMA = network meta-analysis; PASI=psoriasis area and severity index.

^a In the base case assuming a user-defined order of treatment, only the prices of RIS, UST, SEC and ADA were used.

6.47 Table 7 presents the results of the economic evaluation and the incremental impact of changing each parameter on the estimated base case (and re-specified base case) in the March 2022 submission.

Public Summary Document - March 2023 PBAC Meeting

Table 7: Results of the stepped economic evaluation showing model changes (current submission versus March 2022 submission) and the effect of each amendment on the ICER

Step and component	With BKZ	Without BKZ	Increment
Step 1: March 2022 submission base case			
Costs	\$█	\$173,234	\$█
QALY	5.388	5.248	0.140
Incremental cost/extra QALY gained			\$█ ¹
Step 2: March 2022 submission corrected base case^a			
Costs	\$█	\$150,708	\$█
QALY	5.388	5.248	0.140
Incremental cost/extra QALY gained (corrected base case)			\$█ ²
Step 3: PASI response rates use NMA efficacy for all bDMARDs including BKZ			
Costs	\$█	\$150,743	\$█
LYG	5.364	5.238	0.126
Incremental cost/extra LYG gained			\$█ ²
Step 4: Time to QoL benefit the same for all bDMARDs at 16 weeks			
Costs	\$█	\$150,546	\$█
LYG	5.339	5.243	0.097
Incremental cost/extra LYG gained			\$█ ³
Step 5: User-defined order of treatment (RIS, UST, SEC, ADA)			
Costs	\$█	\$161,215	\$█
LYG	5.361	5.298	0.062
Incremental cost/extra LYG gained			\$█ ³
Step 6: BKZ trials as source for utilities			
Costs	\$█	\$161,215	\$█
QALYs	5.491	5.440	0.051
Incremental cost/extra QALY gained (multivariate sensitivity respecified base case)			\$█ ⁴
Step 7: Use effective prices (proposed for BKZ; estimated for other bDMARDs)			
Costs	\$█	\$95,105	\$█
QALYs	5.491	5.440	0.051
Incremental cost/extra QALY gained			\$█ ⁵
Step 8: Indexing of healthcare resource use costs increased to 3 years (base case in current submission)			
Costs	\$█	\$96,677 ^b	\$█
QALYs	5.491	5.440	0.051
Incremental cost/extra QALY gained			\$█ ⁶

Blue shading indicates data previously seen by the PBAC.

Source: Table 3-3, p269 of the current submission. *Italics* indicate results calculated during the evaluation.

^a IXE DPMQ corrected from \$6,842.22 to \$3,421.22, ADA DPMQ corrected from \$1,770.99 to \$885.50, ETN DPMQ corrected from \$4,200.56 to \$1,050.14.

^b A small discrepancy in costs for the comparator arm was found. When working step-wise using the March 2022 corrected base case model and adjusting for effective prices and indexing of healthcare costs, the costs for the comparator arm was \$96,685 compared to \$96,677 from running the model submitted with the current submission.

The redacted values correspond to the following ranges:

¹ \$55,000 to < \$75,000

² \$155,000 to < \$255,000

³ \$255,000 to < \$355,000

⁴ \$355,000 to < \$455,000

⁵ \$45,000 to < \$55,000

6.48 ⁶ \$35,000 to < \$45,000 The current submission stated that the ESC's respecified base case still justified a price advantage for BKZ at an acceptable ICER threshold, even though some of the updated assumptions bias against BKZ. The table illustrates that use of estimated effective prices rather than published prices in the model was the main driver in reducing the respecified base case ICER from

Public Summary Document - March 2023 PBAC Meeting

\$355,000 to < \$455,000/QALY in the March 2022 submission to \$35,000 to < \$45,000/QALY in the current submission.

- 6.49 In the March 2022 consideration, the ESC also noted that the assumed health care resource use and costs were highly uncertain and had noted a sensitivity analysis assuming a 50% reduction in health care resource costs (paragraph 6.78, BKZ PSD, March 2022 PBAC meeting). The assumed health care resource use remained unchanged in the current submission, but the unit costs were inflated from 2021 to 2023 prices. Under the current model specifications, a 50% reduction in health care resource costs increases the ICER by 49% from \$35,000 to < \$45,000/QALY to \$55,000 to < \$75,000 /QALY.
- 6.50 Table 8 summarises the drug costs over the first two years for all current PBS-listed treatments based on the estimated effective prices assumed in the economic analysis, and the corresponding AEMP for BKZ assuming a cost minimisation approach to each treatment. The calculations for the cost-minimisation approach are based on drug costs only with the exception of IFX SC and IFX IV regimens, which include administration costs for IV doses (costed using MBS item 14245, see footnotes). The analysis showed that the requested effective AEMP for BKZ in the current submission is 36% higher than ADA and 8% higher than the most costly treatments on the PBS (RIS, GUS and TIL).

