

5.01 BIMEKIZUMAB,

**Injection 160 mg in 1 mL single use pre-filled syringe;
 Injection 160 mg in 1 mL single use pre-filled pen;
 Injection 320 mg in 2 mL single use pre-filled syringe;
 Injection 320 mg in 2 mL single use pre-filled pen;
 Bimzelx[®],
 UCB Australia Proprietary Limited.**

1 Purpose of submission

- 1.1 The Category 2 submission requested a General Schedule, Authority Required listing for bimekizumab for the treatment of patients with moderate to severe hidradenitis suppurativa (HS). It included a request for listing a new strength, 320 mg/2 mL injection, in both syringe and pen device forms, as well as the existing strength of 160 mg/1 mL, in both syringe and pen device forms.
- 1.2 Listing was requested on the basis of a cost-minimisation approach versus secukinumab, with adalimumab as a secondary comparator.

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

Component	Description
Population	Patients with moderate to severe hidradenitis suppurativa (HS)
Intervention	Bimekizumab (BKZ) 320 mg (given as 2 subcutaneous injections of 160 mg or 1 subcutaneous injection of 320 mg) every 2 weeks up to Week 16 and every 4 weeks thereafter.
Comparator	Primary: Secukinumab (SEC) 300 mg at week 0,1,2,3 and 4 followed by 300 mg every 4 weeks OR 300 mg once every 2 weeks (weighting 80% Q4W, 20% Q2W) Secondary: Adalimumab (ADA) 160 mg at day 1, 80 mg at day 15, followed by 40 mg every week/80 mg fortnightly from day 29
Outcomes	HiSCR50, HiSCR75, HiSCR90 Safety
Clinical claim	In patients with moderate to severe HS: <ul style="list-style-type: none"> BKZ 320 mg Q2W up to Week 16 followed by BKZ 320 mg Q4W up to Week 48 is superior in terms of efficacy over the shorter- (Week 16) and longer-term (Week 48) and similar in terms of safety, compared with SEC BKZ 320 mg Q2W up to Week 16 followed by BKZ 320 mg Q4W up to Week 48 is at least non-inferior in terms of efficacy over the shorter-term (Week 16), and superior over the longer-term (Week 48), and similar in terms of safety, compared with ADA

Source: Table 1.1, p17 of the submission. HiSCR= Hidradenitis Suppurativa Clinical Response; Q2W= every 2 weeks; Q4W= every 4 weeks.

2 Background

Registration status

- 2.1 TGA status at time of PBAC consideration: The submission was made under the TGA/PBS Parallel Process. The Delegate's Overview was provided on 31 January 2025.

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Bimekizumab was TGA registered for hidradenitis suppurativa on 8 April 2025. The approved indication is, 'Bimzelx is indicated for the treatment of adult patients with moderate to severe hidradenitis suppurativa with an inadequate response to conventional systemic HS therapy'.

- 2.2 The registered dosage regimen for bimekizumab is:
- The recommended dose of Bimzelx for adult patients with hidradenitis suppurativa is 320 mg (given as 2 subcutaneous injections of 160 mg or 1 subcutaneous injection of 320 mg) every 4 weeks.
 - If more rapid disease control is desired and after consideration of the individual patient risks and benefits a Bimzelx dose for adult patients with hidradenitis suppurativa of 320 mg (given as 2 subcutaneous injections of 160 mg or 1 subcutaneous injection of 320 mg) every 2 weeks up to 16 weeks and every 4 weeks thereafter may be considered.

Previous PBAC consideration

- 2.3 Bimekizumab has not previously been considered by the PBAC for the indication of HS. It is currently PBS listed for severe chronic plaque psoriasis (considered March 2022 and March 2023), psoriatic arthritis, radiographic axial spondylitis and non-radiographic axial spondylitis (all in March 2024). In relation to the assessment of safety, the dose for HS is significantly higher than that for the other indications.
- 2.4 The most recent PBAC consideration of a drug for HS was of secukinumab in July and November 2023, with listing recommended on the basis of cost minimisation to adalimumab.

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

3 Requested listing

- 3.1 The submission proposed three listings: for initial treatment, for the balance of supply and for continuing treatment. The submission proposed a Special Pricing Arrangement for all listings.

