

5.05 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 Pty Ltd.

1 Purpose of submission

- 1.1 The Category 2 submission requested Authority Required listing for bimekizumab for the treatment of adult patients with non-radiographic axial spondyloarthritis (nr-axSpA).
- 1.2 Listing was requested on the basis of a cost-minimisation approach versus secukinumab. If listed, bimekizumab would be the fifth biologic or targeted synthetic disease modifying anti-rheumatic drug (b/tsDMARD) on the PBS for nr-axSpA, alongside the tumour necrosis factor alpha (TNF α) inhibitors certolizumab pegol and golimumab, the IL-17 inhibitor secukinumab and the Janus kinase (JAK) inhibitor upadacitinib. In addition, the IL-17 inhibitor ixekizumab was recommended for listing in 2021, but had not listed at time of evaluation. The key components of the submission are shown in Table 1.

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

Component	Description
Population	Adults with non-radiographic axial spondyloarthritis (nr-axSpA) who failed to achieve an adequate response following treatment with at least 2 nonsteroidal anti-inflammatory drugs (NSAIDs) or are contraindicated to NSAIDs, while completing an appropriate exercise program, for a total of three months.
Intervention	Bimekizumab (BKZ) 160 mg SC every 4 weeks
Comparator	Secukinumab (SEC) With a loading dose: 150 mg SC with initial dosing at Weeks 0, 1, 2, 3, and 4 followed by the same dose every month. Without a loading dose: 150 mg SC every month*
Outcomes	ASAS40, ASAS20, BASDAI50 Safety
Clinical claim	In adults with nr-axSpA, BKZ 160 mg SC Q4W is noninferior in terms of effectiveness compared with SEC 150 mg Q4W (with and without loading dose) BKZ 160 mg SC Q4W is noninferior in terms of safety compared with SEC 150 mg Q4W (with and without loading dose)

Source: Table 1-1, p16 of the submission. Abbreviations: ASAS = Assessment of SpondyloArthritis International Society ; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index ; SC = subcutaneous;

*PBAC noted the split between loading dose vs. non-loading dose to be 70:30 (para. 7.7) secukinumab-psd-nov-2020.pdf (pbs.gov.au)

2 Background

Registration status

- 2.1 The submission was made under the TGA/PBAC Parallel Process. TGA status at time of PBAC consideration: Not registered. The TGA Delegate’s Overview was provided during the evaluation. The Delegate was inclined to approve the registration of bimekizumab for nr-axSpA.
- 2.2 Bimekizumab is registered in Australia for the treatment of plaque psoriasis in adults. As well as applications for use in radiological and non-radiological axial spondyloarthritis, the TGA is considering an application for use in psoriatic arthritis.

Previous PBAC consideration

- 2.3 Bimekizumab was considered by the PBAC in March 2022 and March 2023, for the indication of severe chronic plaque psoriasis. It has not been previously considered for nr-axSpA.
- 2.4 The sponsor has lodged separate submissions requesting listing of bimekizumab for the treatment of ankylosing spondylitis and psoriatic arthritis for consideration at the March 2024 PBAC meeting.

3 Requested listing

- 3.1 The submission proposed restrictions for initial and continuing treatment as well as a grandfathering restriction, based on the restrictions in the Public Summary Document (PSD) for upadacitinib and the published restriction for golimumab. An abbreviated restriction for initial treatment is shown below.

Essential elements of the requested listing

MEDICINAL PRODUCT medicinal product pack	Dispensed Price for Max. Qty	Max. qty packs	Max. qty units	No. of Rpts	Available brands
BIMEKIZUMAB					
Bimekizumab 160mg/mL, pre-filled syringe, 2.	\$3422.13 published price \$to be confirmed effective price	1	2	2	Bimzelx
Bimekizumab 160mg/mL, pre-filled pen, 2.	\$3422.13 published price \$to be confirmed effective price	1	2	2	Bimzelx

Public Summary Document – March 2024 PBAC Meeting

Category / Program: General Schedule
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/>
Restriction type: <input checked="" type="checkbox"/> Authority Required (in writing only via post/HPOS upload)
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: No increase in the maximum number of repeats may be authorised
Administrative Advice: Special Pricing Arrangements apply.
Indication: Non-radiographic axial spondyloarthritis
Treatment Phase: Initial treatment - Initial 1 (New patient)
Clinical criteria:
Patient must not have received PBS-subsidised treatment with a biological medicine for this condition,
AND
Clinical criteria:
Patient must have had chronic lower back pain and stiffness for 3 or more months that is relieved by exercise but not rest,
AND
Clinical Criteria:
Patient must have failed to achieve an adequate response following treatment with at least 2 non-steroidal anti-inflammatory drugs (NSAIDs), whilst completing an appropriate exercise program, for a total period of 3 months,
AND
Clinical Criteria
Patient must have one or more of the following: (a) enthesitis (heel); (b) uveitis; (c) dactylitis; (d) psoriasis; (e) inflammatory bowel disease; or (f) positive for Human Leukocyte Antigen B27 (HLA-B27),
AND
Clinical Criteria:
The condition must not be radiographically evidenced on plain x-ray of Grade II bilateral sacroiliitis or Grade III or IV unilateral sacroiliitis,
AND
Clinical Criteria:
The condition must be non-radiographic axial spondyloarthritis, as defined by Assessment of Spondyloarthritis International Society (ASAS) criteria,
AND
Clinical Criteria:
The condition must be sacroiliitis with active inflammation and/or oedema on non-contrast Magnetic Resonance Imaging (MRI),
AND
Clinical Criteria:
The condition must have presence of Bone Marrow Oedema (BMO) depicted as a hyperintense signal on a Short Tau Inversion Recovery (STIR) image (or equivalent),
AND
Clinical Criteria:
The condition must have BMO depicted as a hypointense signal on a T1 weighted image (without gadolinium),

Public Summary Document – March 2024 PBAC Meeting

AND
Clinical Criteria:
The treatment must not exceed a maximum of 16 weeks with this drug under this restriction.
Treatment criteria:
Must be treated by rheumatologist; or
Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis.
Prescribing Instructions: The application must include details of the NSAIDs trialed, their doses and duration of treatment. , If the NSAID dose is less than the maximum recommended dose in the relevant TGA-approved Product Information, the application must include the reason a higher dose cannot be used., If treatment with NSAIDs is contraindicated according to the relevant TGA-approved Product Information, the application must provide details of the contraindication., If intolerance to NSAID treatment develops during the relevant period of use which is of a severity to necessitate permanent treatment withdrawal, the application must provide details of the nature and severity of this intolerance.
Prescribing Instructions: The following criteria indicate failure to achieve an adequate response to NSAIDs and must be demonstrated at the time of the initial application: (a) a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of at least 4 on a 0-10 scale; and (b) C-reactive protein (CRP) level greater than 10 mg per L. The baseline BASDAI score and CRP level must be determined at the completion of the 3-month NSAID and exercise trial, but prior to ceasing NSAID treatment. All measures must be no more than 4 weeks old at the time of initial application.
Prescribing Instructions: If the requirement to demonstrate an elevated CRP level could not be met, the reason must be stated in the application. Treatment with prednisolone dosed at 7.5 mg or higher daily (or equivalent) or a parenteral steroid within the past month (intramuscular or intravenous methylprednisolone or equivalent) is an acceptable reason.
Prescribing Instructions: The assessment of the patient's response to the initial course of treatment must be conducted following a minimum of 12 weeks of treatment and no later than 4 weeks from the cessation of that treatment course. If the response assessment is not conducted within these timeframes, the patient will be deemed to have failed this course of treatment in this treatment cycle.
Prescribing Instructions: The authority application must be made in writing and must include: (a) a completed authority prescription form(s); and (b) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
Prescribing Instructions: The baseline BASDAI score and CRP level must also be documented in the patient's medical records.

Administrative Advice:

Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au

Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos

Or mailed to:

Services Australia

Complex Drugs

Reply Paid 9826

HOBART TAS 7001

Source: p42-43 of the submission.

- 3.2 The submission proposed a Special Pricing Arrangement for this listing.

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

4 Population and disease

- 4.1 Spondyloarthritis (SpA) is a group of conditions manifested by varying degrees and combinations of arthritis affecting axial joints, especially the spine and sacro-iliac joints; peripheral arthritis, typically asymmetrical involvement of a few lower limb joints; enthesitis (inflammation of the insertions of tendons or ligaments to bone), especially of the heel; and dactylitis (swelling of the fingers).
- 4.2 SpA with mainly axial manifestations (axSpA) is divided into axSpA with sacro-iliitis on Plain X-ray, called radiographic axial spondyloarthritis (r-axSpA) but usually referred to by its older name, ankylosing spondylitis (AS), and axSpA with no or minimal sacro-iliitis on Plain X-ray, called non-radiographic axial spondyloarthritis (nr-axSpA). AS is more common in men, while nr-axSpA affects men and women equally.
- 4.3 The first line treatment of nr-axSpA is a non-steroidal anti-inflammatory (NSAID). Patients with nr-axSpA not responding adequately to NSAIDs are treated with a biological agent. Efficacy of TNF α inhibitors and IL-17 inhibitors in SpA appears to be similar. Of current guidelines included in the submission, the US and Asia-Pacific based guidelines suggest that a TNF α inhibitor should be preferred. All guidelines suggest that IL-17 inhibitors are to be preferred in psoriasis, but that TNF α inhibitors are to be preferred in inflammatory bowel disease, because IL-17 inhibitors occasionally cause exacerbations of and may cause new-onset Crohn's disease and ulcerative colitis.¹
- 4.4 Bimekizumab is an antibody to IL-17A and IL-17F. IL-17 is a family of pro-inflammatory cytokines, produced by T helper 17 (Th17) cells and playing a role in the innate immune response to pathogens. There are six cytokines in the family, IL-17A, B, C, D,

¹ Ixekizumab PI, 4.4, pp3-4; secukinumab PI, 4.4, p4.