Public Summary Document - March 2023 PBAC Meeting

Table 8: Two-year drug costs of BKZ versus comparators based on effective AEMPs estimated in current submission – ranked by highest to lowest total 2 year cost

Drug	Dosing Regimen	Effective AEMPs (estimated by current submission)	Number of injections or vials	Total 2-year drug cost	BKZ AEMP based on a cost-minimised to each comparator
BKZ	320 mg SC injections (given as 2 SC injections of 160 mg each) at Weeks 0, 4, 8, 12, 16 and Q8W thereafter	\$█ (requested)	15	\$█	-
RIS	150 mg SC injection (2 injections of 75 mg) at Weeks 0, 4 and Q12W thereafter	\$█*	9.33	\$█	\$█
GUS	100 mg SC injection at Weeks 0, 4 and Q8W thereafter	\$█*	13.5	\$█	\$█
TIL	100 mg SC injection at Weeks 0, 4 and Q12W thereafter ^l	\$█ ^b	9.33	\$█	\$█
SEC	300 mg SC injection (2 injections of 150 mg) at Weeks 0,1,2,3,4 then 300 mg monthly	\$█*	29	\$█	\$█
IXE	160 mg SC injection (2 injections of 80 mg) at Week 0, then 80 mg Q2W from Weeks 2 to 12 and Q4W thereafter	\$█*	15	\$█	\$█
IFX SC	120 mg SC injection Q2W (maintenance dosing assumed to start at Week 6, Week 0 and 2 doses assumed to be IFX IV)	\$█ ^c	49 SC injections; 8.96 IV vials (2 doses x 4.48 vials per dose [^])	Drug cost only: \$█; Drug + IV admin. cost: \$█ ^d	Drug cost only: \$█; Drug + IV admin. cost: \$█ ^d
UST [#]	45 mg (weight ≤ 100 kg) or 90 mg (weight > 100 kg) SC injection at Weeks 0, 4 and Q12W thereafter	\$█ ^b	9.33	\$█ [#]	\$█
ETN	50 mg SC injection once weekly (or 25 mg twice weekly)*	\$█ ^c	26.25	\$█	\$█
IFX IV	5 mg/kg IV infusion at Weeks 0,2,6, then Q8W thereafter	\$█ ^c	63.83 IV vials (14.25 doses x 4.48 vials per dose [^])	Drug cost only: \$█; Drug + IV admin. cost: \$█ ^d	Drug cost only: \$█; Drug + IV admin. cost: \$█ ^d
ADA	80 mg SC injection (2 injections of 40 mg) at Week 0, then 40 mg Q2W starting at Week 1	\$█ ^a	26.75	\$█	\$█

Source: constructed during the evaluation based on Figure 0-1, p18 and Figure 3-1, p267 of the current submission.

ADA = adalimumab; BKZ = bimekizumab; ETN = etanercept; GUS = guselkumab; IFX = infliximab; IXE = ixekizumab; RIS = risankizumab; SEC = secukinumab; TIL = tildrakizumab; UST = ustekinumab.

Assuming all patients are on UST 45 mg.

* Imputed by the current submission based on time of listing and expected comparator at that time.

[^] The model in the current submission assumed that an average IFX patient weighed 89.587 kg based on BKZ studies. At a dose of 5 mg/kg, an average IFX patient was assumed to require 4.48 IFX IV 100 mg vials per dose. This number of vials per dose was costed assuming no wastage.

^a ADA: CPP indication specific price from DOHA (April 2022). Published ADA prices were not indication specific. An indication specific discount of 28.5% was applied by the current submission to derive the effective price.

^b UST and TIL: CPP indication specific price obtained during Cimzia CPP pricing negotiations (2020) and applying anniversary price reductions where appropriate.

^c ETN and IFX (F2 products): The current submission stated that published prices from the October 2022 PBS pricing have been used. The ETN price has been reduced to account for indication specific pricing.

^d Including IV administration costs for IFX IV (in calculating cost minimised price for BKZ), as done in the cost minimisation approach of IFX SC versus IFX IV in the IFX SC submission (Table 7, IFX SC PSD, November 2020 PBAC Meeting). Assumed the cost of MBS item number 14245 100% rebate (\$103.55) for each IFX IV dose. The PBAC has previously accepted MBS item number 14245 as an appropriate unit cost for IV infusion up to 2 hours (paragraph 5.7 - table 1, tocilizumab PSD, March 2019 PBAC meeting).

