

5.04 BIMEKIZUMAB,

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

1 Purpose of submission

- 1.1 The Category 2 submission requested Authority Required listing for bimekizumab for the treatment of radiographically confirmed (active) ankylosing spondylitis (AS).
- 1.2 Listing was requested on the basis of a cost-minimisation approach versus secukinumab. If listed, bimekizumab would be the 10th biological or targeted synthetic disease modifying anti-rheumatic drug (b/tsDMARD) listed for AS, alongside five tumour necrosis factor alpha (TNF α) inhibitors (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab), two IL-17 inhibitors (ixekizumab, secukinumab) and two Janus kinase (JAK) inhibitors (tofacitinib, upadacitinib).
- 1.3 The key components of the submission are shown in Table 1.

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

Component	Description
Population	Adults with radiographic confirmed (active) ankylosing spondylitis (AS) who failed to achieve an adequate response following treatment with at least 2 NSAIDs or are contraindicated to NSAIDs, while completing an appropriate exercise program, for a total of three months.
Intervention	Bimekizumab (BKZ) 160 mg subcutaneously (SC) every 4 weeks (Q4W)
Comparator	Secukinumab (SEC) 150 mg SC at Weeks (W) 0, 1, 2, 3, and 4 followed by 150 mg every 4 weeks.
Outcomes	ASAS20, ASAS40, BASDAI50 Safety
Clinical claim	In adults with AS, BKZ 160 mg SC Q4W is noninferior in terms of effectiveness compared with SEC 150 mg SC at W0, W1, W2, W3, W4 and Q4W thereafter in patients with AS. BKZ 160 mg SC Q4W is noninferior in terms of safety compared with SEC 150 mg SC at W0, W1, W2, W3, W4 and Q4W thereafter in patients with AS.

Source: Table ES-1, p2 of the submission.

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 and BE AGILE, no worsening in remaining domain; BASDAI = Bath ankylosing spondylitis disease activity index; BASDAI50 is a 50% reduction in score.

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 AS.
- 2.2 Bimekizumab is registered in Australia for the treatment of plaque psoriasis in adults. In addition to the AS indication, the TGA is also considering applications for bimekizumab for psoriatic arthritis and non-radiological axial spondyloarthritis concurrently.

Previous PBAC consideration

- 2.3 Bimekizumab was assessed by the PBAC in March 2022 and March 2023, for the indication of severe chronic plaque psoriasis and was listed in October 2023 for this indication. It has not been previously considered for AS.
- 2.4 The sponsor has lodged separate submissions to the PBAC for consideration at the March 2024 PBAC meeting, requesting listing of BKZ for the treatment of non-radiographic axial spondyloarthritis and psoriatic arthritis.

3 Requested listing

- 3.1 The submission proposed restrictions for initial and continuing treatment that were the same as for the currently listed b/tsDMARDS for active ankylosing spondylitis. The Pre-PBAC Response acknowledged that for initial treatment, a maximum number of repeats of 1 would be required for the 16-week period.
- 3.2 The submission also proposed a Special Pricing Arrangement, with the same published prices as for the currently listed bimekizumab preparations and an effective price to be based on cost minimisation to secukinumab.

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

- 3.3 An abbreviated restriction is shown below, for initial treatment in a new patient.

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
Indication: Ankylosing spondylitis
Treatment Phase: Initial
Clinical criteria:

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The condition must be radiographically (plain X-ray) confirmed Grade II bilateral sacroiliitis or Grade III unilateral sacroiliitis
AND
Clinical criteria:
Patient must not have received PBS-subsidised treatment with a biological medicine for this condition
AND
Clinical criteria:
Patient must have at least 2 of the following: (i) low back pain and stiffness for 3 or more months that is relieved by exercise but not by rest; or (ii) limitation of motion of the lumbar spine in the sagittal and the frontal planes as determined by a score of at least 1 on each of the lumbar flexion and lumbar side flexion measurements of the Bath Ankylosing Spondylitis Metrology Index (BASMI); or (iii) limitation of chest expansion relative to normal values for age and gender
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 not receive more than 16 weeks of treatment under this restriction
Treatment criteria:
Must be treated by a rheumatologist; or
Must be treated by a clinical immunologist with expertise in the management of ankylosing spondylitis
Population criteria:
Patient must be aged 18 years or older
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 and must be demonstrated at the time of the initial application: (a) a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of at least 4 on a 0-10 scale; AND (b) an elevated erythrocyte sedimentation rate (ESR) greater than 25 mm per hour or a C-reactive protein (CRP) level greater than 10 mg per L. The BASDAI must be determined at the completion of the 3 month NSAID and exercise trial, but prior to ceasing NSAID treatment. The BASDAI must be no more than 1 month old at the time of initial application. Both ESR and CRP measures should be provided with the initial treatment application and both must be no more than 1 month old. If the above requirement to demonstrate an elevated ESR or CRP cannot be met, the application must state the reason this criterion cannot be satisfied.
Prescribing Instructions:
The authority application must be made in writing and must include: (a) a completed authority prescription form; and (b) a completed Ankylosing Spondylitis PBS Authority Application - Supporting Information Form which includes the following: (i) a copy of the radiological report confirming Grade II bilateral sacroiliitis or Grade III unilateral sacroiliitis; and (ii) a completed BASDAI Assessment Form; and (iii) a completed Exercise Program Self Certification Form included in the supporting information form.

<p>Prescribing Instructions: An assessment of a patient's response to an initial course of treatment must be conducted following a minimum of 12 weeks of therapy. An application for the continuing treatment must be accompanied with the assessment of response and submitted no later than 4 weeks from the date of completion of the most recent course of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment.</p>
<p>Prescribing Instructions: Where the response assessment is not submitted within this timeframe, the patient will be deemed to have failed to respond to treatment with this drug.</p>
<p>Prescribing Instructions: If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition. Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.</p>
<p>Administrative Advice: Details of the toxicities, including severity, which will be accepted for the purposes of administering this restriction can be found on the Services Australia website at www.servicesaustralia.gov.au</p>
<p>Administrative Advice: For details on the appropriate minimum exercise program that will be accepted for the purposes of administering this restriction, please refer to the Services Australia website at www.servicesaustralia.gov.au</p>
<p>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. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

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; uveitis; and dactylitis (swelling of the fingers).
- 4.2 SpA with mainly axial manifestations (axSpA) is divided into axSpA with sacro-iliitis on plane XR, called radiographic axial spondyloarthritis (r-axSpA), usually referred to by its older name, ankylosing spondylitis (AS), and axSpA with no or minimal sacro-iliitis on plane XR, called non-radiographic axial spondyloarthritis (nr-axSpA). AS is more common in men, while nr-axSpA is as common in women as in men.
- 4.3 The cardinal feature of axSpA is low back pain. About 5% of patients with chronic back pain have axSpA. About 80% of patients with axSpA have a pattern of symptoms referred to as inflammatory back pain, with at least four of the following five features: improvement with exercise, pain at night, insidious onset, onset at < 40 years, and

lack of improvement with rest.¹ However, this pattern of symptoms is seen in about 25% of patients with chronic back pain who do not have axSpA, so a large majority of patients with these symptoms do not have axSpA.

- 4.4 SpA is associated with psoriasis, inflammatory bowel disease (Crohn Disease and ulcerative colitis) and some infections (reactive arthritis, also called Reiter's Syndrome). The distinction between, e.g., SpA in a patient with psoriasis, and psoriatic arthritis, is not clear-cut.
- 4.5 The first line treatment of axSpA is non-steroidal anti-inflammatory drugs (NSAIDs). NSAID treatment is effective in a majority of patients; e.g., in a trial of patients with active disease, naproxen produced an ASAS20 response in 72.5% and an ASAS40 response in 56.9% at 28 weeks.²
- 4.6 Patients with axSpA not responding adequately to NSAIDs can be treated with a TNF α inhibitor (e.g., etanercept, infliximab, adalimumab, etc) an interleukin-17 (IL-17) inhibitor (secukinumab, ixekizumab or bimekizumab), or a Janus kinase (JAK) inhibitor (tofacitinib or upadacitinib) on the PBS. These drugs and classes have known properties which play a part in treatment choice for individual patients.
- 4.7 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, 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. Bimekizumab binds to both IL-17A and IL-17F, whereas other PBS-listed IL-17 inhibitors (secukinumab and ixekizumab) are specific for IL-17A.
- 4.8 Because of their mechanism of action, IL-17 inhibitors are contra-indicated in active, clinically significant infections, and are associated with an increase in infections, most often nasopharyngitis and muco-cutaneous candidiasis, during treatment.