E and F; IL-17A and F are the best characterised. Bimekizumab also binds to IL-17A/F. Different tissues express different receptors subtypes, which may allow different cell types to have specific responses to IL-17 family cytokines.

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

5 Comparator

- 5.1 The submission nominated secukinumab as the comparator. While secukinumab may be a reasonable comparator for bimekizumab (given both act on the IL-17 pathway, albeit with differences), given the requested listing is the same across b/tsDMARDs for nr-axSpA, any other treatment with a similar listing may be replaced in practice. The submission conceded that, in principle, any other treatment with a similar listing may be replaced. Bimekizumab would be the 5th product listed for this indication.
- 5.2 The submission maintained that practitioners would switch among subcutaneously administered treatments but would not be likely to switch from a treatment given orally (i.e., JAK inhibitors) to one given subcutaneously (such as bimekizumab). Such assumptions around mode of administration may be implausible, as PBS restrictions allow patients to try three b/tsDMARDs before commencing a treatment break and is highly unlikely that patients who use an oral therapy will cease treatment once agents with a specific manner of administration have been exhausted, rather than use the maximum allowable treatments in a cycle. In addition, certolizumab pegol, a TNF α inhibitor given subcutaneously, is PBS-listed for treatment of nr-axSpA.
- 5.3 In the context of the cost-minimisation approach taken by the submission, a further consideration for PBAC is that, under Section 101(3B) of the National Health Act 1953, when the proposed medicine is substantially more costly than an alternative therapy, the committee cannot make a positive recommendation unless it is satisfied that, for some patients, the proposed medicine provides a significant improvement in efficacy and/or reduction of toxicity over the alternative therapy. If the committee is so satisfied, it must make a statement to this effect.
- 5.4 For the requested population, the following PBS-listed medicines may be considered alternative therapies because they could be replaced in practice: certolizumab pegol, golimumab, secukinumab and upadacitinib.
- 5.5 The Pre-Sub-Committee Response (PSCR) argued that UPA should not be considered a comparator, as it is an oral therapy, and it would not be replaced as clinicians opting to use UPA for a patient would have considered existing subcutaneous options and elected not to use them.

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 and the concurrent application for non-ankylosing spondylitis as a single hearing, as the two conditions are related. The clinician discussed the evidence of effectiveness bimekizumab and outlined the likely place in therapy as being after most patients who had failed treatment with a TNF α inhibitor, as these were considered highly effective and the most commonly used first line b/tsDMARDs for these conditions. The clinician also discussed the weaknesses of the PBS subpopulation analyses (see ‘comparative effectiveness’ section) due to the small sizes of these subgroups in the clinical trials and the implications for how these should be interpreted.

Consumer comments

- 6.2 The PBAC noted and welcomed the input from organisations (2) via the Consumer Comments facility on the PBS website. The comments from health professionals and individuals described bimekizumab as being a needed option with high efficacy which may also have reduced risk of inflammatory bowel disease compared to some other options. The PBAC noted the input from CreakyJoints Australia described the need for additional treatment options for the numerous conditions for which b/tsDMARDs are listed, as different treatments work best for individual patients and more options gives patients more flexibility to find the therapy that best works for them. The PBAC also noted the input from Ankylosing Spondylitis Victoria supported the listing of bimekizumab.

Clinical trials

- 6.3 The submission was based on one trial, BE MOBILE 1 (NCT03928704), comparing bimekizumab to placebo, and an indirect treatment comparison (ITC) with secukinumab using one trial, PREVENT (NCT02696031), comparing secukinumab to placebo.
- 6.4 Details of the trials presented in the submission are provided in Table 2.

Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
BE MOBILE 1 (AS0010) NCT03928704	<p>A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating The Efficacy And Safety Of Bimekizumab In Subjects With Active Nonradiographic Axial Spondyloarthritis.</p> <p>van der Heijde D et al. Efficacy and safety of bimekizumab in axial spondyloarthritis: results of two parallel phase 3 randomised controlled trials</p> <p>Baraliakos X et al. Bimekizumab treatment in patients with active axial spondyloarthritis: 52-week efficacy and safety from the randomised parallel phase 3 BE MOBILE 1 and BE MOBILE 2 studies.</p>	<p>1 February, 2023</p> <p><i>Ann Rheum Dis</i> 2023; 82:515–526. doi:10.1136/ard-2022-223595; and supplemental material.</p> <p><i>Ann Rheum Dis</i>, Published Online First: 04 October 2023. doi: 10.1136/ard-2023-224803; correction published <i>Ann Rheum Dis</i> 2023; 82:e213.</p>
PREVENT NCT02696031	<p>A Randomized, Double-blind, Placebo-controlled Multicenter Study of Secukinumab 150 mg in Patients With Active nr-axSpA to Evaluate the Safety, Tolerability and Efficacy up to 2 Yrs, Followed by an Opt Phase of Either 150 mg or 300 mg Randomized Dose Escalation for up to Another 2 Yrs</p> <p>Deodhar A et al. Improvement of Signs and Symptoms of Nonradiographic Axial Spondyloarthritis in Patients Treated With Secukinumab: Primary Results of a Randomized, Placebo-Controlled Phase III Study.</p> <p>Braun J et al. Secukinumab in non-radiographic axial spondyloarthritis: subgroup analysis based on key baseline characteristics from a randomized phase III study, PREVENT.</p>	<p>Not reported.</p> <p><i>Arthritis Rheumatol</i> 2021; 73:110-120.</p> <p><i>Arthritis Res Ther</i> 2021, 23: 231.</p>

Source: Table 2-5, p60 of the submission and <https://clinicaltrials.gov/study/NCT02696031> accessed 12 December 2023.

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

Table 3: Key features of the relevant randomised controlled trials

Trial	N	Design/duration	Risk of bias	Patient population	Primary Outcome	Use in Modelled Evaluation
Bimekizumab vs placebo						
BE MOBILE 1	254	R, DB, 16 wk, randomised to bim 160 mg 4 wkly or placebo, then 36 wk OLE	Low	Adults; axSpA by ASAS criteria <i>except no sacro-iliitis</i> by Plain X-ray \geq grade 2 bilateral or \geq 3 unilateral within 6 mo; duration > 3 mo, onset age < 45 years; BASDAI \geq 4, and BASDAI item 2 (spinal pain) \geq 4; \geq 2 failed NSAID; if prior TNF α inhibitor must have failed or been intolerant.	ASAS40 at 16 wk	Used
Secukinumab vs placebo						
PREVENT	555	R, DB, 52 wk, randomised to secLD = with loading dose = 150 mg wks 0,1,2,3,4 then 150 mg 4 wkly or secNL = no loading dose = 150 mg 4 wkly or placebo; placebo could escape to sec after 20 wk.	Low	Adults; axSpA by ASAS criteria, <i>except no sacro-iliitis</i> by Plain X-ray \geq grade 2 bilateral or \geq 3 unilateral; duration > 6 mo; onset age < 45 years; BASDAI \geq 4, and BASDAI item 2 (spinal pain) \geq 4; \geq 2 failed NSAID; if prior TNF α inhibitor must have failed or been intolerant.	ASAS40 for secLD in TNF α inhibitor naïve patients at 16 wk (EU reg req) and secLD and secNL in TNF α inhibitor naïve patients at 52 wk (USA reg req)	Pooled 16 wk data used

Source: constructed during the evaluation from: Submission, Figure 2-5, p63; Tables 2-10, p64; 2-12, p67; Figure 2-7, p68; Tables 2-15, p71, 2-16, p72.

ASAS = Assessment of SpondyloArthritis international Society; ASAS score is calculated from 4 symptom domains (patient global assessment, pain, function and inflammation) rated on a 10-point scale. ASAS40 requires reduction of \geq 40% *and* \geq 2 points in at least 3 domains *and* no worsening in the remaining domain; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; bim = bimekizumab; DB = double blind; LD = loading dose; NL = no loading dose; NSAID = non-steroidal anti-inflammatory drug; OLE = open-label extension; R = randomised; reg req = regulatory requirement; sec = secukinumab; TNF α = tissue necrosis factor alpha.