6.51 The PSCR stated that across the totality of evidence, whilst Armstrong 2022 supports a clinical claim of superior effectiveness of BKZ versus all PBS-listed bDMARDs, it is acknowledged that the Cochrane review concluded that BKZ and RIS have the most optimal benefit-risk profiles, excluding IFX and IXE from this grouping on the grounds of their inferior safety profiles. As such, the PSCR stated it may be appropriate to

Public Summary Document - March 2023 PBAC Meeting

consider RIS the most relevant lowest cost alternative in the context of a PBAC recommendation. The PSCR stated the sponsor would be willing to accept the RIS price for BKZ. The ESC noted that the authors of the Cochrane NMA had lower confidence in the reported safety outcomes, and that in the longer term NMA (Armstrong 2022a) BKZ had (one of) the lowest SUCRA scores for all three safety outcomes. The ESC considered any claim that BKZ was of superior safety compared to IXE and IFX was not supported by this data.

Drug cost/patient: \$ [REDACTED] (first two years)

- 6.52 Using the proposed effective DPMQ of \$ [REDACTED] per pack of two 160 mg injections, and assuming 15 BKZ packs per patient over the first two years (including both induction and the maintenance treatment phases), the drug cost of BKZ was estimated to be \$ [REDACTED] (over the first two years of treatment). This compares to an estimated two-year cost of \$ [REDACTED] in the March 2022 submission, based on the requested published DPMQ of \$ [REDACTED].

Estimated PBS usage & financial implications

- 6.53 This current submission was not considered by DUSC. The current submission presented updated estimates for the utilisation and financial impact of the requested listing based on the market share approach presented in the March 2022 submission with changes to the following parameters:
- Drug costs for BKZ and comparators (estimated effective rather than published prices).
 - Estimates of the current bDMARD market size, market shares and average co-payments (updated from PBS statistics for the 12 months ending August 2022).
 - Correction of cross-referencing errors identified in the March 2022 evaluation.
- 6.54 Table 9 summarises the key inputs in the financial estimates.

Public Summary Document - March 2023 PBAC Meeting

Table 9: Key inputs for financial estimates

Data	March 2022 submission			Current submission			Source	Comment
Market size and share								
Packs for bDMARDs	Yr 0 (2021):			Yr 0 (2022):			PBS/RPBS prescription data for 12 months period from Sept. 2021 to Aug. 2022 (updated from Sept. 2020 to Aug. 2021).	Reasonable. The current submission acknowledged that inclusion of IFX SC may modify the financial impact, but expected this to be minor.
	UST	11,725		UST	10,935			
	SEC	18,857		SEC	19,931			
	IXE	8,439		IXE	9,597			
	GUS	16,521		GUS	20,802			
	TIL	3,756		TIL	4,767			
	RIS	5,767		RIS	9,755			
	ADA	9,929		ADA	8,963			
	ETN	5,628		ETN	3,523			
IFX IV was excluded given low market share (2%).			IFX IV was excluded given low market share (2%).					
Market growth (per annum)		Group1	Group2	No change.			PBS trends based on PBS data from Jan 2013 to Aug 2021	May not be reasonable to split the market into two groups of drugs given PBS data shows differences in rates of growth for different bDMARDs (paragraph 6.82, BKZ PSD, March 2022 PBAC Meeting).
	Yr0	10%	-1%					
	Yr1	7%	-1%					
	Yr2	6%	-1%					
	Yr3	5%	-1%					
	Yr4	4%	-1%					
	Yr5	3.5%	-1%					
	Group1: SEC, IXE, GUS, TIL, RIS Group2: ETN, ADA, UST							
Treatment utilisation								
BKZ market share (uptake)	Y1: 7.5% Y2: 15% Y3: 20% Y4: 25% Y5: 30% Y6: 35% BKZ was assumed to take market share from listed bDMARDs at the same rate			No change.			Assumption.	May not be reasonable. It was noted in the March 2022 submission that BKZ may be more likely to substitute products with a similar mechanism of action (paragraph 6.82, BKZ PSD, March 2022 PBAC Meeting).
BKZ pack equivalence (substitution rate)	BKZ substitution	Init	Cont	No change.			Number of packs supplied for initial and continuing treatment for BKZ relative to comparator	The number of packs estimated to be supplied for SEC initial treatment could not be verified
	UST	1.67	1.5					
	SEC	1.53	0.5					
	IXE	1.11	1.0					
	GUS	1.67	1.0					
	TIL	1.67	1.5					
	RIS	1.67	1.5					
	ADA	1.0	0.5					
	ETN	1.25	0.5					
Costs								
BKZ and comparators	BKZ	\$3,908.88		BKZ	\$		Requested effective DPMQ for BKZ and estimated effective DPMQs for comparators (updated from published prices in March 2022).	The current submission noted that estimated effective prices of ADA and ETN used in the financial estimates are higher than the prices used in the economic analysis, because they do not account for the indication specific discount.
	UST	\$3,943.23		UST	\$			
	SEC	\$1,403.68		SEC	\$			
	IXE	\$3,421.22		IXE	\$			
	GUS	\$3,795.84		GUS	\$			
	TIL	\$3,271.27		TIL	\$			
	RIS	\$5,400.51		RIS	\$			
	ADA	\$885.50		ADA	\$			
	ETN	\$1,050.14		ETN	\$			