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

5 Comparator

- 5.1 The submission nominated secukinumab as the comparator.

¹ Sieper J, van der Heijde D, Landewe R, et al. New criteria for inflammatory back pain in patients with chronic back pain: A real patient exercise by experts from the Assessment of SpondyloArthritis international Society (ASAS). *Ann Rheum Dis* 2009;68:784-788.

² Sieper J, Lenaerts J, Wollenhaupt J, et al. Efficacy and safety of infliximab + naproxen vs naproxen alone in patients with early, active axial spondyloarthritis: results from the double-blind, placebo-controlled INFAST study, Part 1. *Ann Rheum Dis* 2014; 73:101-107.

- 5.2 While secukinumab may be a reasonable comparator for bimekizumab (given both act on the IL-17 pathway, albeit with differences), the proposed listing was for all patients failing NSAID treatment, and, in principle, any other treatment with a similar listing may be replaced. It was conceded by the submission that, absent other factors, a TNF α inhibitor would be the appropriate comparator. The submission also included other treatments in its estimates of use and financial impact.
- 5.3 The submission maintained that one such other factor affecting comparator selection was that practitioners would switch among subcutaneously administered treatments but would not be likely to switch from a treatment given orally (i.e., JAK inhibitors) or intravenously (such as infliximab) 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 IV or 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 AS.
- 5.4 In the context of the cost-minimisation approach taken by the submission, a further consideration for PBAC is that, under Section 101(3B) of the National Health Act 1953, when the proposed medicine is substantially more costly than an alternative therapy, the committee cannot make a positive recommendation unless it is satisfied that, for some patients, the proposed medicine provides a significant improvement in efficacy and/or reduction of toxicity over the alternative therapy. If the committee is so satisfied, it must make a statement to this effect.
- 5.5 For the requested population, the following PBS-listed medicines may be considered alternative therapies because they could be replaced in practice: adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, ixekizumab, secukinumab, tofacitinib and upadacitinib.
- 5.6 The Pre-PBAC Response (pp. 2-3) argued that while bimekizumab could replace any listed b/tsDMARD in practice, a combination of the mechanism of action and route of administration meant replacement of some therapies was more likely than others. The Response also argued that bimekizumab was more likely to be used after a TNF α inhibitor (i.e. second line) and that BKZ may offer a safer and/or more effective treatment option. The PBAC considered that while a combination of these factors may impact that rate at which bimekizumab replaces some agents, also considered the PBS listings for b/tsDMARDs for AS were line agnostic, and therefore any treatment could be chosen in any line within a treatment cycle.

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-radiographic axial spondylarthritis as a single hearing, as the two conditions are related. The clinician discussed the evidence of effectiveness for 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.

Consumer comments

- 6.2 The PBAC noted and welcomed the input from individuals (1), health care professionals (1) and 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 highlighted the importance of having ongoing availability of different medications for AS, as patients often lose response to treatments over time and new options are needed.

Clinical trials

- 6.3 The submission was based on two trials, BE MOBILE 2 (NCT 03928743) and BE AGILE, comparing bimekizumab to placebo, and an indirect treatment comparison (ITC) with secukinumab using three trials, MEASURE 2, MEASURE 4, and MEASURE 5, comparing secukinumab to placebo. BE AGILE 2, an open-label extension (OLE) of BE AGILE, provided longer term safety data.
- 6.4 Trial AS0013 (NCT03215277) was excluded because it used “the wrong comparator”. This was randomised, double-blind comparison of bimekizumab and certolizumab pegol, a subcutaneously administered TNF α inhibitor, in patients with AS. It was stated in the submission that “results of this trial are expected in 2024”, but results are available on the clinical trials.gov website.³
- 6.5 Trial AS0014 (NCT04436640) was excluded because it included “patients with both AS and non-radiographic axSpA”. AS0014 is an open label extension (OLE) of two separate trials, NCT03928704, BE MOBILE 1, which enrolled patients with nr-axSpA, and the included trial NCT03928743, BE MOBILE 2, which enrolled patients with AS, so there

³ <https://clinicaltrials.gov/study/NCT03215277?tab=results> accessed 9 December 2023.

were two distinct groups, not a single group of patients with undifferentiated axSpA. The start date for NCT04436640 is listed as June 2020, and the estimated completion date as August 2026, so there may not yet be any data from this study, but if there is, the data for AS patients should have been included.

6.6 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
Bimekizumab vs placebo		
BE MOBILE 2 (AS0011) NCT03928743	A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating The Efficacy And Safety Of Bimekizumab In Subjects With Active Ankylosing Spondylitis van der Heijde D, Deodhar A, Baraliakos X, et al., 2023. Efficacy and safety of bimekizumab in axial spondyloarthritis: results of two parallel phase 3 randomised controlled trials."	<i>Ann Rheum Dis</i> 2023; 82: 515-526. Correction published in <i>Ann Rheum Dis</i> 2023; 82:e213.
BE AGILE (AS0008) NCT02963506	A Multicenter, Phase 2B, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Dose-Ranging Study to Evaluate the Efficacy and Safety of Bimekizumab in Study participants with Active Ankylosing Spondylitis van der Heijde D, Gensler L, Deodhar A, et al. Dual neutralisation of interleukin-17A and interleukin-17F with bimekizumab in patients with active ankylosing spondylitis: results from a 48-week phase IIb, randomised, double-blind, placebo-controlled, dose-ranging study.	<i>Ann Rheum Dis</i> 2020; 79: 595-604. Corrections published in <i>Ann Rheum Dis</i> 2020; 79:e121, and in <i>Ann Rheum Dis</i> 2021; 80:e186.
Bimekizumab open-label extension		
BE AGILE 2 (AS0009) NCT03355573	A Multicenter, Open-Label Extension Study to Evaluate the Long-Term Safety and Efficacy of Bimekizumab in Subjects with Ankylosing Spondylitis Baraliakos X, Deodhar A, Dougados M, et al. Safety and efficacy of bimekizumab in patients with active ankylosing spondylitis: Three-year results From a Phase IIb randomized controlled trial and its open-label extension study.	<i>Arthritis Rheumatol</i> 2022; 74: 1943-1958.
Secukinumab vs placebo		
MEASURE 2 NCT01649375	A Randomized, Double-blind, Placebo-controlled Phase III Study of Subcutaneous Secukinumab in Prefilled Syringes to Demonstrate Efficacy at 16 Weeks and to Assess Long-term Efficacy, Safety and Tolerability up to 5 Years in Patients With Active Ankylosing Spondylitis Baeten D, Sieper J, Braun J, et al. Secukinumab, an interleukin-17A inhibitor, in ankylosing spondylitis. Sieper J, Deodhar A, Marzo-Ortega H, et al. Secukinumab efficacy in anti-TNF-naïve and anti-TNF-experienced subjects with ankylosing spondylitis: results from the MEASURE 2 study. Marzo-Ortega H, Sieper J, Kivitz A, et al. Secukinumab and sustained improvement in signs and symptoms of patients with active ankylosing spondylitis through two years: Results from a Phase III study.	<i>N Engl J Med</i> 2015; 373: 2534-2548 <i>Ann Rheum Dis</i> 2017; 76:571-592. <i>Arthritis Care Res</i> 2017; 69: 1020-1029.
	Marzo-Ortega H, Sieper J, Kivitz A, et al. Secukinumab provides sustained improvements in the signs and symptoms of active ankylosing spondylitis with high retention rate: 3-year results from the phase III trial, MEASURE 2.	<i>RMD Open</i> 2017; 3: e000592.