- 6.6 The primary outcome in PREVENT specified two independent analyses: (1) for TNF α inhibitor naïve patients treated with a loading dose and assessing outcomes at 16 weeks, to satisfy EU requirements, and (2) for TNF α inhibitor naïve patients treated without a loading dose and assessing outcomes at 52 weeks, to satisfy FDA requirements. Most trials of biologicals for axSpA have assessed outcomes at 16 weeks, and the Australian approved indication (based on the trial) allows secukinumab to be given for nr-axSpA with or without a loading dose. The PBS listings of secukinumab for nr-axSpA also has provisions for loading dose or no loading dose options.
- 6.7 There were minor differences between the trials in terms of diagnostic criteria. Both trials referred to the ASAS criteria for diagnosis of nr-axSpA, which require the presence of one of the following if sacro-iliitis is present on Plain X-ray or MRI (but is not severe enough on Plain X-ray to meet criteria for ankylosing spondylitis), or two

of the following and HLA-B27 if sacro-iliitis is absent on Plain X-ray and MRI: inflammatory back pain (see 4.3, above); arthritis; heel enthesitis; uveitis; dactylitis; psoriasis; Crohn’s disease or ulcerative colitis; a good response to NSAID; a family history of SpA; elevated C-reactive protein (CRP). The trials did not follow these criteria, in that in both PREVENT and BE MOBILE 1 patients with no sacro-iliitis on MRI were required to have elevated CRP, and in BE MOBILE 1 a good response to NSAID and a family history of SpA were not allowed as criteria for diagnosis. The threshold for elevated CRP was different: 5 mg/L in PREVENT, and 6 mg/L in BE MOBILE 1. The Australian approved indication for secukinumab, based on PREVENT, requires either MRI change or elevated CRP.²

- 6.8 Patients with uveitis or Crohn’s disease or ulcerative colitis were eligible for BE MOBILE 1, provided that they had “no active symptomatic disease” at enrolment. The wording in PREVENT may have been more restrictive: “active ongoing” uveitis and inflammatory bowel disease required exclusion.
- 6.9 There was a minor difference in the definition of ASAS20 used in the trials. The definition in the Assessment of Spondyloarthritis international Society (ASAS) handbook is improvement of $\geq 20\%$ and ≥ 1 unit in at least 3 of 4 domains and no worsening of $\geq 20\%$ and ≥ 1 unit in the remaining domain.³ This definition was used in PREVENT, but in BE MOBILE 1 no worsening at all in the fourth domain was allowed.
- 6.10 Baseline characteristics of patients enrolled in the included trials were generally similar.

Comparative effectiveness

- 6.11 The results of the trials are shown in Table 4.

² Secukinumab PI, 4.1, p1.

³ Sieper J, Rudwaleit M, Baraliakos X, et al. The Assessment of SpondyloArthritis international Society (ASAS) handbook: A guide to assess spondyloarthritis. *Ann Rheum Dis* 2009; 68:ii1-ii44.

Table 4: Primary outcomes and secondary outcomes used in the indirect treatment comparison in the trials presented in the submission; ITT population.

	BE MOBILE 1		PREVENT		
	Bimekizumab N = 128	Placebo N = 126	Secukinumab LD N = 185	Secukinumab NL N = 184	Placebo N = 186
ASAS40 at 16 wk, n (%) RR (95% CI) vs placebo	61 (47.7%) 2.22 (1.52, 3.25)	27 (21.4%)	74 (40.0%) 1.43 (1.07, 1.91)	75 (40.8%) 1.46 (1.09, 1.95)	52 (28.0%)
ASAS20 at 16 wk, n (%) RR (95% CI) vs placebo	88 (68.8%) 1.80 (1.40, 2.32)	43 (38.1%)	105 (56.8%) 1.24 (1.02, 1.52)	107 (58.2%) 1.27 (1.04, 1.55)	85 (45.7%)
BASDAI change from baseline, LS mean (SE) Mean difference vs placebo (95% CI)	-3.07 (0.21) -1.52 (-2.12, -0.92)	-1.55 (0.22)	-2.35 (0.20) -0.89 (-1.46, -0.32)	-2.43 (0.20) -0.97 (-1.54, -0.40)	-1.46 (0.21)
BASDAI50 at 16 wk, n (%) RR (95% CI) vs placebo	60 (46.9%) 2.19 (1.49, 3.20)	27 (21.4%)	69 (37.3%) 1.78 (1.27, 2.49)	69 (37.5%) 1.79 (1.28, 2.50)	39 (21.0%)

Source: Submission Tables 2-35, p92; 2-43, p102; Figures 2-17, p123; 2-19, p125; 2-23, p129.

Statistically significant results are in **bold**.

ASAS = Assessment of SpondyloArthritis international Society score; ASAS is calculated from 4 symptom domains (patient global assessment, pain, function and inflammation) rated on a 10-point scale. ASAS40 requires reduction of $\geq 40\%$ and ≥ 2 points in at least 3 domains and no worsening in the remaining domain. ASAS20 requires improvement of $\geq 20\%$ and ≥ 1 unit in at least 3 domains and no worsening of $\geq 20\%$ and ≥ 1 unit in remaining domain, or, in BE MOBILE 1, no worsening in remaining domain; BASDAI = Bath ankylosing spondylitis disease activity index; BASDAI50 = 50% fall in BASDAI; CI = confidence interval; ITT = intent to treat; LD = loading dose; LS = least squares; NL = no loading dose; RR = risk ratio; SE = standard error.

- 6.12 Overall, in the ITT population both active treatments were superior to placebo, and there no obvious differences in the size or frequency of responses between bimekizumab and secukinumab.
- 6.13 The PREVENT trial suggested that the benefit of secukinumab was greater in patients with the most active inflammation, as evidenced by MRI change and elevated CRP. The proposed restriction for bimekizumab, modelled on that for secukinumab, requires MRI change and elevated CRP (> 10 mg/L). Approximately 30% of patients in the trials met this criterion.
- 6.14 In BE MOBILE 1, there was a pre-specified subgroup analysis of patients with MRI change and elevated CRP (> 6 mg/L), and in the submission this analysis was compared to a post-hoc analysis of a similar subgroup in PREVENT (MRI change and CRP > 5 mg/L). However, this subgroup is not the same as the proposed PBS-population, because, as well as the difference in threshold (5 or 6 vs 10 mg/L), in the proposed restriction an elevated CRP is not a criterion for diagnosis, as it was in BE MOBILE 1 and in PREVENT, but for NSAID failure, and must be measured while the patient is taking NSAID, which was not the case in BE MOBILE 1 and PREVENT (how this requirement can be applied in patients in whom NSAIDs are contra-indicated or not tolerated is unclear).

- 6.15 The results for the MRI+/CRP+ subgroups are shown in Table 5.
- 6.16 The data for the MRI+/CRP+ subgroup from BE MOBILE 1 used the trial definition of elevated CRP (> 6 mg/L). The data for the MRI+/CRP+ subgroup for ASAS40 and BASDAI50 from PREVENT also used the trial definition (> 5 mg/L). These values were the upper limits of normal at the central laboratories used for the trials and can probably be regarded as not meaningfully different.
- 6.17 Results for ASAS20 for the MRI+/CRP+ subgroup were not reported in the PREVENT publications. The submission presents results for ASAS20 taken from the secukinumab PSD (November 2020). However, these ASAS20 results are for a different population, with CRP > 10 mg/L. Braun, 2021, gives the number of patients in the MRI+/CRP+ group, using the > 5 mg/L threshold, as 166 (111 allocated to secukinumab and 55 to placebo), while Table 5 of the PSD gives the number of MRI+/CRP+ patients as 88 (63 allocated to secukinumab and 25 to placebo). The change of threshold had, therefore, a significant effect on the population selected.
- 6.18 Overall, the point estimates for the effect of bimekizumab were lower in the MRI+/CRP+ population, and for ASAS20 did not achieve statistical significance, while the point estimates for the effect of secukinumab were higher.

Table 5: Efficacy outcomes for the MRI+/CRP+ subgroups

	BE MOBILE 1		PREVENT	
	Bimekizumab	Placebo	Secukinumab (pooled)	Placebo
ASAS40 at 16 wk, n/N (%)	23/41 (56.1%)	13/40 (32.5%)	58/111 (52.3%)	12/55 (21.8%)
RR vs placebo (95% CI)	1.73 (1.02, 2.91)		2.39 (1.41, 4.07)	
ASAS20 at 16 wk, n/N (%)	30/41 (73.2%)	21/40 (52.5%)	44/63 (69.8%)	7/25 (28.0%)
RR vs placebo (95% CI)	1.39 (0.98, 1.97)		2.49 (1.55, 4.00)	
BASDAI50, n/N (%)	24/41 (58.5%)	12/40 (30.0%)	50/111 (45.0%)	7/55 (12.7%)
RR vs placebo (95% CI)	1.95 (1.14, 3.34)		3.54 (1.72, 7.29)	

Source: Submission Tables 2-57, p115; 2-58, p115; 2-59, p115; 2-60, p116; 2-61, p118; Figures 2-18, p124; 2-22, p128.