Public Summary Document - March 2023 PBAC Meeting

Data	March 2022 submission	Current submission	Source	Comment
				The estimated effective price for SEC also differed slightly.

Source: p272 of the current submission; Section 4 spreadsheet

ADA = adalimumab; BSC = best supportive care; BKZ = bimekizumab; ETN = etanercept; GUS = guselkumab; IFX = infliximab; IXE = ixekizumab; RIS = risankizumab; SEC = secukinumab; TIL = tildrakizumab; UST = ustekinumab.

6.55 Table 10 presents the estimated use and financial implications of BKZ listing.

Table 10: Estimated use and financial implications (using effective prices)

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of scripts dispensed	1	6	6	8	8	13
	1	6	8	8	13	13
Estimated financial implications of BKZ						
Cost to PBS/RPBS less copayments	\$2	\$7	\$9	\$11	\$14	\$14
	3	2	10	12	7	15
Estimated financial implications for UST, SEC, IXE, GUS, TIL, RIS, ADA, ETN						
Cost to PBS/RPBS less copayments ^a	4	4	4	4	4	4
	4	4	4	4	4	4
Net financial implications						
Net cost to PBS/RPBS/MBS ^a	\$5	\$2	\$2	\$2	\$2	\$10
	5	5	5	5	5	5

Blue shading indicates data previously seen by the PBAC.

Source: '3c. Impact – proposed (eff)' worksheet and '5. Impact – net' worksheet of the model submitted with the current submission.

^a An error in the model submitted with the current submission in calculating the wholesale markup for SEC was corrected in the '4c. Impact – affected (eff)' worksheet, cell E302.

The redacted values correspond to the following ranges:

¹ 5,000 to < 10,000

² \$20 million to < \$30 million

³ \$10 million to < \$20 million

⁴ Net cost saving

⁵ \$0 to < \$10 million

⁶ 10,000 to < 20,000

⁷ \$50 million to < \$60 million

⁸ 20,000 to < 30,000

⁹ \$70 million to < \$80 million

¹⁰ \$30 million to < \$40 million

¹¹ \$90 million to < \$100 million

¹² \$40 million to < \$50 million

¹³ 30,000 to < 40,000

¹⁴ \$100 million to < \$200 million

¹⁵ \$60 million to < \$70 million

6.56 The total net cost to the PBS/RPBS of listing BKZ was estimated to be \$4.0 million in Year 6 (compared to \$31.7m in the March 2022 submission), and a total of \$20.4 million in the first 6 years of listing (compared to \$128.9m in the March 2022 submission). Compared to the March 2022, the reduction in the estimated net cost to

Public Summary Document - March 2023 PBAC Meeting

the PBS/RPBS for the proposed listing of BKZ was driven almost entirely by the use of the estimated effective prices in the current submission rather than published prices.

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

7 PBAC Outcome

- 7.1 The PBAC recommended the Authority Required listing of bimekizumab (BKZ) for the treatment of severe chronic plaque psoriasis (CPP). The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of BKZ would be acceptable if it were cost minimised to the least costly alternative therapy of infliximab (IFX), guselkumab (GUS), ixekizumab (IXE), risankizumab (RIS), tildrakizumab (TIL) and secukinumab (SEC). The PBAC considered there is sufficient evidence to conclude that BKZ provides, for some patients, a significant improvement in efficacy compared to adalimumab (ADA), etanercept (ETN) and ustekinumab (UST).
- 7.2 The PBAC recalled that BKZ was recommended at the March 2022 PBAC meeting on the basis of cost minimisation to the least costly alternative bDMARD for severe CPP, consistent with previous recommendations for GUS, RIS and IXE. Compared to the submission considered in March 2022, the current submission:
 - Requested a lower price (\$23,923 vs \$58,633 per patient over 2 years);
 - Presented additional clinical data (one additional short term NMA, one long term NMA, subgroup analyses, data with longer term follow-up);
 - Provided a comparison vs IFX; and
 - Presented a cost minimisation approach (excluding ADA, TIL and UST) as an alternative to the cost utility analysis, in the event the PBAC not accept the superiority claim versus all currently PBS-listed bDMARDs.
- 7.3 The PBAC is satisfied that BKZ provides, for some patients, a significant improvement in efficacy over ADA, ETN and UST.
- 7.4 The PBAC noted the consumer comments regarding the significant quality of life impact severe CPP has on patients and the importance of having additional treatment options available.
- 7.5 The PBAC agreed with the ESC that the mechanism of action and mode of administration of BKZ was not unique and the clinical need for additional treatment options for severe CPP was low. However, acknowledging the consumer comments (see paragraph above), the PBAC reiterated its previous consideration that the addition of another option which may offer a higher chance of achieving a PASI 90 response compared with some of the alternative bDMARDs, may be useful in particular patients.
- 7.6 The PBAC noted the current submission nominated all currently PBS-listed bDMARDs for severe CPP as comparators. The PBAC reaffirmed its previous consideration that