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Trial ID	Protocol title/ Publication title	Publication citation
Bimekizumab vs placebo		
	<p>Deodhar A, Conaghan P, Kvien T, et al. Secukinumab provides rapid and persistent relief in pain and fatigue symptoms in patients with ankylosing spondylitis irrespective of baseline C-reactive protein levels or prior tumour necrosis factor inhibitor therapy: 2-year data from the MEASURE 2 study.</p> <p>Marzo-Ortega H, Sieper J, Kivitz A, et al. 5-year efficacy and safety of secukinumab in patients with ankylosing spondylitis: end-of-study results from the phase 3 MEASURE 2 trial.</p> <p>Kishimoto, M, Taniguchi A, Fujishige A, et al. Efficacy and safety of secukinumab in Japanese patients with active ankylosing spondylitis: 24-week results from an open-label phase 3 study (MEASURE 2-J).</p> <p>Kvien T, Conaghan P, Gossec L, et al. Secukinumab and sustained reduction in fatigue in patients with ankylosing spondylitis: Long-term Results of two Phase III randomized controlled trials.</p>	<p><i>Clin Exp Rheumatol</i> 2018; 37: 260-269.</p> <p><i>Lancet Rheumatology</i>, 2020; 2: E339-E346.</p> <p><i>Modern Rheumatol</i> 2020; 30: 132-140.</p> <p><i>Arthritis Care Res</i> 2022; 74:759-767.</p>
MEASURE 4 NCT02159053	<p>A Randomized, Double-blind, Placebo-controlled, Phase III Multicenter Study of Subcutaneous Secukinumab (150 mg) With and Without a Subcutaneous Loading Regimen to Assess Efficacy, Safety, and Tolerability up to 2 Years in Patients With Active Ankylosing Spondylitis</p> <p>Kivitz A, Wagner U, Dokoupilova E, et al. Efficacy and safety of secukinumab 150 mg with and without loading regimen in ankylosing spondylitis: 104-week results from MEASURE 4 study.</p>	<p><i>Rheumatol Ther</i> 2018; 5: 447-462.</p>
MEASURE 5 ¹ NCT02896127	<p>Randomized, Double-blind, Placebo-controlled, Phase III Multicenter Study of Subcutaneous Secukinumab to Compare Efficacy at 16 Weeks With Placebo and Assess Safety and Tolerability up to 52 Weeks in Subjects With Active Ankylosing Spondylitis</p> <p>Huang F, Sun F, Wan W, et al. Secukinumab provided significant and sustained improvement in the signs and symptoms of ankylosing spondylitis: results from the 52-week, Phase III China-centric study, MEASURE 5.</p>	<p><i>Chin Med J (Engl)</i> 2020; 133: 2521-2531.</p>

Source: Table 2.5, pp67-8 of the submission.

NR = not reported.

¹ MEASURE 5 is referred to as a China-centric study because 24/44 study centres were in China; other sites were in Czechia, Republic of Korea, and UK. Eighty-one per cent of participants were categorised as Asian. <https://clinicaltrials.gov/study/NCT02896127> accessed 10 December 2023.

6.7 The key features of these 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 2	332	R, DB, 16 wk, randomised 2:1 to bim 160 mg 4 wkly or placebo, then 36 wk OLE	Low	Adults; AS by Modified NY criteria, 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
BE AGILE	285, 114 randomised to bim 160 mg or placebo	R, DB, 12 wk, randomised to bim 4 wkly, 16 mg, 64 mg, 160 mg, 320 mg or placebo; after DB period patients on placebo or bim 16 mg or 64 mg re-randomised to bim 160 mg or 320 mg for 36 wk dose-blind OLE	Low	Adults; AS by Modified NY criteria, 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 or lost access for other reasons.	ASAS40 at 12 wk	Data from patients randomised to 160 mg dose or placebo used
Secukinumab vs placebo						
MEASURE 2		R, DB, 16 wk, randomised to sec 150 mg wk 0, 1,2,3 then 4 wkly, or sec 75 mg wk 0,1,2,3 then 4 wkly or placebo; after DB phase re-randomised to 150 mg or 75 mg 4 wkly for 244 wk dose-blind OLE	Low	Adults; AS by Modified NY criteria; 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.	ASAS20 at 16 wk; ASAS40 at 16 wk was a secondary outcome.	Data from patients randomised to 150 mg dose or placebo used.
MEASURE 4	350, 233 randomised to sec 150 mg with loading doses or placebo	R, DB, 16 wk, randomised to sec 150 mg 4 wkly with loading doses, 150 mg 4 wkly without loading doses or placebo; then 96 wk OLE	Low	Adults; AS by Modified NY criteria; 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.	ASAS20 at 16 wk; ASAS40 at 16 wk was a secondary outcome.	Data from patients randomised to 150 mg dose with loading doses or placebo used.

Trial	N	Design/duration	Risk of bias	Patient population	Primary Outcome	Use in Modelled Evaluation
MEASURE 5	458	R, DB, 16 wk, randomised to sec 150 mg wk 0, 1,2,3,4 then 4 wkly or placebo; then 36 wk OLE	Low	Adults; AS by Modified NY criteria; BASDAI ≥ 4 , and BASDAI item 2 (spinal pain) ≥ 4 and total back pain ≥ 40 mm on 100 mm VAS; ≥ 2 failed NSAID; if prior TNF α inhibitor must have failed or been intolerant.	ASAS20 at 16 wk; ASAS40 at 16 wk was a secondary outcome.	Used

Source: constructed during the evaluation from: Submission Figures 2-4, 2-5, 2-6, 2-7, 2-8, pp71-74; Tables 2.12, pp80-1; 2.13, pp82-3; 2.21, p91; 2.22, p92.

AS = ankylosing spondylitis; 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 and BE AGILE, no worsening in remaining domain; ASDAS = Ankylosing Spondylitis Disease Activity Score, calculated as the sum of $0.121 \times$ BASDAI item 2 = spinal pain, $0.058 \times$ BASDAI item 6 = duration of morning stiffness, $0.110 \times$ PGADA = patient's global assessment of disease activity, $0.073 \times$ BASDAI item 3 = peripheral joint pain and swelling, $0.579 \times$ (natural logarithm of C-reactive protein [mg/L] + 1). There is a minimum score of 0.98, because values of C-reactive protein below the lower limit of quantification are assigned a value of 2, but no maximum. Reduced scores indicate improvement. BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; bim = bimekizumab; DB = double blind; NSAID = non-steroidal anti-inflammatory drug; NY = New York; OLE = open-label extension; R = randomised; sec = secukinumab; VAS = visual analog scale

- 6.8 The definition of ASAS20 used in the MEASURE trials was that of the Assessment of Spondyloarthritis international Society (ASAS) handbook: 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.⁴ A slightly different definition was used in BE MOBILE 2, in that no worsening in the fourth domain was allowed (CSR, p65/375).
- 6.9 Baseline characteristics of patients enrolled in the included trials are shown in Table 4 and Table 5. Characteristics were similar across the trials.

⁴ 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: Baseline characteristics of patients enrolled in bimekizumab trials

	BE MOBILE 2		BE AGILE	
	Bimekizumab N= 221	Placebo N = 111	Bimekizumab N = 60	Placebo N = 60
Age, years, mean (SD)	41.0 (12.1)	39.1 (12.6)	42.4 (13.1)	39.7 (10.3)
Male, n (%)	160 (72.4%)	80 (72.1%)	52 (86.7%)	49 (81.7%)
Time since diagnosis of AS, years, mean (SD)	6.7 (8.3)	5.7 (6.9)	8.8 (9.2)	6.6 (7.2)
HLA-B27, n (%)	191 (86.4%)	93 (83.8%)	52 (86.7%)	57 (95.0%)
TNF α inhibitor naïve, n (%)	184 (83.3%)	94 (84.7%)	53 (88.3%)	53 (86.9%)
BASDAI total score, mean (SD)	6.45 (1.33)	6.51 (1.31)	6.25 (1.32)	6.51 (1.43)

Source: Table 2-14, p84 of the submission.

AS = ankylosing spondylitis; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; HLA = human leukocyte antigen; TNF α = tissue necrosis factor alpha.