ASAS = Assessment of SpondyloArthritis international Society score; ASAS is calculated from 4 symptom domains (patient global assessment, pain, function and inflammation) rated on a 10-point scale. ASAS40 requires reduction of $\geq 40\%$ and ≥ 2 points in at least 3 domains and no worsening in the remaining domain. ASAS20 requires improvement of $\geq 20\%$ and ≥ 1 unit in at least 3 domains and no worsening of $\geq 20\%$ and ≥ 1 unit in remaining domain, or, in BE MOBILE 1, no worsening in remaining domain; BASDAI = Bath ankylosing spondylitis disease activity index; BASDAI50 = 50% fall in BASDAI; CRP = C-reactive protein; MRI = magnetic resonance image.

- 6.19 The results of the indirect treatment comparison for efficacy variables are shown in Table 6.
- 6.20 Because the ASAS20 results for MRI+/CRP+ patients in PREVENT are from a population with CRP > 10 mg/L, rather than > 5 mg/L in the case of ASAS40 and BASDAI50 in the PREVENT data and > 6 mg/L in the case of all three outcome measures for the BE MOBILE 1 population.

Table 6: Results of the indirect treatment comparison

	RR (95% CI) BKZ vs SEC LD	RR (95% CI) BKZ vs SEC NL	RD (95% CI) BKZ- SEC LD	RD (95% CI) BKZ - SEC NL	MD (95% CI) BKZ - SEC LD	MD (95% CI) BKZ - SEC NL
ASAS20	1.45 (1.05, 2.00)	1.42 (1.03, 1.96)	0.20 (0.04, 0.36)	0.19 (0.03, 0.35)	NA	
ASAS40	1.55 (0.96, 2.50)	1.52 (0.94, 2.45)	0.14 (-0.01, 0.29)	0.13 (-0.02, 0.28)	NA	
BASDAI change from baseline	-	-	-	-	-0.63 (-1.46, 0.20)	-0.55 (-1.38, 0.28)
BASDAI50	1.23 (0.74, 2.05)	1.22 (0.74, 2.03)	0.09 (-0.05, 0.23)	0.08 (-0.07, 0.23)	NA	
MRI+/CRP+ subgroup	RR (95% CI) BKZ vs SEC (pooled)		RD (95% CI) BKZ vs SEC (pooled)		NA	
ASAS20	0.56 (0.31, 1.01)		-0.21 (-0.48, 0.06)			
ASAS40	0.72 (0.34, 1.53)		-0.06 (-0.31, 0.19)			
BASDAI50	0.55 (0.22, 1.36)		-0.03 (-0.27, 0.21)			

Source: Submission Table 2-67, p122. Statistically significant results are in **bold**.

ASAS20 = Assessment in Ankylosing Spondylitis Response 20% response; ASAS40 = Assessment in Ankylosing Spondylitis Response 40% response; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASDAI50 = 50% fall in BASDAI; BXZ = bimekizumab; CI = confidence interval; CRP = C-reactive protein; MD = mean difference; MRI = magnetic resonance image; NA = not applicable; RD = risk difference; RR = risk ratio; SEC = secukinumab.

- 6.21 The submission nominated a non-inferiority margin for the risk ratio for ASAS40 of 0.43. This non-inferiority margin has been accepted for ASAS20 by the PBAC when it considered other biological treatments for AS, including secukinumab. The condition for accepting non-inferiority, that the 95% CI of the RR in the ASAS40 response included 1.00 and the lower CI margin was > 0.43, was satisfied for the trials overall. The ESC considered the analyses based on the ITT populations of the BKZ and SEC trials supported a conclusion of non-inferiority between BKZ and SEC at the whole-trial population level.
- 6.22 The condition for accepting non-inferiority was not satisfied for the MRI+/CRP+ subgroup. The lower bound of the 95% CI was less than 0.43 for all comparisons of the PBS population (MRI+/CRP+ subgroup), and the point estimates consistently favoured secukinumab (although not to the level of statistical significance for any comparison). For contrast with a recent submission for nr-axSpA with a non-inferiority claim, the submission for upadacitinib (November 2022/March 2023 PBAC), the lower bounds of the 95% CIs in the PBS population comparison of upadacitinib and golimumab also were less than 0.43 for the outcomes of ASAS20 and ASAS40 (Table 7, upadacitinib PSD, November 2022 PBAC meeting with March 2023 addendum).
- 6.23 The PSCR argued the approach applied to inform the clinical claim is consistent with previous b/tsDMARD submissions, and the clinical claim is based upon the results in both the ITT and PBS subpopulations. The Response further argued the results of subgroup analyses of the BE MOBILE 1 trial demonstrate the MRI+/CRP- and MRI-/CRP+ groups have similar outcomes to the MRI+/CRP+ group, which when considering the evidence on the whole, given the uncertainties of small patient

numbers in these subgroups, support a conclusion of non-inferior comparative effectiveness, despite the NIMs not being met in the PBS subpopulation analyses.

- 6.24 The ESC considered the differences between the trials made a robust comparison of bimekizumab and secukinumab challenging, particularly in the PBS subpopulation as the uncertainty of these differences is compounded in smaller post-hoc subgroup analyses. The Pre-PBAC Response argued that the totality of the evidence, when considering the limitations of the PBS subpopulation analyses, supports a conclusion that bimekizumab can reasonably be expected to be non-inferior in the intended PBS population. The Response also argued the ITT population of a trial is the most robust evidence for treatment effect, and argued the sample size and post hoc nature of the PBS subpopulation analyses means they should be interpreted in this context. The Response further noted the differences in the PBS subpopulation were not statistically significant.

Comparative harms

- 6.25 Adverse events in the trials are presented in Table 7. There may have been an excess of minor infections, as expected, but this did not appear to be different for the two active treatments.
- 6.26 Treatment-emergent inflammatory bowel disease was reported as an adverse event in one patient receiving secukinumab; the trial publications did not report whether this led to discontinuation.

Table 7: Adverse events in the trials presented in the submission

	Bimekizumab	Placebo
BE MOBILE 1	N = 128	N = 126
Patients with TEAE to 16 wk, n (%)	80 (62.5%)	71 (56.3%)
URTI or Nasopharyngitis, n (%)	22 (17.2%)	16 (12.7%)
Oral candidiasis, n (%)	4 (3.1%)	0
Patients with STEAE to 16 wk, n (%)	0	1 (0.8%)
Discontinuation due to AE, n (%)	2 (1.6%)	5 (4.0%)
Ulcerative colitis, n (%)	0	1 (0.8%)
Death to 16 wk	0	0
	Secukinumab	Placebo
PREVENT	N = 369	N = 186
Patients with AE to 20 wk, n (%)	226 (61.2%)	101 (54.3%)
URTI or Nasopharyngitis, n (%)	68 (18.4%)	30 (16.1%)
Inflammatory bowel disease, n (%)	1 (0.3%)	0
Patients with SAE to 20 wk, n (%)	6 (1.6%)	5 (2.7%)
Discontinuation due to AE to 20 wk, n (%)	3 (0.8%)	3 (1.6%)
Death	0	0

Source: Submission Tables 2-44, p103; 2-46, p105; 2-50, p108; 2-54, p111.

AE = adverse event; SAE = serious adverse event; STEAE – serious treatment emergent adverse event; TEAE = treatment emergent adverse event; URTI = upper respiratory tract infection.

- 6.27 There was no evidence of severe adverse events or adverse events leading to discontinuation that were not identified as risks with bimekizumab during development. Post-marketing data has led to vulvovaginal candidiasis being noted as

a common adverse event, and oesophageal candidiasis as an uncommon adverse event.

Benefits/harms

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

Clinical claim

6.29 The submission described bimekizumab as non-inferior in terms of effectiveness compared to secukinumab. This claim was adequately supported for patients meeting clinical criteria for nr-axSpA at the whole-trial/ITT population level. The evaluation considered the claim did not appear to be adequately supported for patients meeting the criteria of the proposed restriction/PBS population. The PSCR reiterated the Sponsor's view that whilst there were uncertainties with the comparisons in the PBS population that overall the evidence supported the claim of non-inferior comparative effectiveness. The ESC considered the PBS subgroup analyses were uncertain and it was unclear if they were sufficient to support the claim of non-inferiority.

6.30 The submission described bimekizumab as non-inferior in terms of safety compared to secukinumab. This evaluation and ESC considered this claim was adequately supported.

6.31 The PBAC considered that the claim of non-inferior comparative effectiveness was, on balance, likely to be reasonable.