Public Summary Document - March 2023 PBAC Meeting

BKZ was more likely to substitute for the recently listed bDMARDs that tended to be the more effective treatment options (i.e., IXE and RIS); however, all currently PBS-subsidised bDMARDs for severe CPP were relevant alternative therapies.

- 7.7 The PBAC noted the clinical claim in the current submission was that BKZ is more effective than all currently PBS-listed bDMARDs at achieving a PASI 90 and PASI 100 response and similar in safety. This is consistent with the clinical claim in the previous submission with the exception of the removal of reference to the PASI 75 outcome as part of the claim.
- 7.8 The PBAC noted the key clinical evidence presented to support the clinical claim consisted of 3 direct randomised controlled trials of BKZ vs ADA, UST and SEC, two short term NMAs [Armstrong 2022 (86 studies, 34,476 patients), Sbidian 2022 (167 studies, 58,912 patients)] and one long term NMA [Armstrong 2002a (14 studies)]. The current submission also presented clinical data from a subgroup of patients with severe CPP in high impact areas (scalp, nails and palmoplantar).
- 7.9 The PBAC noted the interpretation of the results from the indirect treatment comparisons and the NMAs was inconsistent and varied based on the risk statistic (see paragraph 6.17). The PBAC considered the evidence presented did not support the claim that BKZ is more effective than all currently PBS-listed bDMARDs at achieving a PASI 90 response. The PBAC considered that PASI 75 remained a relevant outcome for severe CPP and the evidence also did not support a claim that BKZ is superior to all currently PBS-listed bDMARDs based on the PASI 75 response.
- 7.10 The PBAC considered that, based on the totality of evidence, with a consistent conclusion across direct trials, two short term NMAs and one long term NMA, BKZ provides, for some patients, a significant improvement in efficacy (as measured by PASI 75 and PASI 90) compared to ADA and UST. The PBAC noted there was no direct evidence comparing BKZ and ETN but considered that, based on previous consideration of the efficacy of ETN (see paragraph 6.17), and supported by the conclusion in the two short term NMAs and one long term NMA, BKZ provides, for some patients, a significant improvement in efficacy (as measured by PASI 75 and PASI 90) compared to ETN.
- 7.11 The PBAC recalled it had previously considered a claim of non-inferior safety compared to all currently PBS-listed bDMARDs to be reasonable (paragraph 7.9, BKZ PSD, March 2022 PBAC meeting).
- 7.12 The PBAC agreed with the ESC that the economic model was not informative given the clinical evidence presented in the current submission did not support the clinical claim that BKZ was superior to all PBS-listed bDMARDs.
- 7.13 The PBAC noted the PSCR proposed a cost minimisation approach versus RIS, excluding ADA, ETN, UST, SEC, TIL, GUS, IFX and IXE on the basis that BKZ has demonstrated a significant improvement in efficacy and/ or toxicity versus these