Table 5: Baseline characteristics of patients enrolled in secukinumab trials

	MEASURE 2		MEASURE 4		MEASURE 5	
	Secukinumab N = 72	Placebo N = 74	Secukinumab N = 116	Placebo N = 117	Secukinumab N = 305	Placebo N = 153
Age, years, mean (SD)	41.9 (12.5)	43.6 (13.2)	44.5 (11.6)	43.4 (12.5)	35.1 (10.4)	33.0 (10.0)
Male, n (%)	46 (64%)	56 (76%)	81 (70%)	76 (65%)	252 (83%)	132 (86%)
Time since diagnosis of AS, years, mean (SD)	7.0 (8.2)	6.4 (8.9)	8.4 (10.8)	7.1 (9.2)	5.7 (6.4)	5.3 (6.0)
HLA-B27, n (%)	57 (79%)	58 (78%)	100 (86%)	93 (80%)	276 (90%)	142 (93%)
TNF α inhibitor naïve, n (%)	44 (61%)	45 (61%)	85 (73%)	83 (71%)	240 (79%)	122 (80%)
BASDAI total score, mean (SD)	6.6 (1.5)	6.8 (1.3)	7.0 (1.2)	7.1 (1.3)	6.9 (1.4)	6.9 (1.2)

Source: Table 2-15, p86 of the submission.

AS = ankylosing spondylitis; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; HLA = human leukocyte antigen; TNF α = tissue necrosis factor alpha.

Comparative effectiveness

6.10 The results of the trials are shown in Table 6.

Table 6: Primary outcomes and secondary outcomes used in the indirect treatment comparison for the trials presented in the submission.

	Bimekizumab	Placebo
BE MOBILE 2	N = 221	N = 111
ASAS40 at 16 wk, n (%)	99 (44.8%)	25 (22.5%)
RR vs placebo (95% CI)	1.99 (1.37, 2.89)	
ASAS20 at 16 wk, n (%)	146 (66.1%)	48 (43.2%)
RR vs placebo (95% CI)	1.53 (1.21, 1.93)	
BASDAI change from baseline, LS mean (SE)	-2.74 (0.17)	-1.70 (0.21)
Mean difference bimekizumab – placebo (95% CI)	-1.04 (-1.57, -0.51)	
BE AGILE	N = 60	N = 60
ASAS40 at 12 wk, n (%)	28 (46.7%)	8 (13.3%)
RR vs placebo (95% CI)	3.50 (1.74, 7.04)	
ASAS20 at 12 wk, n (%)	35 (58.3%)	17 (28.3%)
RR vs placebo (95% CI)	2.06 (1.31, 3.25)	
BASDAI change from baseline, LS mean (SE)	-2.60 (0.38)	-1.0 (0.38)
Mean difference bimekizumab – placebo (95% CI)	-1.60 (-2.65, -0.55)	
	Secukinumab	Placebo
MEASURE 2	N = 72	N = 74
ASAS40 at 16 wk, n (%)	26 (36.1%)	8 (10.8%)
RR vs placebo (95% CI)	3.34 (1.62, 6.88)	
ASAS20 at 16 wk, n (%)	44 (61.1%)	21 (28.4%)
RR vs placebo (95% CI)	2.15 (1.43, 3.23)	
BASDAI change from baseline, LS mean (SE)	-2.19 (0.25)	-0.85 (0.25)
Mean difference, secukinumab – placebo (95% CI)	-1.30 (-2.01, -0.59)	
MEASURE 4	N = 116	N = 117
ASAS40 at 16 wk, n (%)	45 (38.8%)	33 (28.2%)
RR vs placebo (95% CI)	1.38 (0.95, 1.99)	
ASAS20 at 16 wk, n (%)	69 (59.5%)	55 (47.0%)
RR vs placebo (95% CI)	1.27 (0.99, 1.62)	
BASDAI change from baseline, LS mean (SE)	-2.39 (0.20)	-1.86 (0.20)
Mean difference, secukinumab – placebo (95% CI)	-0.53 (-1.08, 0.02)	
MEASURE 5	N = 305	N = 153
ASAS40 at 16 wk, n (%)	134 (43.9%)	26 (17.0%)
RR vs placebo (95% CI)	2.59 (1.78, 3.75)	
ASAS20 at 16 wk, n (%)	178 (58.4%)	56 (36.6%)
RR vs placebo (95% CI)	1.59 (1.27, 2.00)	
BASDAI change from baseline, LS mean (SE)	-2.79 (0.13)	-1.50 (0.18)
Mean difference, secukinumab – placebo (95% CI)	-1.29 (-1.73, -0.85)	

Source: Submission Tables 2-26, p99; 2-27, p101; 2-31, p105; 2-34, p107. For consistency of methods, all RR results and mean differences for BASDAI are taken from the meta-analyses, Figures 2-19, 2-21, 2-23, pp129-133. 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 and BE AGILE, no worsening in remaining domain; CI = confidence interval; LS = least squares; RR = risk ratio; SE = standard error.

- 6.11 Overall, both active treatments were consistently superior to placebo, and there were no obvious differences in the size or frequency of responses between bimekizumab and secukinumab.
- 6.12 The rate of response to placebo was higher in MEASURE 4, and the effect of secukinumab was not statistically significant in this trial.

- 6.13 The focus of the analyses was identifying heterogeneity in the trial outcomes. One meta-analysis compared the two included bimekizumab trials (BE MOBILE 2 and BE AGILE), and another the three secukinumab trials (MEASURE 2, MEASURE 4 and MEASURE 5). The meta-analysis of secukinumab trials found that MEASURE 4 had less favourable results than MEASURE 2 and MEASURE 5 because of a higher rate of responses in the placebo-treated group.
- 6.14 The results of the indirect treatment comparison for the outcome measures for efficacy is shown in Table 7.

Table 7: Results of the indirect treatment comparison

	RR (95% CI) Bimekizumab vs secukinumab	OR (95% CI) Bimekizumab vs secukinumab	RD (95% CI) Bimekizumab - secukinumab	MD (95% CI) Bimekizumab - secukinumab
ASAS20	1.06 (0.73, 1.53)	1.16 (0.65, 2.08)	0.03 (-0.11, 0.17)	-
ASAS20 excluding MEASURE 4	0.94 (0.65, 1.38)	0.98 (0.54, 1.79)	-0.01 (-0.15, 0.13)	
ASAS40	1.12 (0.53, 2.38)	1.22 (0.48, 3.11)	0.05 (-0.09, 0.19)	-
ASAS40 excluding MEASURE 4	0.89 (0.48, 1.67)	0.90 (0.41, 1.98)	0.00 (-0.12, 0.12)	
BASDAI change from baseline	-	-	-	-0.11 (-0.81, 0.59)
BASDAI change from baseline excluding MEASURE 4	-	-	-	0.14 (-0.47, 0.75)

Source: Submission Table 2-69, p143.

ASAS20 = Assessment in Ankylosing Spondylitis Response 20% response; ASAS40 = Assessment in Ankylosing Spondylitis Response 40% response; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; CI = confidence interval; MD = mean difference; OR = odds ratio; RD = risk difference; RR = risk ratio.

- 6.15 The submission nominated a non-inferiority margin for the risk ratio for ASAS20 of 0.43. This non-inferiority margin has been accepted by the PBAC when it considered other biological treatments for AS, including secukinumab. The condition for non-inferiority, that the 95% CI of the RR in the ASAS20 response included 1.00 and the lower CI margin was > 0.43, was satisfied.
- 6.16 The PBAC has previously noted that differences in the rate of response to placebo among trials, such as that seen in MEASURE 4, suggest differences in baseline risk or other factors that may make indirect treatment comparisons unreliable. The indirect treatment comparison was, therefore, conducted with the results of MEASURE 4 included and with them excluded. Excluding MEASURE 4 changed the point estimates from marginally favouring bimekizumab to marginally favouring secukinumab, but the conclusion of non-inferiority was not affected.

Comparative harms

- 6.17 Adverse events in the trials are presented in Table 8. The expected excess of nasopharyngitis and oral candidiasis was observed but did not appear to be different for the two active treatments, and only one event of oral candidiasis was reported as leading to discontinuation.

6.18 Treatment-emergent inflammatory bowel disease was reported as an adverse event in two patients receiving bimekizumab, and one lead to discontinuation.

Table 8: Adverse events in the trials presented in the submission.