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

Economic analysis

6.33 The submission presented a cost-minimisation approach. The key assumptions and components are shown in Table 8.

Table 8: Key components and assumptions of the cost-minimisation approach

Component	Claim or assumption
Therapeutic claim: effectiveness	Based on evidence presented in the submission, the effectiveness of bimekizumab is assumed to be non-inferior to secukinumab
Therapeutic claim: safety	Based on evidence presented in the submission, the safety of bimekizumab is assumed to be non-inferior to secukinumab
Evidence base	Indirect comparison of bimekizumab and secukinumab
Equi-effective doses	The EEDs are based on the maintenance doses for BKZ and SEC. With loading doses: SEC 150 mg at weeks 0,1,2,3 and 4 then every 4 weeks = BKZ 160 mg every 4 weeks. Without loading doses: SEC 150 mg every 4 weeks = BKZ 160 mg every 4 weeks.
Direct medicine costs	Cost minimisation of BKZ and SEC is based on the dosage recommendations in the PIs over a 2-year period, which captures the loading and maintenance doses. Total costs of treatment are calculated over the 2-year period and the AEMP is calculated for BKZ based on the required number of packs. Bimekizumab: Bimekizumab comes in a pack with 2x160 mg pre-filled pens. Thus 26 doses (13 packs) are required to treat a patient for 2 years. Secukinumab: Twenty-nine doses are required to treat a patient that requires loading doses for two years, at a total AEMP of \$19,090.12 (DPMQ \$20,506.96). Without a loading dose, the recommended dose is 150 mg by subcutaneous injection every month. Twenty-six doses are required to treat a patient that does not require loading doses for two years at a total AEMP of \$17,115.28 (DPMQ \$18,474.56). Based on a 70:30 split of patients with and without loading doses, the AEMP cost per dose of BKZ is calculated to be \$1,422.90 (DPMQ \$1,558.88), when cost-minimised to the published price of SEC in nr-axSpA.
Other costs or cost offsets	None

Source: Table 3.1, pp 146-147 of the submission.

Abbreviations: BKZ = bimekizumab; SEC = secukinumab; EEDs = equi-effective doses; nr-axSpA = non-radiographic axial spondyloarthritis; mg = milligram; AEMP = approved ex-manufacturer price; DPMQ = dispensed price for maximum quantity.

- 6.34 Based on previous recommendations of the PBAC for calculating equi-effective doses, the equi-effective doses were estimated as bimekizumab 160 mg every 4 weeks over 2 years and secukinumab 150 mg every 4 weeks over 2 years. Calculations were presented with and without the loading dose of secukinumab. These results were based on the published price of the comparator. No other costs were included.
- 6.35 The cost per patient over two years depends on the price used for secukinumab and whether a loading dose is included. If a loading dose is used and the published price of secukinumab, the cost over 2 years is \$19,090.12 AEMP / \$20,506.96 DPMQ. Without a loading dose, it is \$17,115.28/\$18,474.56 respectively. If the cost is calculated using a weighted average price of 70%:30% with and without a loading dose, the AEMP is \$18,497.67. The cost minimised price of bimekizumab using these prices is therefore \$1,422.90 per pack AEMP / \$1,558.88 DPMQ.

Estimated PBS usage & financial implications

- 6.36 This submission was not considered by DUSC.
- 6.37 The submission appropriately presented a market share approach to estimating PBS usage and the financial impact of listing bimekizumab for nr-axSpA. The medicines included in the estimate of market size were secukinumab, certolizumab pegol and golimumab. Upadacitinib was excluded as having been listed only in August 2023. Ixekizumab has not been listed in the PBS although recommended by the PBAC in 2021.
- 6.38 Key inputs and assumptions for the financial estimates are shown in Table 9.
- 6.39 The submission assumed that there would be no market expansion due to listing of bimekizumab and that market growth would be the same as population growth.
- 6.40 The submission assumed that the main market substitution would be for secukinumab.

Table 9: Key inputs for financial estimates

Parameter	Source	Estimate						Justification		
		Year 1	Year 2	Year 3	Year 4	Year 5	Year 6			
Estimated annual growth rate of all bDMARDs	Services Australia - PBS data /population growth, July 2022-June 2023.	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	Assumed to be indexed against population growth given the number of existing products in the market.		
Market share of bimekizumab vs secukinumab	Sponsor patient forecast model	█%	█%	█%	█%	█%	█%	Sponsor assumption		
Proportion of substitution of each medicine affected by bimekizumab	Sponsor estimates	Substitution rates for each medicine		Proportion of each medicine substituted						Not stated – presumed to be sponsor assumption
				Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	
		SEC		█%	█%	█%	█%	█%	█%	
		UPA		█%	█%	█%	█%	█%	█%	
		CER		█%	█%	█%	█%	█%	█%	
		GOL		█%	█%	█%	█%	█%		
Calculation of substituted scripts from utilisation data Initial +continuing		Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Table 4-4 of the submission		
		█ ¹	█ ¹	█ ²	█ ²	█ ²	█ ²			
Grandfathered patients	Not included in estimates although submission proposed a patient familiarisation program. The Pre-PBAC Response stated the Sponsor anticipated fewer than █ ¹ grandfather patients were expected for nr-axSpA.									
Costs (published DPMQ)	Secukinumab: \$710.56, \$3453.52		Certolizumab pegol : \$1,026.68, \$3018.54			Golimumab: \$1161.49				
Patient copayment	PBS: \$34.05 75; RPBS: \$5.30 for all medicines									

Source: Tables 4.2, 4.3, 4.4, 4.10, pp, 185 of the submission; bDMARD = biological disease modifying antirheumatic drug; CER = certolizumab pegol; GOL= golimumab; SEC = secukinumab; UPA = upadacitinib

The redacted values correspond to the following ranges

¹ < 500

² 500 to < 5,000

6.41 The estimated financial implications presented in the submission, using the cost minimised price for bimekizumab based on the published price of secukinumab are summarised in Table 10.

Table 10: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated financial implications of bimekizumab – using secukinumab published price						
Cost to PBS/RPBS less copayments	1	1	1	1	1	1
Estimated financial implications for other medicines						
Cost to PBS/RPBS less copayments	2	2	2	2	2	2
Net financial implications						
Net cost to PBS/RPBS	2	2	2	2	2	2
Estimated financial implications of bimekizumab – using proposed bimekizumab published price						
Cost to PBS/RPBS less copayments	1	1	1	1	1	1
Net financial implications						
Net cost to PBS/RPBS	1	1	1	1	1	1

Source: Tables 4.5, 4.6, 4.12, 4.13 pp158, 165 of the submission

The redacted values correspond to the following ranges

¹\$0 to < \$10 million

² net cost saving

6.42 A Risk Sharing Arrangement remains in place for b/tsDMARDs in nr-axSpA. If listed, it would be appropriate that bimekizumab is included in the arrangement.

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

7 PBAC Outcome

7.1 The PBAC recommended the General Schedule, Authority Required (in writing) listing of bimekizumab for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA). The PBAC’s recommendation was based on, among other matters, its assessment the cost effectiveness of bimekizumab would be acceptable if it were cost minimised to the least costly alternative of certolizumab pegol, golimumab, secukinumab or upadacitinib (as well as ixekizumab if listed on the PBS prior to the listing of bimekizumab).

7.2 The PBAC considered the equi-effective doses of bimekizumab and the alternative biologic or targeted synthetic disease modifying anti-rheumatic drugs (b/tsDMARDs) could be derived with reference to the relevant Product Information documents, noting the bimekizumab equi-effective dose component was 1 x 160 mg injection given at 4-weekly intervals.

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

7.4 The PBAC noted a grandfather restriction was requested for bimekizumab for nr-axSpA and considered this was reasonable, and the grandfather listing should remain

in place for 12 months from the date of listing, per standard policy. The grandfather restriction will have similar eligibility criteria to the initial restriction. A grandfather patient would be required to have met these criteria prior to the non-PBS supply of bimekizumab.

- 7.5 The PBAC noted the only registered and marketed pack size for bimekizumab provides 2 x 160 mg injections per pack. The PBAC noted this pack size is currently PBS listed for psoriasis and provides 8 weeks of therapy at a dose of 320 mg (given as 2 x 160 mg injections) every 8 weeks. The PBAC noted a pack size of 2 injections would also provide 8 weeks of therapy for nr-axSpA patients at a dose of 160 mg (given as 1 x 160 mg injection) every 4 weeks. The PBAC noted it was of a mind to revise the PBS listings for other b/tsDMARD if the listing of this pack size for bimekizumab creates inconsistencies across the listings for nr-axSpA.
- 7.6 The PBAC noted that four treatments were currently PBS listed for nr-axSpA and considered the clinical need for additional therapies for this indication that were of similar effectiveness and safety to other options was low. The Committee noted the IL-17 inhibitor secukinumab was currently listed for nr-axSpA and there was a standing recommendation for ixekizumab (also an IL-17 inhibitor), with further advice noted above.
- 7.7 The PBAC noted the submission nominated secukinumab as the main comparator and considered this was reasonable, given the similar mechanism of action of these two agents. However, the Committee considered that bimekizumab could substitute for any of the PBS listed b/tsDMARDs for nr-axSpA in practice. The Committee noted the advice from the clinician in the Sponsor hearing that tumour necrosis factor inhibitors are generally the first line agent of choice in spondyloarthropathies (AS & nr-axSpA), however noted the restrictions for nr-axSpA are line-agnostic, therefore considered there was no basis to exclude any therapies as alternatives on that basis. The PBAC also did not accept the submission argument that upadacitinib, as an oral therapy, should be excluded as alternative therapies, as clinicians will use the maximum number of treatments allowable under PBS treatment cycle rules, rather than decide to cease treatment based on whether additional options with a similar manner of administration are available.
- 7.8 The PBAC noted no direct trials comparing bimekizumab to secukinumab (or any of the alternative b/tsDMARDs) were available, and the submission relied on an indirect treatment comparison (ITC) with placebo as the common comparator. The Committee noted the ITCs presented were based on comparisons using both the whole trial/intention to treat (ITT) populations of bimekizumab and secukinumab, and also based on the PBS subpopulations using post-hoc subgroup analyses in the MRI+/CRP+ populations of these trials. The Committee noted the analyses presented for the outcomes of Assessment of SpondyloArthritis International Society 20 or 40 (ASAS20/ASAS40) and Bath Ankylosing Spondylitis Disease Activity Index 50 (BASDAI50) were similar to those presented in previous b/tsDMARD submissions for nr-axSpA.