Public Summary Document - March 2023 PBAC Meeting

- bDMARDs. However, the PBAC accepted a superiority claim versus ADA, ETN and UST only.
- 7.14 The PBAC considered a standard cost minimisation approach with costs over two years was appropriate, consistent with the previous approach for bDMARDs. The PBAC considered the cost minimisation approach should be based on an equi-effective dose of BKZ of 320 mg at weeks 0, 4, 8, 12, 16 and then every 8 weeks and the doses of alternative bDMARDs (excluding ADA, ETN and UST) could be derived with reference to the relevant Product Information documents. The PBAC considered the cost of BKZ should be no greater than the least costly of the alternative therapies (excluding ADA, ETN and UST).
- 7.15 The PBAC considered the listing included in Section 8 of the March 2022 PSD remained appropriate (including a reduction in the number of repeats from 5 to 4) with flow-on changes to the other bDMARD listings to include BKZ in the list of eligible treatments as part of a treatment cycle. The PBAC considered it remained reasonable to apply a grandfather restriction for the listing of BKZ, which should be reviewed after 12 months, as per standard practice.
- 7.16 The PBAC considered that, given its recommendation was on a cost minimisation basis to the least costly alternative bDMARD (excluding ADA, ETN and UST), the listing of BKZ on this basis was likely to be cost neutral or modestly cost saving to the PBS as it may substitute for more costly bDMARDs. The PBAC noted BKZ may be more costly than ADA, ETN and UST but considered BKZ was less likely to substitute for these therapies. The PBAC reiterated its previous consideration that, as BKZ would be the tenth bDMARD available on the PBS, the listing was unlikely to accelerate growth in the market.
- 7.17 The PBAC recommended that BKZ should be treated as interchangeable on an individual patient basis with IFX, GUS, IXE, RIS, TIL and SEC.
- 7.18 The PBAC advised that BKZ is not suitable for prescribing by nurse practitioners, consistent with other bDMARD listings for severe CPP.
- 7.19 The PBAC recommended that the Early Supply Rule should apply.
- 7.20 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because BKZ is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over all the PBS-listed bDMARDs, or not expected to address a high and urgent unmet clinical need given the presence of alternative therapies, the criteria prescribed by the National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009 for Pricing Pathway A were not met.
- 7.21 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Public Summary Document - March 2023 PBAC Meeting

Outcome:

Recommended

8 Recommended listing**8.1 Add new item/s as follows:**

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Manufacturer	Name and
BIMEKIZUMAB 160mg/mL injection, 2 x 1 mL syringe	NEW	1	2	4	Bimelx®	UCB Australia Proprietary Limited
160mg/mL injection, 2 x 1 mL pen device	NEW	1	2	4		

Minor amendments based on Benefit Type 49345 (guselkumab)

Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: ☒ Medical Practitioners
	Restriction Level / Method: ☒ Authority Required – In Writing
	Administrative Advice: Advices 7606, 7607 and 7608 (standard 'no increases' and special pricing arrangement) clauses should apply. Minor amendments to Administrative Advice 27644 should apply (noted at end) and flowed on to other bDMARD listings for severe chronic plaque psoriasis.
	Episodicity:
	Severity: Severe
	Condition: Chronic plaque psoriasis
	Indication: Severe chronic plaque psoriasis
	Same as RS 11141/ToC 11114 with the following differences
	Treatment Phase: Initial treatment - Initial 1, Whole body (new patient)
	Clinical criteria:
	Patient must not receive more than 24 weeks of treatment under this restriction.
	Prescribing Instructions: Items 26651, 26652, 26653, 26386, 23217, 25769, 23934 and 23935 should apply
	Administrative Advice: 26654 and 25744 should apply.
	Same as RS 10856/ToC 10742 with the following differences
	Treatment Phase: Initial treatment - Initial 2, Whole body (change or re-commencement of treatment after a break in biological medicine of less than 5 years)
	Clinical criteria:
	Patient must not receive more than 24 weeks of treatment under this restriction.
	Prescribing Instructions: Items 24057, 22873, 25769, 23934, 23954, 23935 and 23943 should apply
	Administrative Advice: 25744 should apply.
	Same as RS 11150/ToC 11097 with the following differences
	Treatment Phase: Initial treatment - Initial 3, Whole body (re-commencement of treatment after a break in biological medicine of more than 5 years)
	Clinical criteria:
	Patient must not receive more than 24 weeks of treatment under this restriction.
	Prescribing Instructions: Items 26387, 23957, 25769, 23934 and 23935 should apply
	Administrative Advice: 25744 should apply.
	Same as RS 11150/ToC 11097 with the following differences