	Bimekizumab	Placebo
BE MOBILE 2	N = 221	N = 111
Patients with TEAE to 16 wk, n (%)	120 (54.3%)	48 (43.2%)
Nasopharyngitis, n (%)	17 (7.7%)	4 (3.6%)
Oral candidiasis, n (%)	10 (4.5%)	0
Patients with STEAE to 16 wk, n (%)	5 (2.3%)	1 (0.9%)
Crohn's disease + ulcerative colitis, n (%)	2 (0.9%)	0
Discontinuation due to AE to 16 wk, n (%)	6 (2.7%)	0
Crohn's disease, n (%)	1 (0.5%)	0
Oral candidiasis, n (%)	1 (0.5%)	0
BE AGILE	N = 60	N = 60
Patients with TEAE to 12 wk, n (%)	20 (31.7%)	26 (43.3%)
Nasopharyngitis, n (%)	3 (4.8%)	0
Oral candidiasis, n (%)	NR	NR
Patients with STEAE to 12 wk	1 (1.7%)	2 (3.3%)
Discontinuation due to AE to 12 wk, n (%)	1 (1.7%)	1 (1.7%)
Death to 12 wk	1 (1.6%)	0
	Secukinumab	Placebo
MEASURE 2	N = 72	N = 74
Patients with TEAE to 16 wk, n (%)	47 (65%)	47 (64%)
Nasopharyngitis, n (%)	8 (11%)	3 (4%)
Patients with STEAE to 16 wk	4 (6%)	3 (4%)
Discontinuation due to AE to 16 wk, n (%)	5 (7%)	4 (5%)
Death to 16 wk	0	0
MEASURE 4	N = 116	N = 117
Patients with TEAE to 16 wk, n (%)	72 (62.1%)	64 (64.7%)
Nasopharyngitis, n (%)	17 (14.7%)	10 (8.5%)
Patients with STEAE to 16 wk	2 (1.7%)	4 (3.4%)
Discontinuation due to AE to 16 wk, n (%)	1 (0.9%)	1 (0.9%)
Death to 16 wk	0	0
MEASURE 5	N = 305	N = 153
Patients with TEAE to 16 wk, n (%)	206 (67.8%)	91 (59.5%)
Nasopharyngitis + upper respiratory tract infection, n (%)	84 (27.6%)	39 (25.5%)
Patients with STEAE to 16 wk	10 (3.3%)	3 (2.0%)
Discontinuation due to AE to 16 wk, n (%)	2 (0.7%)	1 (0.7%)
Death to 16 wk	0	0

Source: Submission Tables 2-39, p110; 2-41, 2-42, p112; 2-45, 2-46, p114; 2-55, p120, 2-57, 2-58, 2-59, p121.

AE = adverse event; STEAE = severe treatment-emergent adverse event; TEAE = treatment-emergent adverse event.

Benefits/harms

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

Clinical claim

6.20 The submission described bimekizumab as non-inferior in terms of effectiveness compared to secukinumab. The evaluation considered this claim was adequately supported.

- 6.21 The submission described bimekizumab as non-inferior in terms of safety compared to secukinumab. The evaluation considered this claim was adequately supported.
- 6.22 The PBAC considered that the claim of non-inferior comparative effectiveness and safety was reasonable.

Economic analysis

- 6.23 The submission presented a cost minimisation approach to the economic analysis using the published price of secukinumab as the basis for the comparison. The key components and assumptions are summarised in Table 9.

Table 9: 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 loading and maintenance doses for BKZ and SEC over two-years of treatment. SEC 150 mg at weeks 0,1,2,3 and 4 then every 4 weeks = BKZ 160 mg every 4 weeks
Direct medicine costs	Costs of treatment are calculated over 2 years and the AEMP for bimekizumab is calculated on the required number of packs: Bimekizumab: Bimekizumab comes in a pack with 2x160 mg pre-filled syringes or 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 for two years at a total AEMP of \$19,090.12 (DPMQ \$20,548.45). The AEMP per pack of BKZ is calculated to be \$1,468.47 (DPMQ \$1,606.73).
Other costs or cost offsets	None

Source: Table 3.1, pp 163-4 of the submission AEMP = approved ex-manufacture price; AS = ankylosing spondylitis, BKZ = bimekizumab, DPMQ = dispensed price max quantity; mg = milligram, EED = equi-effective dose, PBS = Pharmaceutical Benefits Scheme, SEC = secukinumab.

- 6.24 The submission stated that the approach to the cost minimisation calculations was based on previous PBAC recommendations that the costs should be calculated over 2 years, based on equi-effective doses derived from the relevant Product Information documents (noted in various b/tsDMARD Public Summary Documents (PSDs), including most recently paragraphs 7.2 and 7.7, upadacitinib PSD, July 2023 PBAC meeting).
- 6.25 The equi-effective doses were estimated as bimekizumab 160 mg for every 4 weeks over 2 years and secukinumab 50 mg administered at weeks 0,1,2,3 and 4 followed by 150 mg every 4 weeks over 2 years.
- 6.26 Based on this dose equivalence and using the published AEMP for secukinumab, the submission calculated that the AEMP per pack for bimekizumab to be \$1,468.47.

- 6.27 Should the PBAC accept the clinical claim of overall non-inferior effectiveness and safety, the cost-minimisation approach must establish that the cost per patient for treatment with bimekizumab would be no more than the cost per patient with the other listed options for AS. Where these cost per patient calculations are uncertain, the guiding principle is that the Australian Government should not bear the financial risk of this uncertainty because the Australian population already has access to therapy that is at least as effective and safe. Given the claim of non-inferior comparative effectiveness and safety to secukinumab, and the existing therapeutic relativities for AS have not established the superiority of any therapy over any other, there does not appear to be a basis for bimekizumab to be more costly than any of the alternative therapies.

Drug cost/patient/year

- 6.28 Assuming a DPMQ of \$3,422.13 (i.e. requested published price) and 13 scripts required over 2 years, the cost per patient per year is \$22,243.85.

Estimated PBS usage & financial implications

- 6.29 This submission was not considered by DUSC.
- 6.30 The submission appropriately presented a market share approach to estimating PBS usage and financial implications of listing bimekizumab.
- 6.31 The key inputs used in the financial estimates are shown in Table 10. Year 1 is assumed to be 2025.

Table 10: 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						See para 6.33 Estimates not provided for golimumab and infliximab
				Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	
		SEC		█%	█%	█%	█%	█%	█%	
		IXE		█%	█%	█%	█%	█%	█%	
		ADA		█%	█%	█%	█%	█%	█%	
		ETA		█%	█%	█%	█%	█%	█%	
		UPA		█%	█%	█%	█%	█%	█%	
		CER		█%	█%	█%	█%	█%	█%	
Calculation of substituted scripts from utilisation data		Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	calculated		
		█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ²			
Grandfathered patients	Not included in estimates although submission proposed a patent familiarisation program									
Costs (published DPMQ's)	Adalimumab: \$827.02, \$676.79		Etanercept: \$845.63			Certolizumab: \$1,026.28, \$3018.54				
	Secukinumab: \$710.56, \$2784.45		Ixekizumab: \$3,259.13			Upadacitinib: \$1272.31				
	Infliximab: \$252.52, \$272.03, \$1267.60, \$1315.97, \$272.03, \$577.89, \$759.43									
Patient copayment	PBS: \$22.04 75; RPBS: \$4.21 for all medicines except infliximab, which had a PBS copayment of \$22.88 and RPBS \$7.30.									

Source: Tables 4.2, 4.3, 4.4, 4.10, pp172-73, 185 of the submission;. ADA = adalimumab; AS = ankylosing spondylitis; bDMARD = biological disease modifying antirheumatic drug; CER = certolizumab; ETA = etanercept; IXE = ixekizumab; Jan = January; PsA = psoriatic arthritis; SEC = secukinumab; UPA = upadacitinib

The redacted values correspond to the following ranges

¹ 500 to < 5,000

² 5,000 to < 10,000

6.32 The estimates included the following assumptions:

- That there would be no market growth beyond the predicted population growth;
- That the main products substituted by bimekizumab would be secukinumab, ixekizumab and the other bDMARDs that are administered subcutaneously;

- Conversely, that bimekizumab would not be substituted for JAK inhibitors or products requiring IV administration (stated to be golimumab and infliximab). (The Australian PI states that golimumab is administered by subcutaneous injection so this appears to be an error and golimumab should have been included in the estimates of market size.)

6.33 The estimates did not include the number of patients proposed for the grandfathering restriction. The Pre-PBAC Response stated the Sponsor anticipated fewer than < 500 grandfather patients were expected for AS.