- 7.9 The PBAC noted the results of the whole trial/ITT population analyses found no statistically significant differences between bimekizumab and secukinumab for the outcomes of ASAS40 and BASDAI50, and the lower bound of the 95% CI remained within the nominated non-inferiority margin of 0.43 previously accepted by the Committee. The PBAC noted the results for the outcome of ASAS20 was statistically favoured, however noted the lower bound of the 95% CI approached the null and considered the difference unlikely to be clinically important. Based on the available data, the PBAC considered the submission's claim of non-inferior comparative effectiveness for the whole trial/ITT population level was adequately supported.
- 7.10 With regards to the PBS subgroup analyses, the PBAC noted the lower bounds of the 95% CI for the comparisons of bimekizumab and secukinumab exceeded the non-inferiority margin of 0.43 for all comparisons, however noted the sample sizes for these subgroup analyses were small and this resulted in wide 95% CIs. The PBAC recalled it had previously considered that a claim of non-inferior comparative effectiveness of upadacitinib and golimumab was reasonable, despite the non-inferiority margin for some PBS subgroup analyses not being met (paragraph 7.6, upadacitinib Public Summary Document, November 2022-March 2023 PBAC meeting). Overall, despite the uncertainty of the PBS subgroup analyses, the PBAC considered the claim of non-inferior comparative effectiveness of bimekizumab and secukinumab was, on balance, overall likely to be reasonable.
- 7.11 With respect to comparative safety, the PBAC noted the submission presented a summary of adverse events across the bimekizumab and secukinumab trials and considered that on balance, the safety profiles of these agents appeared to be similar. Overall, the Committee considered the claim of non-inferior comparative safety was reasonable.
- 7.12 The PBAC noted no clinical evidence was provided to support BKZ having superior effectiveness or safety versus any of the alternative therapies for nr-axSpA.
- 7.13 The PBAC considered that a listing based on a cost minimisation approach with costs over two years, consistent with the approach previously used for b/tsDMARDs, was appropriate to determine the cost minimised price of bimekizumab. The PBAC considered the cost of bimekizumab should be no greater than the alternative therapies.
- 7.14 The PBAC noted the utilisation and financial estimates as presented in the submission resulted in an incremental cost for the listing of bimekizumab, however also noted the estimates were based on a price of bimekizumab calculated from a cost minimisation approach using the published price of secukinumab (rather than the least costly alternative). The PBAC considered the uptake and rate of replacement of specific b/tDMARDs to be uncertain, however considered that if listed on a cost minimisation basis with the least costly alternative, the listing would most likely be cost neutral or modestly cost saving to the PBS as it will only replace therapies that are either of

equivalent cost or more expensive. The PBAC also considered it was appropriate for bimekizumab to join the existing Risk Sharing Arrangement (RSA) for nr-axSpA.

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

Outcome:

Recommended

8 Recommended listing

- 8.1 Add new indication/s to bimekizumab as follows:

Initial Treatment/Balance of Supply

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
BIMEKIZUMAB					
bimekizumab 160 mg/mL injection, 2 x 1 mL pen devices	NEW	1	2	1	Bimzelx
bimekizumab 160 mg/mL injection, 2 x 1 mL syringes	NEW	1	2	1	Bimzelx

Restriction Summary [New] / Treatment of Concept: [New]

Edit Restriction Summary 14201 / Treatment of Concept: 14216

Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required – In Writing/HPOS upload
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Indication: Non-radiographic axial spondyloarthritis
	Treatment Phase: Initial treatment - Initial 1 (New patient)
	Clinical criteria: Patient must not have received PBS-subsidised treatment with a biological medicine for this condition
	AND

Public Summary Document – March 2024 PBAC Meeting

Clinical criteria:
Patient must have had chronic lower back pain and stiffness for 3 or more months that is relieved by exercise but not rest
AND
Clinical criteria:
Patient must have failed to achieve an adequate response following treatment with at least 2 non-steroidal anti-inflammatory drugs (NSAIDs), whilst completing an appropriate exercise program, for a total period of 3 months
AND
Clinical criteria:
Patient must have one or more of the following: (a) enthesitis (heel); (b) uveitis; (c) dactylitis; (d) psoriasis; (e) inflammatory bowel disease; or (f) positive for Human Leukocyte Antigen B27 (HLA-B27)
AND
Clinical criteria:
The condition must not be radiographically evidenced on plain x-ray of Grade II bilateral sacroiliitis or Grade III or IV unilateral sacroiliitis
AND
Clinical criteria:
The condition must be non-radiographic axial spondyloarthritis, as defined by Assessment of Spondyloarthritis International Society (ASAS) criteria
AND
Clinical criteria:
The condition must be sacroiliitis with active inflammation and/or oedema on non-contrast Magnetic Resonance Imaging (MRI)
AND
Clinical criteria:
The condition must have presence of Bone Marrow Oedema (BMO) depicted as a hyperintense signal on a Short Tau Inversion Recovery (STIR) image (or equivalent)
AND
Clinical criteria:
The condition must have BMO depicted as a hypointense signal on a T1 weighted image (without gadolinium)
AND
Clinical criteria:
The treatment must not exceed a maximum of 16 weeks with this drug under this restriction
AND
Treatment criteria:
Must be treated by a rheumatologist; or
Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
Prescribing Instructions: The application must include details of the NSAIDs trialled, their doses and duration of treatment. , If the NSAID dose is less than the maximum recommended dose in the relevant TGA-approved Product Information, the application must include the reason a higher dose cannot be used., If treatment with NSAIDs is contraindicated according to the relevant TGA-approved Product Information, the application must provide details of the contraindication., If intolerance to NSAID treatment develops during the relevant period of use which is of a severity to necessitate permanent treatment withdrawal, the application must provide details of the nature and severity of this intolerance.
Prescribing Instructions: The following criteria indicate failure to achieve an adequate response to NSAIDs and must be demonstrated at the time of the initial application:., (a) a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of at least 4 on a 0-10 scale; and, (b) C-reactive protein (CRP) level greater than 10 mg per L., The baseline BASDAI score and CRP level must be determined at the completion of the 3-month NSAID and exercise trial, but prior to ceasing NSAID treatment. All measures must be no more than 4 weeks old at the time of initial application.
Prescribing Instructions: If the requirement to demonstrate an elevated CRP level could not be met, the reason must be stated in the application. Treatment with prednisolone dosed at 7.5 mg or higher daily (or equivalent) or a parenteral steroid within the past month (intramuscular or intravenous methylprednisolone or equivalent) is an acceptable reason.
Prescribing Instructions: The assessment of the patient's response to the initial course of treatment must be conducted following a minimum of 12 weeks of treatment and no later than 4 weeks from the cessation of that treatment course. If the

Public Summary Document – March 2024 PBAC Meeting

	response assessment is not conducted within these timeframes, the patient will be deemed to have failed this course of treatment in this treatment cycle.
	Prescribing Instructions: The authority application must be made in writing and must include: (a) a completed authority prescription form(s); and, (b) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	Prescribing Instructions: The baseline BASDAI score and CRP level must also be documented in the patient's medical records.
	Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au . Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos . Or mailed to: Services Australia, Complex Drugs, Reply Paid 9826, HOBART TAS 7001
Restriction Summary [New] / Treatment of Concept: [New]	
Edit Restriction Summary 14221 / Treatment of Concept: 14208	
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required – Telephone/Electronic
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Indication: Non-radiographic axial spondyloarthritis
	Treatment Phase: Initial treatment - Initial 2 (Change or recommencement of treatment after a break in biological medicine of less than 5 years)
	Clinical criteria:
	Patient must have received prior PBS-subsidised treatment with a biological medicine for this condition in this treatment cycle
	AND
	Clinical criteria:
	The condition must not have responded inadequately to biological medicine on 4 occasions within the same treatment cycle
	AND
	Clinical criteria:
	Patient must not have failed PBS-subsidised therapy with this biological medicine for this PBS indication more than once in the current treatment cycle
	AND
	Clinical criteria:
	The treatment must not exceed a maximum of 16 weeks with this drug under this restriction
	AND
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
	Prescribing Instructions: An application for Initial 2 treatment must indicate whether the patient has demonstrated an adequate response (an absence of treatment failure), failed or experienced an intolerance to the most recent supply of biological medicine treatment. A new baseline Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score and C-reactive protein (CRP) level may be provided at the time of this application.