Public Summary Document - March 2023 PBAC Meeting

Treatment Phase: Initial treatment - Initial 1, Face, hand, foot (new patient)						
Clinical criteria:						
Patient must not receive more than 24 weeks of treatment under this restriction.						
Prescribing Instructions:						
Items 26651, 26652, 26653, 26388, 16804, 24055, 25769, 23934 and 23935 should apply						
Administrative Advice:						
Items 26654 and 25744 should apply.						
Same as RS 11175/ToC 11130 with the following differences						
Treatment Phase: Initial treatment - Initial 2, Face, hand, foot (change or re-commencement of treatment after a break in biological medicine of less than 5 years)						
Clinical criteria:						
Patient must not receive more than 24 weeks of treatment under this restriction.						
Prescribing Instructions:						
Items 23226, 16804, 22873, 25769, 23934, 23942, 23935 and 23943 should apply						
Administrative Advice:						
25744 should apply.						
Same as RS 10907/ToC 10901 with the following differences						
Treatment Phase: Initial treatment - Initial 3, Face, hand, foot (re-commencement of treatment after a break in biological medicine of more than 5 years)						
Clinical criteria:						
Patient must not receive more than 24 weeks of treatment under this restriction.						
Prescribing Instructions:						
Items 26387, 16804, 23948, 25769, 23934, and 23935 should apply						
Administrative Advice:						
25744 should apply.						
Same as RS 10874/ToC 8877 with the following differences						
Treatment Phase: Initial treatment - Initial 1, Whole body or Face, hand, foot (new patient) or Initial 2, Whole body or Face, hand, foot (change or re-commencement of treatment after a break in biological medicine of less than 5 years) or Initial 3, Whole body or Face, hand, foot (re-commencement of treatment after a break in biological medicine of more than 5 years) - balance of supply						
Clinical criteria:						
The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restrictions.						
Administrative Advice:						
25745 should apply.						
Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Manufacturer	Name and
BIMEKIZUMAB	NEW	1	2	2	Bimelx®	UCB Australia Proprietary Limited
160mg/mL injection, 2 x 1 mL syringe 160mg/mL injection, 2 x 1 mL pen device	NEW	1	2	2		

Notes on continuing restrictions under Benefit Type 49345 (Separate listing required due to difference in proposed repeats)

Concept ID	Category / Program:
	GENERAL – General Schedule (Code GE)
	Prescriber type: ☒ Medical Practitioners
	Restriction Level / Method:
	☒ Authority Required – In Writing
	Administrative Advice:
	Advices 7606, 7607 and 7608 (standard 'no increases' and special pricing arrangement) clauses should apply. Minor amendments to Administrative Advice 27644 should apply (noted at end) and flowed on to other bDMARD listings for severe chronic plaque psoriasis.
	Episodicity:
	Severity: Severe
	Condition: Chronic plaque psoriasis
	Indication: Severe chronic plaque psoriasis

Public Summary Document - March 2023 PBAC Meeting

	Same as RS 10736/ToC 10806
	Treatment Phase: Continuing treatment, Whole body
	Nil changes to continuing restriction.
	Prescribing Instructions: Items 24057, 26389, 26394, 23934, 23935 and 23943 should apply
	Administrative Advice: 25744 should apply.
	Same as RS 10737/ToC 10889
	Treatment Phase: Continuing treatment, Face, hand, foot
	Nil changes to continuing restriction.
	Prescribing Instructions: Items 23226, 23240, 26387, 23239, 16804, 26394, 23934, 23935 and 23943 should apply
	Administrative Advice: 25744 should apply.
	Same as RS 10805/ToC 10807
	Treatment Phase: Continuing treatment, Whole body or Continuing treatment, Face, hand, foot - balance of supply
	Nil changes to continuing balance of supply restriction
	Administrative Advice: 25744 should apply.

Grandfather restriction:

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Manufacturer	Name and
BIMEKIZUMAB 160mg/mL injection, 2 x 1 mL syringe	NEW	1	2	2	Bimelx®	UCB Australia Proprietary Limited
160mg/mL injection, 2 x 1 mL pen device	NEW	1	2	2		

Notes on continuing restrictions under Benefit Type 49345 (Separate listing required due to difference in proposed repeats)

Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: ☒ Medical Practitioners
	Restriction Level / Method: ☒ Authority Required – In Writing
	Administrative Advice: Advices 7606, 7607 and 7608 (standard 'no increases' and special pricing arrangement) clauses should apply. Minor amendments to Administrative Advice 27644 should apply (noted at end) and flowed on to other bDMARD listings for severe chronic plaque psoriasis.
	Episodicity:
	Severity: Severe
	Condition: Chronic plaque psoriasis
	Indication: Severe chronic plaque psoriasis
	Same as RS 10736/ToC 10806
	Treatment Phase: Initial treatment, Whole body – Grandfather patients
	Clinical criteria:
	Patient must have a documented severe chronic plaque psoriasis where lesions have been present for at least 6 months prior to commencing non-PBS-subsidised treatment with this drug for this condition
	AND
	Clinical criteria:
	Patient must have received non-PBS subsidised therapy with this drug for this condition prior to [list date]
	AND
	Clinical criteria:
	Patient must have a documented failure to achieve an adequate response, as demonstrated by a Psoriasis Area and Severity Index (PASI) assessment, to at least 2 of the following 5 treatments prior to commencing non-PBS-subsidised treatment with this drug for this condition:

Public Summary Document - March 2023 PBAC Meeting

	(i) phototherapy (UVB or PUVA) for 3 treatments per week for at least 6 weeks; (ii) methotrexate at a dose of at least 10 mg weekly for at least 6 weeks; (iii) cyclosporin at a dose of at least 2 mg per kg per day for at least 6 weeks; (iv) acitretin at a dose of at least 0.4 mg per kg per day for at least 6 weeks, (v) apremilast at a dose of 30 mg twice a day for at least 6 weeks
	AND
	Clinical criteria:
	Patient must have a documented Psoriasis Area and Severity Index (PASI) score of greater than 15 prior to commencing non-PBS subsidised treatment with this drug for this condition
	AND
	Clinical criteria:
	The treatment must be as systemic monotherapy (other than methotrexate)
	AND
	Clinical criteria:
	Patient must not receive more than 24 weeks of treatment under this restriction
	AND
	Population criteria:
	Patient must be aged 18 years or older
	Prescribing Instructions: Items 24057, 26389, 26394 should apply.
	Insert also: The most recent PASI assessment must be no more than 1 month old at the time of application. A Grandfather patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria. This restriction is only valid for 12 months following [list date].
	Administrative Advice: 25744 should apply.
	Same as RS 10737/ToC 10889
	Treatment Phase: Initial treatment, Face, hand, foot – Grandfather patients
	Clinical criteria:
	Patient must have a documented severe chronic plaque psoriasis of the face, or palm of a hand or sole of a foot where lesions have been present for at least 6 months prior to commencing non-PBS-subsidised treatment with this drug for this condition
	AND
	Clinical criteria:
	Patient must have received non-PBS subsidised therapy with this drug for this condition prior to [list date]
	AND
	Clinical criteria:
	Patient must have a documented failure to achieve an adequate response, as demonstrated by a Psoriasis Area and Severity Index (PASI) assessment, to at least 2 of the following 5 treatments prior to commencing non-PBS-subsidised treatment with this drug for this condition: (i) phototherapy (UVB or PUVA) for 3 treatments per week for at least 6 weeks; (ii) methotrexate at a dose of at least 10 mg weekly for at least 6 weeks; (iii) cyclosporin at a dose of at least 2 mg per kg per day for at least 6 weeks; (iv) acitretin at a dose of at least 0.4 mg per kg per day for at least 6 weeks, (v) apremilast at a dose of 30 mg twice a day for at least 6 weeks
	AND
	Clinical criteria:
	The treatment must be as systemic monotherapy (other than methotrexate)
	AND
	Clinical criteria:

Public Summary Document - March 2023 PBAC Meeting

	Patient must not receive more than 24 weeks of treatment under this restriction
	AND
	Population criteria:
	Patient must be aged 18 years or older
	Prescribing Instructions: Items 24057, 26389, 26394 should apply The most recent PASI assessment must be no more than 1 month old at the time of application. A Grandfather patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria. This restriction is only valid for 12 months following [list date].
	Administrative Advice: Items 25744 should apply.

	Amend the following paragraphs as outlined: [Paragraph 1]: The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of the biological medicines adalimumab, <i>bimekizumab</i>, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab and ustekinumab for adult patients with severe chronic plaque psoriasis. Therefore, where the term 'biological medicines' appears in notes and restrictions, it refers to adalimumab, bimekizumab, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab only. [Paragraph 3]: A patient who received PBS-subsidised adalimumab, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab treatment prior to 1 February 2019 is considered to start their first cycle as of 1 February 2019. [Paragraph 16]: An application for initial treatment will be limited to provide for a maximum of 16 weeks of therapy for adalimumab, etanercept, ixekizumab, and secukinumab, 20 weeks of therapy for guselkumab, 22 weeks of therapy for infliximab, 24 weeks for <i>bimekizumab</i> and 28 weeks of therapy for risankizumab, tildrakizumab and ustekinumab. [Paragraph 17]: It is recommended that a patient is reviewed for response following a minimum of 12 weeks of therapy; or a minimum of 16 weeks for bimekizumab. (4) 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 requalify with respect to the indices of disease severity (i.e. a PASI score of greater than 15), or the prior non-biological therapy requirements, except if the patient has had a break in therapy of more than 5 years who would need to requalify with respect to the indices of disease severity. A patient who is not able to complete a minimum of 12 weeks, or a <i>minimum of 16 weeks for bimekizumab</i>, 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...
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This restriction may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

9 Context for Decision

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

Public Summary Document - March 2023 PBAC Meeting

through the PBS. The PBAC welcomes applications containing new information at any time.

10 Sponsor's Comment

The sponsor had no comment.