6.34 There are multiple biosimilars for adalimumab and at least one for etanercept, with multiple indications and indication-specific prices at least at the DPMQ level. The submission may have used a reasonable approach to estimate substitution but did not appear to take account of the impact of biosimilar listings, although these may have a minimal impact on the uptake of a new b/tsDMARD. The Pre-PBAC Response acknowledged the complexity of pricing arrangements and stated the Sponsor will work collaboratively with the Department following a recommendation to ensure the financial estimates are robust.

Table 11: 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 and published prices of other products						
Cost to PBS/RPBS less copayments	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹
Estimated financial implications for substituted bDMARDS						
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 published price and published prices of other products						
Cost to PBS/RPBS less copayments	■ ¹	■ ¹	■ ³	■ ³	■ ³	■ ³
Estimated financial implications for substituted bDMARDS						
Cost to PBS/RPBS less copayments	■ ²	■ ²	■ ²	■ ²	■ ²	■ ²
Net financial implications						
Net cost to PBS/RPBS	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹

Source: Tables 4.12 and 4.13 p187 of the submission.

The redacted values correspond to the following ranges

¹ \$0 to < \$10 million

² net cost saving

³ \$10 million to < \$20 million

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 ankylosing spondylitis (AS). 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 therapy of adalimumab, etanercept, infliximab, golimumab, certolizumab pegol, ixekizumab, secukinumab, tofacitinib and upadacitinib.
- 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 AS, 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 AS 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 AS and considered this was reasonable, and the grandfather listing should remain in place for 12 months from the date of listing, per standard policy.
- 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 AS 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 AS.
- 7.6 The PBAC noted that nine treatments were currently PBS listed for AS and considered the clinical need for additional therapies for AS that were of similar effectiveness and safety to other options was low. The Committee further noted two other IL-17 inhibitors (secukinumab and ixekizumab) were listed for AS, but that bimekizumab has a different affinity for IL-17 subunits than secukinumab or ixekizumab.
- 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 (noting ixekizumab is also an IL-17A inhibitor like secukinumab). However, the Committee considered that bimekizumab could substitute for any of the PBS listed b/tsDMARDs for AS 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 and nr-axSpA), however considered that given the available evidence is not in a specific line of therapy and the restrictions for AS are line-agnostic, there was no compelling basis to exclude any of the b/tsDMARDs currently listed for AS as alternative therapies. The PBAC also did not accept the

- submission argument that intravenous (IV) or oral therapies 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 to support the clinical claims. The PBAC noted the clinical claim was that bimekizumab was of non-inferior comparative effectiveness and safety to secukinumab. These claims are discussed further below.
- 7.9 The Committee noted the results of the ITC versus secukinumab for the outcomes of ASAS20, ASAS40 and BASDAI change from baseline did not find any statistically significant differences for any of the analyses presented (see Table 7), and the lower bound of the 95% CI remained within the nominated non-inferior margin of 0.43 (which has been previously accepted for upadacitinib for AS). Overall, the PBAC considered based on the available evidence that the claim of non-inferior comparative effectiveness of bimekizumab and secukinumab was adequately supported.
- 7.10 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 safety data in AS to be consistent with the known safety profiles of these agents in other indications, and overall, the claim of non-inferior comparative safety was reasonable.
- 7.11 The PBAC noted no clinical evidence was provided to support BKZ having superior effectiveness or safety versus any of the alternative therapies for AS.
- 7.12 The PBAC considered that a listing based on a cost minimisation approach with costs over two years, consistent with the approach previously used for b/tsDMARDs, was appropriate to determine the cost minimised price of bimekizumab. The PBAC considered the cost of bimekizumab should be no greater than the alternative therapies.
- 7.13 The PBAC noted the utilisation and financial estimates as presented in the submission resulted in an incremental cost for the listing of bimekizumab, however also noted the estimates were based on a price of bimekizumab calculated from a cost minimisation approach using the published price of secukinumab (rather than the least costly alternative). The PBAC considered the uptake and rate of replacement of specific b/tsDMARDs to be uncertain, however considered that if listed on a cost minimisation basis with the least costly alternative, the listing would most likely be cost neutral or modestly cost saving to the PBS as it will only replace therapies that are either of equivalent cost or more expensive.

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

Outcome:

Recommended

8 Recommended listing

8.1 Add new indication/s to bimekizumab as follows:

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]					
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required – Written/HPOS upload				
	Administrative Advice: See below				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: Special Pricing Arrangements apply.				
	Indication: Ankylosing spondylitis				
	Treatment Phase: Initial 1 (new patient)				
	Clinical criteria:				
	The condition must be either radiologically (plain X-ray) confirmed: (i) Grade II bilateral sacroiliitis; (ii) Grade III unilateral sacroiliitis				
	AND				
	Clinical criteria:				
	Patient must not have received PBS-subsidised treatment with a biological medicine for this condition				
	AND				

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	Clinical criteria:
	Patient must have at least 2 of the following: (i) low back pain and stiffness for 3 or more months that is relieved by exercise but not by rest; (ii) limitation of motion of the lumbar spine in the sagittal and the frontal planes as determined by a score of at least 1 on each of the lumbar flexion and lumbar side flexion measurements of the Bath Ankylosing Spondylitis Metrology Index (BASMI); (iii) limitation of chest expansion relative to normal values for age and gender
	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 not receive more than 16 weeks of treatment under this restriction
	Population criteria:
	Patient must be at least 18 years of age
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of ankylosing spondylitis
	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 and must be demonstrated at the time of the initial application: (a) a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of at least 4 on a 0-10 scale; and (b) an elevated erythrocyte sedimentation rate (ESR) greater than 25 mm per hour or a C-reactive protein (CRP) level greater than 10 mg per L. The baseline BASDAI score and ESR or CRP level must be determined at the completion of the 3 month NSAID and exercise trial, but prior to ceasing NSAID treatment. All measurements must be no more than 4 weeks old at the time of initial application. If the above requirement to demonstrate an elevated ESR or CRP cannot be met, the application must state the reason this criterion cannot be satisfied.
	Prescribing Instructions: The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	Prescribing Instructions: The following must be provided at the time of application and documented in the patient's medical records: (i) details (name of the radiology report provider, date of the radiology report and unique identifying number/code that links report to the individual patient) of the radiological report confirming Grade II bilateral sacroiliitis or Grade III unilateral sacroiliitis; and (ii) a baseline BASDAI score; and (iii) a completed Exercise Program Self Certification Form included in the supporting information form; and

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	(iv) baseline ESR and/or CRP level.
	Prescribing Instructions: An assessment of a patient's response to this initial course of treatment must be conducted following a minimum of 12 weeks of therapy and no later than 4 weeks prior the completion of this course of treatment.
	Prescribing Instructions: Where a response assessment is not conducted within these timeframes, the patient will be deemed to have failed to respond to treatment with this drug.
	Prescribing Instructions: If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition within this treatment cycle. Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.
	Administrative Advice: Details of the toxicities, including severity, which will be accepted for the purposes of administering this restriction can be found on the Services Australia website at www.servicesaustralia.gov.au
	Administrative Advice: For details on the appropriate minimum exercise program that will be accepted for the purposes of administering this restriction, please refer to the Services Australia website at www.servicesaustralia.gov.au
	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]	
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required – Written/HPOS upload
	Administrative Advice: See below
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Indication: Ankylosing spondylitis
	Treatment Phase: Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 5 years)
	Clinical criteria:
	Patient must have received prior PBS-subsidised treatment with a biological medicine for this condition in this treatment cycle
	AND

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	Clinical criteria:
	Patient must not have already failed/ceased to respond to PBS-subsidised treatment with this drug for this condition during the current treatment cycle
	AND
	Clinical criteria:
	Patient must not receive more than 16 weeks of treatment under this restriction
	Population criteria:
	Patient must be at least 18 years of age
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of ankylosing spondylitis
	Prescribing Instructions: The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	Prescribing Instructions: An application for a patient who is either changing treatment from another biological medicine to this drug or recommencing therapy with this drug after a treatment break of less than 5 years, must be accompanied with details of the evidence of a response to the patient's most recent course of PBS-subsidised biological medicine within the timeframes specified below.
	Prescribing Instructions: To demonstrate a response to treatment the application must be accompanied with the assessment of response, conducted following a minimum of 12 weeks of therapy and no later than 4 weeks from cessation of the most recent course of biological medicine. It is recommended that an application for the continuing treatment be submitted no later than 4 weeks from the date of completion of the most recent course of treatment. This is to ensure treatment continuity for those who meet the continuing restriction.
	Prescribing Instructions: Where a patient is changing from PBS-subsidised treatment with a biosimilar medicine for this condition, the prescriber must submit baseline disease severity indicators with this application, in addition to the response assessment outlined below.
	Prescribing Instructions: An adequate response is defined as an improvement from baseline of at least 2 units (on a scale of 0-10) in the BASDAI score combined with at least 1 of the following: (a) an ESR measurement no greater than 25 mm per hour; or (b) a CRP measurement no greater than 10 mg per L; or (c) an ESR or CRP measurement reduced by at least 20% from baseline. Where only 1 acute phase reactant measurement is supplied in the first application for PBS-subsidised treatment, that same marker must be measured and used to assess all future responses to treatment.
	Prescribing Instructions: The assessment of response to treatment must be documented in the patient's medical records.
	Prescribing Instructions: Where a response assessment is not conducted within these timeframes, the patient will be deemed to have failed to respond to treatment with this drug.
	Prescribing Instructions: If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition within this treatment cycle. Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.