Public Summary Document – March 2024 PBAC Meeting

	Prescribing Instructions: An adequate response to therapy with this biological medicine is defined as a reduction from baseline in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score by 2 or more units (on a scale of 0-10) and 1 of the following: (a) a CRP measurement no greater than 10 mg per L; or, (b) a CRP measurement reduced by at least 20% from baseline.
	Prescribing Instructions: The assessment of the patient's response to the most recent supply of biological medicine must be conducted following a minimum of 12 weeks of treatment.
	Prescribing Instructions: BASDAI scores and CRP levels must be documented in the patient's medical records.
	Prescribing Instructions: The assessment of the patient's response to the initial course of treatment must be conducted following a minimum of 12 weeks of treatment and no later than 4 weeks from the cessation of that treatment course. If the response assessment is not conducted within these timeframes, the patient will be deemed to have failed this course of treatment in this treatment cycle.
	Prescribing Instructions: The following must be provided at the time of application and documented in the patient's medical records: (a) the BASDAI score; and, (b) the C-reactive protein (CRP) level.
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).
Restriction Summary [New] / Treatment of Concept: [New]	
Edit Restriction Summary 14222 / Treatment of Concept: 14213	
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required – Telephone/Electronic
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Indication: Non-radiographic axial spondyloarthritis
	Treatment Phase: Initial treatment - Initial 3 (Recommencement of treatment after a break in biological medicine of more than 5 years)
	Clinical criteria:
	Patient must have received prior PBS-subsidised treatment with a biological medicine for this condition
	AND
	Clinical criteria:
	Patient must have had chronic lower back pain and stiffness for 3 or more months that is relieved by exercise but not rest
	AND
	Clinical criteria:
	Patient must have had a break in treatment of 5 years or more from the most recently approved PBS-subsidised biological medicine for this condition
	AND
	Clinical criteria:
	Patient must have one or more of the following: (a) enthesitis (heel); (b) uveitis; (c) dactylitis; (d) psoriasis; (e) inflammatory bowel disease; or (f) positive for Human Leukocyte Antigen B27 (HLA-B27)
	AND
	Clinical criteria:
	The condition must not be radiographically evidenced on plain x-ray of Grade II bilateral sacroiliitis or Grade III or IV unilateral sacroiliitis
	AND
	Clinical criteria:

Public Summary Document – March 2024 PBAC Meeting

	The condition must be non-radiographic axial spondyloarthritis, as defined by Assessment of Spondyloarthritis International Society (ASAS) criteria
	AND
	Clinical criteria:
	The condition must be sacroiliitis with active inflammation and/or oedema on non-contrast Magnetic Resonance Imaging (MRI)
	AND
	Clinical criteria:
	The condition must have presence of Bone Marrow Oedema (BMO) depicted as a hyperintense signal on a Short Tau Inversion Recovery (STIR) image (or equivalent)
	AND
	Clinical criteria:
	The condition must have BMO depicted as a hypointense signal on a T1 weighted image (without gadolinium)
	AND
	Clinical criteria:
	The treatment must not exceed a maximum of 16 weeks with this drug under this restriction
	AND
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
	Prescribing Instructions: The following must be provided at the time of application and documented in the patient's medical records:; (a) a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of at least 4 on a 0-10 scale; and, (b) C-reactive protein (CRP) level greater than 10 mg per L.
	Prescribing Instructions: The BASDAI score and CRP level must be no more than 4 weeks old at the time of this application.
	Prescribing Instructions: If the requirement to demonstrate an elevated CRP level could not be met, the reason must be stated in the application. Treatment with prednisolone dosed at 7.5 mg or higher daily (or equivalent) or a parenteral steroid within the past month (intramuscular or intravenous methylprednisolone or equivalent) is an acceptable reason.
	Prescribing Instructions: The assessment of the patient's response to the initial course of treatment must be conducted following a minimum of 12 weeks of treatment and no later than 4 weeks from the cessation of that treatment course. If the response assessment is not conducted within these timeframes, the patient will be deemed to have failed this course of treatment in this treatment cycle.
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).
Restriction Summary [New] / Treatment of Concept: [New]	
Edit Restriction Summary 14193 / Treatment of Concept: 14217	
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required – Telephone/Electronic
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Indication: Non-radiographic axial spondyloarthritis

Public Summary Document – March 2024 PBAC Meeting

	Treatment Phase: Initial 1 (New patient), Initial 2 (Change or recommencement of treatment after a break in biological medicine of less than 5 years) or Initial 3 (Recommencement of treatment after a break in biological medicine of more than 5 years) - balance of supply
	Clinical criteria:
	Patient must have received insufficient therapy with this drug for this condition under the Initial 1 (new patient) restriction to complete 16 weeks treatment; or Patient must have received insufficient therapy with this drug for this condition under the Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 5 years) restriction to complete 16 weeks treatment; or Patient must have received insufficient therapy with this drug for this condition under the Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years) restriction to complete 16 weeks treatment
	AND
	Clinical criteria:
	The treatment must provide no more than the balance of up to 16 weeks treatment
	AND
	Treatment criteria:
	Must be treated by a rheumatologist; or Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
BIMEKIZUMAB					
bimekizumab 160 mg/mL injection, 2 x 1 mL pen devices	NEW	1	2	2	Bimzelx
bimekizumab 160 mg/mL injection, 2 x 1 mL syringes	NEW	1	2	2	Bimzelx
Restriction Summary [New] / Treatment of Concept: [New] Edit Restriction Summary 14192 / Treatment of Concept: 14199					
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required – Telephone/Electronic				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: Special Pricing Arrangements apply.				
	Indication: Non-radiographic axial spondyloarthritis				
	Treatment Phase: Continuing treatment				
	Clinical criteria:				

Public Summary Document – March 2024 PBAC Meeting

	Patient must have received this drug as their most recent course of PBS-subsidised biological medicine treatment for this condition
	AND
	Clinical criteria:
	Patient must have demonstrated an adequate response to treatment with this drug for this condition
	AND
	Clinical criteria:
	The treatment must not exceed a maximum of 24 weeks with this drug per authorised course under this restriction
	AND
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
	Prescribing Instructions: An adequate response to therapy with this biological medicine is defined as a reduction from baseline in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score by 2 or more units (on a scale of 0-10) and 1 of the following; (a) a CRP measurement no greater than 10 mg per L; or, (b) a CRP measurement reduced by at least 20% from baseline.
	Prescribing Instructions: If the requirement to demonstrate an elevated CRP level could not be met under an initial treatment restriction, a reduction in the BASDAI score from baseline will suffice for the purposes of administering this continuing treatment restriction.
	Prescribing Instructions: The patient remains eligible to receive continuing treatment with the same biological medicine in courses of up to 24 weeks providing they continue to sustain an adequate response. It is recommended that a patient be reviewed in the month prior to completing their current course of treatment.
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).
Restriction Summary [New] / Treatment of Concept: [New]	
Edit Restriction Summary 14215 / Treatment of Concept: 10434	
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required – Telephone/Electronic
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Indication: Non-radiographic axial spondyloarthritis
	Treatment Phase: Continuing treatment – balance of supply
	Clinical criteria:
	Patient must have received insufficient therapy with this drug under the Continuing treatment restriction to complete 24 weeks of treatment
	AND
	Clinical criteria:
	The treatment must provide no more than the balance of up to 24 weeks treatment
	AND
	Treatment criteria:
	Must be treated by a rheumatologist; or

Public Summary Document – March 2024 PBAC Meeting

	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).
Restriction Summary [New] / Treatment of Concept: [New]	
Edit Restriction Summary 14198 / Treatment of Concept: 14198	
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required – Telephone/Electronic
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Indication: Non-radiographic axial spondyloarthritis
	Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply - Grandfather arrangements
Placeholder	Clinical criteria:
Placeholder	Patient must have commenced treatment with this biological medicine for this condition prior to [PBS listing date]
	AND
	Clinical criteria:
	<i>Patient must have demonstrated an adequate response following at least 12 weeks of non-PBS-subsidised treatment with this drug for this condition</i>
	AND
	Clinical criteria:
	The condition must not have responded inadequately to biological medicine on 4 occasions within the same treatment cycle
	AND
	Clinical criteria:
	Patient must have had chronic lower back pain and stiffness for 3 or more months that is relieved by exercise but not rest
	AND
	Clinical criteria:
	Patient must have failed to achieve an adequate response following treatment with at least 2 non-steroidal anti-inflammatory drugs (NSAIDs), whilst completing an appropriate exercise program, for a total period of 3 months
	AND
	Clinical criteria:
	Patient must have one or more of the following: (a) enthesitis (heel); (b) uveitis; (c) dactylitis; (d) psoriasis; (e) inflammatory bowel disease; or (f) positive for Human Leukocyte Antigen B27 (HLA-B27)
	AND
	Clinical criteria:
	The condition must not be radiographically evidenced on plain x-ray of Grade II bilateral sacroiliitis or Grade III or IV unilateral sacroiliitis
	AND
	Clinical criteria:
	The condition must be non-radiographic axial spondyloarthritis, as defined by Assessment of Spondyloarthritis International Society (ASAS) criteria
	AND
	Clinical criteria:

Public Summary Document – March 2024 PBAC Meeting

	The condition must be sacroiliitis with active inflammation and/or oedema on non-contrast Magnetic Resonance Imaging (MRI)
	AND
	Clinical criteria:
	The condition must have presence of Bone Marrow Oedema (BMO) depicted as a hyperintense signal on a Short Tau Inversion Recovery (STIR) image (or equivalent)
	AND
	Clinical criteria:
	The condition must have BMO depicted as a hypointense signal on a T1 weighted image (without gadolinium)
	AND
	Clinical criteria:
	The treatment must not exceed a maximum of 24 weeks with this drug per authorised course under this restriction
	AND
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
	Prescribing Instructions: An adequate response to therapy with this biological medicine is defined as a reduction from baseline in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score by 2 or more units (on a scale of 0-10) and 1 of the following: (a) a CRP measurement no greater than 10 mg per L; or, (b) a CRP measurement reduced by at least 20% from baseline.
	Prescribing Instructions: The application must include details of the NSAIDs trialled, their doses and duration of treatment. , If the NSAID dose is less than the maximum recommended dose in the relevant TGA-approved Product Information, the application must include the reason a higher dose cannot be used., If treatment with NSAIDs is contraindicated according to the relevant TGA-approved Product Information, the application must provide details of the contraindication., If intolerance to NSAID treatment develops during the relevant period of use which is of a severity to necessitate permanent treatment withdrawal, the application must provide details of the nature and severity of this intolerance.
	Prescribing Instructions: The following criteria indicate failure to achieve an adequate response to NSAIDs and must be demonstrated at the time of the initial application: (a) a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of at least 4 on a 0-10 scale; and, (b) C-reactive protein (CRP) level greater than 10 mg per L., The baseline BASDAI score and CRP level must be determined at the completion of the 3-month NSAID and exercise trial, but prior to ceasing NSAID treatment. All measures must be no more than 4 weeks old at the time of initial application.
	Prescribing Instructions: If the requirement to demonstrate an elevated CRP level could not be met, the reason must be stated in the application. Treatment with prednisolone dosed at 7.5 mg or higher daily (or equivalent) or a parenteral steroid within the past month (intramuscular or intravenous methylprednisolone or equivalent) is an acceptable reason.
	Prescribing Instructions: The assessment of the patient's response to the initial course of treatment must be conducted following a minimum of 12 weeks of treatment and no later than 4 weeks from the cessation of that treatment course. If the response assessment is not conducted within these timeframes, the patient will be deemed to have failed this course of treatment in this treatment cycle.
	Prescribing Instructions: The authority application must be made in writing and must include: (a) a completed authority prescription form(s); and, (b) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	Prescribing Instructions: The baseline BASDAI score and CRP level must also be documented in the patient's medical records.
	Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday)., Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au , Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos , Or mailed to: Services Australia, Complex Drugs, Reply Paid 9826, HOBART TAS 7001

Common administrative note: Concept 30890

PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS - TREATMENT CYCLES AND TREATMENT PHASES, Where the term 'biological medicine' appears in notes and restrictions, it refers to pharmaceutical benefits listed specifically for the indication of: non-radiographic axial spondyloarthritis. Some listed pharmaceutical benefits are technically not biological medicines (e.g. Janus-kinase inhibitors), but for practical purposes, have been included under the broad term of 'biological medicine'. A patient is eligible for PBS-subsidised treatment with only 1 biological medicine at any one time. Treatment cycles: A treatment cycle commences when the authority application for first PBS-subsidised biological medicine is approved for a given patient under the 'Initial 1' treatment phase. The treatment cycle continues until a fourth biological medicine fails to provide the patient with an adequate response. A new treatment cycle begins each time PBS subsidy is obtained through the 'Initial 3' treatment phase. Within a treatment cycle, the same PBS-subsidised biological medicine must not be subsidised more than once where it has failed to provide the patient with an adequate response on any occasion that a response assessment is conducted. Once biological medicines have failed to provide a patient with an adequate response 4 times (once with any biological medicine) within the same treatment cycle, the treatment cycle has been completed and the patient must have, at a minimum, a 5-year break in PBS-subsidised biological medicine therapy before they are eligible to commence the next cycle. The 5-year break is measured from the date of the last prescription for PBS-subsidised biological medicine treatment in the most recent cycle to the date of the first application for initial treatment with a biological medicine under the new treatment cycle. A serious adverse reaction requiring permanent withdrawal of treatment, including serious infusion or injection related reactions, Steven's Johnson Syndrome, development of a demyelinating lesion, progressive multifocal leukoencephalopathy and malignancy related to treatment with the biological medicine, is not considered as a completed treatment attempt. Where there have been fewer than 4 inadequate responses with biological medicine therapy in a treatment cycle and there has been a break in therapy of less than 5 years, the patient may continue treatment within the same treatment cycle. A patient who has had a break in therapy of more than 5 years may commence a new treatment cycle with up to 4 treatment attempts. There is no limit to the number of treatment cycles a patient may undertake in their lifetime. Treatment phases: (1) Initial treatment. Applications for initial treatment should be made where: (i) no prior PBS-subsidised biological medicine treatment has been prescribed - apply through the 'Initial 1 - New patient' treatment phase, (ii) a patient has received prior PBS-subsidised (initial or continuing) biological medicine therapy, but is prescribed an alternate biological medicine - apply through the 'Initial 2 - Change or Recommencement of treatment after a break in therapy of less than 5 years' [further details are under 'Changing the prescribed biological medicine' below]; or, (iii) a patient is recommencing treatment following a break in PBS-subsidised therapy of less than 5 years - apply through the 'Initial 2 - Change or Recommencement of treatment after a break in therapy of less than 5 years' treatment phase (note that where there is both a change and recommencement after less than 5 years occurring simultaneously, Initial 2 is the correct treatment phase to apply through); or, (iv) a patient is recommencing treatment with a biological medicine following a break in PBS-subsidised therapy of more than 5 years - apply through the 'Initial 3 - Recommencement of treatment after a break in biological medicine of more than 5 years' treatment phase. A patient must be assessed for response to a course of initial PBS-subsidised treatment following a minimum of 12 weeks of therapy. (2) Continuing treatment. For continuing PBS subsidy of biological medicine it is recommended that a patient be reviewed the month prior to when the continuing dose is due to ensure uninterrupted biological medicine supply. Continuing PBS subsidy is available in quantities/repeats that provide up to 24 weeks of continuing treatment where an adequate response to the immediately preceding supply of treatment has been experienced. A patient must be assessed for response to a course of continuing therapy, and the assessment must be conducted no later than 4 weeks from the cessation of that treatment course. Where a response assessment is not conducted within the required timeframe, the treatment will be deemed to have failed to provide an adequate response, unless the patient has experienced a serious adverse reaction requiring permanent treatment withdrawal. (3) Changing the prescribed biological medicine. Once initial treatment with the first PBS-subsidised biological medicine is approved, an alternate biological medicine may be prescribed within the same treatment cycle without having to requalify with respect to the indices of disease severity (i.e. the C-reactive protein (CRP) level and the BASDAI score), or the prior NSAID therapy and exercise program requirements. An authority application must be made under the 'Initial 2' treatment phase and must indicate the response to the preceding biological medicine in terms of whether the response was adequate or not. The prescription for the discontinued biological medicine must be marked as cancelled by the prescriber. (4) Baseline measurements to determine response. A response to treatment is based on the baseline BASDAI score and CRP level documented in the patient's medical records. For a patient untreated with biological medicines, the BASDAI score used to determine baseline disease severity must be measured while the patient is receiving NSAID therapy and completing their exercise program. To ensure consistency in determining response, the same indices of disease severity used to establish baseline must be used for all subsequent continuing treatment

applications., Prescribers may provide new baseline measurements any time that an 'Initial treatment' authority application is submitted and the eligibility for continuing treatment must be assessed according to these revised baseline measurements., (5) Recommencement of treatment after a 5-year break in PBS-subsidised therapy., A second or subsequent course of treatment following a break in PBS-subsidised biological medicine therapy of at least 5 years, must occur through the Initial 3 treatment restriction. The same clinical criteria and indices of disease severity (i.e. the C-reactive protein (CRP) levels and the BASDAI) as for the Initial 1 (New patient) restriction will need to be met, but a re-trial of NSAID therapy and exercise therapy is not required., (6) Balance of Supply, Where the full number of repeat prescriptions have not been requested under any initial or continuing listing, apply for the balance of the supply of the repeats under any treatment phase listing containing the words 'balance of supply'.

This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.

9 Context for Decision

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

10 Sponsor's Comment

The sponsor had no comment.