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	<p>Prescribing Instructions: A patient may re-trial this drug after a minimum of 5 years have elapsed between the date the last prescription for a PBS-subsidised biological medicine was approved in this cycle and the date of the first application under a new cycle under the Initial 3 treatment restriction.</p>
	<p>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</p>
Restriction Summary [New] / Treatment of Concept: [New]	
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required – Written/HPOS upload
	Administrative Advice: See below
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Indication: Ankylosing spondylitis
	Treatment Phase: 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 a break in treatment of at least 5 years from the most recently approved PBS-subsidised biological medicine for this condition
	AND
	Clinical criteria:
	The condition must be either radiologically (plain X-ray) confirmed: (i) Grade II bilateral sacroiliitis; (ii) Grade III unilateral sacroiliitis
	AND
	Clinical criteria:
	Patient must have at least 2 of the following: (i) low back pain and stiffness for 3 or more months that is relieved by exercise but not by rest; (ii) limitation of motion of the lumbar spine in the sagittal and the frontal planes as determined by a score of at least 1 on each of the lumbar flexion and lumbar side flexion measurements of the Bath Ankylosing Spondylitis Metrology Index (BASMI); (iii) limitation of chest expansion relative to normal values for age and gender

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AND
Clinical criteria:
Patient must have a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of at least 4 on a 0-10 scale that is no more than 4 weeks old at the time of application
AND
Clinical criteria:
Patient must have an elevated erythrocyte sedimentation rate (ESR) greater than 25 mm per hour that is no more than 4 weeks old at the time of application; or
Patient must have a C-reactive protein (CRP) level greater than 10 mg per L that is no more than 4 weeks old at the time of application; or
Patient must have a clinical reason as to why demonstration of an elevated ESR or CRP cannot be met and the application must state the reason
AND
Clinical criteria:
Patient must not receive more than 16 weeks of treatment under this restriction
Population criteria:
Patient must be at least 18 years of age
Treatment criteria:
Must be treated by a rheumatologist; or
Must be treated by a clinical immunologist with expertise in the management of ankylosing spondylitis
Prescribing Instructions: The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
Prescribing Instructions: The following must be provided at the time of application and documented in the patient's medical records: (i) details (name of the radiology report provider, date of the radiology report and unique identifying number/code that links report to the individual patient) of the radiological report confirming Grade II bilateral sacroiliitis or Grade III unilateral sacroiliitis; and (ii) a baseline BASDAI score; and (iii) a baseline ESR and/or CRP level.
Prescribing Instructions: To demonstrate a response to treatment the application must be accompanied with the assessment of response, conducted following a minimum of 12 weeks of therapy and no later than 4 weeks from cessation of the most recent course of biological medicine. It is recommended that an application for the continuing treatment be submitted no later than 4 weeks from the date of completion of the most recent course of treatment. This is to ensure treatment continuity for those who meet the continuing restriction.
Prescribing Instructions: Where a response assessment is not conducted within these timeframes, the patient will be deemed to have failed to respond to treatment with this drug.
Prescribing Instructions: If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition within this treatment cycle. Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.
Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

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	<p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au</p> <p>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</p> <p>Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
Restriction Summary [New] / Treatment of Concept: [New]	
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required – Telephone/Electronic
	Administrative Advice: See below
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Indication: Ankylosing spondylitis
	Treatment Phase: Initial 1 (new patient) or Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 5 years) or Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years) - balance of supply
	Clinical criteria:
	Patient must have received insufficient therapy with this drug for this condition under the Initial 1 (new patient) restriction to complete 16 weeks treatment; or
	Patient must have received insufficient therapy with this drug for this condition under the Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 5 years) restriction to complete 16 weeks treatment; or
	Patient must have received insufficient therapy with this drug for this condition under the Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years) restriction to complete 16 weeks treatment
	AND
	Clinical criteria:
	The treatment must provide no more than the balance of up to 16 weeks treatment available under the above restrictions
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of ankylosing spondylitis
	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).

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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]					
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required – Written/HPOS upload				
	Administrative Advice: See below				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: Special Pricing Arrangements apply.				
	Indication: Ankylosing spondylitis				
	Treatment Phase: Continuing treatment				
	Clinical criteria:				
	Patient must have received this drug as their most recent course of PBS-subsidised biological medicine treatment for this condition				
	AND				
	Clinical criteria:				
	Patient must have demonstrated an adequate response to treatment with this drug				
	AND				
	Clinical criteria:				
	Patient must not receive more than 24 weeks of treatment under this restriction				
	Population criteria:				
	Patient must be at least 18 years of age				
	Treatment criteria:				
	Must be treated by a rheumatologist; or				
	Must be treated by a clinical immunologist with expertise in the management of ankylosing spondylitis				
	Prescribing Instructions				
	The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).				
	Prescribing instructions:				
	An adequate response is defined as an improvement from baseline of at least 2 units (on a scale of 0-10) in the BASDAI score combined with at least 1 of the following: (a) an ESR measurement no greater than 25 mm per hour; or				

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	(b) a CRP measurement no greater than 10 mg per L; or (c) an ESR or CRP measurement reduced by at least 20% from baseline. Where only 1 acute phase reactant measurement is supplied in the first application for PBS-subsidised treatment, that same marker must be measured and used to assess all future responses to treatment.
	Prescribing Instructions: The assessment of response to treatment must be documented in the patient's medical records.
	Prescribing instructions: An application for the continuing treatment must be accompanied with the assessment of response conducted following a minimum of 12 weeks of therapy and no later than 4 weeks from cessation of the most recent course of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment.
	Prescribing Instructions: Where a response assessment is not conducted within these timeframes, the patient will be deemed to have failed to respond to treatment with this drug.
	Prescribing Instructions: If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition within this treatment cycle. Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.
	Prescribing Instructions: A patient may re-trial this drug after a minimum of 5 years have elapsed between the date the last prescription for a PBS-subsidised biological medicine was approved in this cycle and the date of the first application under a new cycle under the Initial 3 treatment restriction.
	Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001
Restriction Summary [New] / Treatment of Concept: [New]	
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required
	Administrative Advice: See below
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Indication: Ankylosing spondylitis
	Treatment Phase: Continuing treatment – balance of supply

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	Clinical criteria:
	Patient must have received insufficient therapy with this drug under the Continuing treatment restriction to complete 24 weeks treatment
	AND
	Clinical criteria:
	The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restriction
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of ankylosing spondylitis
	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]	
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required
	Administrative Advice: See below
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Indication: Ankylosing spondylitis
	Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply - Grandfather arrangements
	Clinical criteria:
	The condition must be either radiologically (plain X-ray) confirmed: (i) Grade II bilateral sacroiliitis; (ii) Grade III unilateral sacroiliitis
	AND
	Clinical criteria:
	<i>Patient must have received non-PBS-subsidised treatment with this drug for this PBS indication prior to [listing date]</i>
	AND
	Clinical criteria:
	Patient must have had at least 2 of the following prior to commencing non-PBS-subsidised treatment <i>with this drug for this condition</i> : (i) low back pain and stiffness for 3 or more months that is relieved by exercise but not by rest; (ii) limitation of motion of the lumbar spine in the sagittal and the frontal planes as determined by a score of at least 1 on each of the lumbar flexion and lumbar side flexion measurements of the Bath Ankylosing Spondylitis Metrology Index (BASMI); (iii) limitation of chest expansion relative to normal values for age and gender
	AND

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	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 prior to commencing non-PBS-subsidised treatment
	AND
	Clinical criteria:
	<i>Patient must have demonstrated an adequate response after 16 weeks of treatment if the patient has been treated with this drug for this condition for 16 weeks or longer</i>
	AND
	Clinical criteria:
	Patient must not receive more than 24 weeks of treatment under this restriction
	Population criteria:
	Patient must be at least 18 years of age
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of ankylosing spondylitis
	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 have been demonstrated prior to initiation of non-PBS subsidised treatment with this biological medicine for this condition: (a) a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of at least 4 on a 0-10 scale; and (b) an elevated erythrocyte sedimentation rate (ESR) greater than 25 mm per hour or a C-reactive protein (CRP) level greater than 10 mg per L. The baseline BASDAI score and ESR or CRP level must have been determined at the completion of the 3 month NSAID and exercise trial, but prior to ceasing NSAID treatment. If the above requirement to demonstrate an elevated ESR or CRP could not be met, the application must state the reason this criterion could not be satisfied.
	Prescribing Instructions: The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	Prescribing Instructions: The following must be provided at the time of application and documented in the patient's medical records: (i) details (name of the radiology report provider, date of the radiology report and unique identifying number/code that links report to the individual patient) of the radiological report confirming Grade II bilateral sacroiliitis or Grade III unilateral sacroiliitis; and (ii) baseline <i>and current</i> BASDAI scores; and (iii) a completed Exercise Program Self Certification Form included in the supporting information form; and (iv) baseline ESR and/or CRP level.
	Prescribing Instructions:

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	<p>An adequate response is defined as an improvement from baseline of at least 2 units (on a scale of 0-10) in the BASDAI score combined with at least 1 of the following:</p> <p>(a) an ESR measurement no greater than 25 mm per hour; or</p> <p>(b) a CRP measurement no greater than 10 mg per L; or</p> <p>(c) an ESR or CRP measurement reduced by at least 20% from baseline.</p> <p>Where only 1 acute phase reactant measurement is supplied in the first application for PBS-subsidised treatment, that same marker must be measured and used to assess all future responses to treatment.</p>
	<p>Prescribing Instructions: The assessment of response to treatment must be documented in the patient's medical records.</p>
	<p>Prescribing Instructions: To demonstrate a response to treatment the application must be accompanied with the assessment of response, conducted following a minimum of 12 weeks of therapy and no later than 4 weeks from cessation of the most recent course of biological medicine. It is recommended that an application for the continuing treatment be submitted no later than 4 weeks from the date of completion of the most recent course of treatment. This is to ensure treatment continuity for those who meet the continuing restriction.</p>
	<p>Prescribing Instructions: Where a response assessment is not conducted within these timeframes, the patient will be deemed to have failed to respond to treatment with this drug.</p>
	<p>Prescribing Instructions: If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition within this treatment cycle. Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.</p>
	<p>Administrative Advice: A patient may only qualify for PBS-subsidised treatment under this restriction once in a lifetime.</p>
	<p>Administrative Advice: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.</p>
	<p>Administrative Advice: Details of the toxicities, including severity, which will be accepted for the purposes of administering this restriction can be found on the Services Australia website at www.servicesaustralia.gov.au</p>
	<p>Administrative Advice: For details on the appropriate minimum exercise program that will be accepted for the purposes of administering this restriction, please refer to the Services Australia website at www.servicesaustralia.gov.au</p>
	<p>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</p>

Overarching administrative advice:

	<p>Administrative advice: TREATMENT OF ADULT PATIENTS WITH ANKYLOSING SPONDYLITIS</p> <p>The following information applies to Pharmaceutical Benefits Scheme (PBS) benefits listed for adult patients with the indication of ankylosing spondylitis (AS).</p>
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Public Summary Document – March 2024 PBAC Meeting

<p>Where the term 'biological medicine' appears in notes and restrictions, it refers to any PBS benefit where the PBS indication specifies: Ankylosing spondylitis. Some benefits are not biological medicines, but are small molecules. However, for administrative purposes, these benefits are included within the term 'biological medicine'.</p> <p>Treatment cycles:</p> <p>Under these arrangements, within a single treatment cycle, a patient may continue to receive long-term treatment with a biological medicine while they continue to show a response to therapy. A patient who has been receiving PBS-subsidised adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, ixekizumab and secukinumab treatment prior to 1 October 2021 is considered to start their first cycle as of 1 October 2021.</p> <p>Within the same treatment cycle, a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised biological medicine more than once.</p> <p>Where treatment has resulted in an inadequate response on 3 occasions a treatment cycle is considered to have been completed and there must be a 5-year break in PBS subsidy from all medicines with the PBS indication: 'Ankylosing spondylitis' before starting a new treatment 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.</p> <p>Where treatment has resulted in an inadequate response on fewer than 3 occasions in a treatment cycle and where a break in therapy of less than 5 years has occurred, a further course of treatment may be commenced within the same treatment cycle.</p> <p>There is no limit to the number of treatment cycles a patient may undertake in their lifetime.</p> <p>Prescribing under the correct 'Treatment phase' listing for the authority application:</p> <p>(1) Initial treatment.</p> <p>Apply under the 'Initial 1' treatment listing where the patient has never received a biological medicine for ankylosing spondylitis.</p> <p>(2) Grandfather patients (<i>bimekizumab</i> and tofacitinib only).</p> <p>A patient who commenced treatment with <i>bimekizumab</i> prior to [listing date] or tofacitinib for ankylosing spondylitis prior to 1 August 2023 for ankylosing spondylitis and who continues to receive treatment at the time of application, may qualify for treatment under the 'Grandfather' treatment restriction.</p> <p>A patient may only qualify for PBS-subsidised treatment under this restriction once. A maximum of 24 weeks of treatment will be authorised under this criterion. Following completion of the initial PBS-subsidised course, further subsidised treatment must be prescribed under the continuing treatment restriction of the relevant drug. 'Grandfather' arrangements will only apply for the first treatment cycle.</p> <p>For the second and subsequent cycles, a 'grandfather' patient must qualify for continuing treatment under the criteria that apply to a continuing patient.</p> <p>(3) Continuing treatment.</p> <p>Apply under the 'Continuing treatment' listing where the patient is experiencing an adequate response as defined in the restriction where there has been no change in prescribed biological medicine. Under no circumstance is continuing treatment to proceed initial treatment. An authority application for continuing treatment is not to be made on the same day as initial treatment.</p>
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<p>(4) Changing therapy.</p> <p>Apply under the 'Initial 2' treatment listing. Once initial treatment with the first PBS-subsidised biological medicine is prescribed, a patient may swap to an alternate biological medicine without having to requalify with respect to prior NSAID therapy and exercise program requirements. Where a patient is changing from a biosimilar medicine the prescriber must submit baseline indices of disease severity (i.e. the erythrocyte sedimentation rate (ESR), the C-reactive protein (CRP) levels and the BASDAI). A patient may trial an alternate biological medicine at any time, regardless of whether they are receiving therapy (initial or continuing) with a biological medicine at the time of the application. However, they cannot change to a particular biological medicine if it has failed to provide the patient with an adequate response within the same treatment cycle. A response assessment to the preceding supply of biological medicine must accompany this initial 2 treatment authority application.</p> <p>(5) Baseline measurements to determine response.</p> <p>A response to treatment is to be determined by comparison of current disease activity measurements relative to the baseline measurements of the BASDAI, ESR and/or CRP submitted with the first authority application for a biological medicine. 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 an 'Initial treatment' authority application is submitted within a treatment cycle and the eligibility for continuing treatment must be assessed according to these revised baseline measurements.</p> <p>(6) Recommencement of treatment after a 5-year break in PBS-subsidised therapy.</p> <p>Apply under the 'Initial 3' treatment listing. Prior NSAID and exercise therapies need not be re-trialled.</p>
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This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.

9 Context for Decision

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

10 Sponsor's Comment

The sponsor had no comment.