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MEDICINAL PRODUCT medicinal product pack	Dispensed Price for Max. Qty	Max. qty packs	Max. qty units	No. of Rpts	Available brands
BIMEKIZUMAB (INITIAL AND BALANCE OF SUPPLY)					
bimekizumab 160 mg/mL injection, 2 x 1 mL pen devices	\$6,682.60 published price \$ tbc effective price	2	4	3	Bimzelx
bimekizumab 160 mg/mL injection, 2 x 1 mL syringe	\$6,682.60 published price \$ tbc effective price	2	4	3	Bimzelx
bimekizumab 320mg/2 mL injection, 1 x 2 mL pen devices	\$6,682.60 published price \$ tbc effective price	2	2	3	Bimzelx
bimekizumab 320mg/2 mL injection, 1 x 2 mL syringe	\$6,682.60 published price \$ tbc effective price	2	2	3	Bimzelx
BIMEKIZUMAB (CONTINUING AND GRANDFATHER)					
bimekizumab 160 mg/mL injection, 2 x 1 mL pen devices	\$3,422.60 published price \$ tbc effective price	1	2	5	Bimzelx
bimekizumab 160 mg/mL injection, 2 x 1 mL syringe	\$3,422.60 published price \$ tbc effective price	1	2	5	Bimzelx
bimekizumab 320mg/2 mL injection, 1 x 2 mL pen devices	\$3,422.60 published price \$ tbc effective price	1	1	5	Bimzelx
bimekizumab 320mg/2 mL injection, 1 x 2 mL syringe	\$3,422.60 published price \$ tbc effective price	1	1	5	Bimzelx

tbc = to be confirmed

- 3.2 The submission proposed restrictions for: initial treatment for new patients; initial treatment after a break in biological medicine treatment of less than 5 years; initial treatment after a break in therapy of more than 5 years; balance of supply for each of these restrictions; continuing treatment; and a grandfathering restriction. The restrictions were modelled on the existing restrictions for adalimumab and secukinumab for HS.
- 3.3 The proposed restriction does not match the inclusion criteria for the BE HEARD I/II trials in relation to prior antibiotic use. The trials required an inadequate response only to a single antibiotic, with no minimum duration of the course, and allowed enrolment of patients who had an adequate response but relapsed when the antibiotic was stopped.
- 3.4 A similar discrepancy between the proposed restriction and the trial eligibility criteria was noted by PBAC in its consideration of secukinumab (paragraph 3.4, 6.13, 6.14, secukinumab Public Summary Document (PSD), July 2023 PBAC Meeting). The sponsor of secukinumab responded in the Pre-Sub-Committee Response (PSCR) that "more than 80%" of the trial population had received antibiotics for HS and about 60% had stopped them for lack of efficacy. In BE HEARD I 80% of patients, and in BE HEARD II 90% had received prior antibiotics (BE HEARD I CSR; BE HEARD II CSR), and most of the antibiotics reported were those commonly used for HS.
- 3.5 The proposed restriction requires an abscess + nodule count of at least three, while the BE HEARD I/II trials required a count of at least five. The same discrepancy was noted by PBAC in relation to secukinumab (paragraph 3.4, secukinumab PSD, July 2023 PBAC Meeting), however the listing of secukinumab ultimately reflected that of adalimumab with respect to abscess and nodule counts.

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3.6 An abridged initial treatment restriction is shown below (without prescriber instructions and administrative advice). Continuing and grandfather restrictions are not presented for brevity reasons. Full restrictions recommended by the PBAC are in Section 8.

Category / Program: General Schedule
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/>
Restriction type: <input checked="" type="checkbox"/> Authority Required (in writing only via post/HPOS upload)
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Administrative advice: Special pricing arrangements apply.
Severity: Moderate to severe
Condition: Hidradenitis suppurativa
Indication: Moderate to severe hidradenitis suppurativa
Treatment Phase: Initial treatment – Initial 1 (new patient)
Clinical criteria:
Patient must have at the time of application, a Hurley stage II or III grading with an abscess and inflammatory nodule (AN) count greater than or equal to 3
AND
Clinical criteria:
Patient must have failed to achieve an adequate response to 2 courses of different antibiotics each for 3 months prior to initiation of PBS subsidised treatment with this drug for this condition;
OR
Patient must have had an adverse reaction to an antibiotic of a severity necessitating permanent treatment withdrawal resulting in the patient being unable to complete treatment with 2 different courses of antibiotics each for 3 months prior to initiation of PBS-subsidised treatment with this drug for this condition;
OR
Patient must be contraindicated to treatment with an antibiotic due to an allergic reaction of a severity necessitating permanent treatment withdrawal resulting in the patient being unable to complete treatment with 2 different courses of antibiotics each for 3 months prior to initiation of PBS-subsidised treatment with this drug for this condition;
AND
Clinical criteria:
Patient must not have received PBS-subsidised treatment with a biological medicine for this condition
AND
Clinical criteria:
Patient must not receive more than 16 weeks of treatment under this restriction
Treatment criteria:
Must be treated by a dermatologist

3.7 The submission proposed that the published price for the HS indication for bimekizumab should be the same as the current published price for the other indications. The effective price was proposed to be based on the effective price for secukinumab used in the cost minimisation approach.

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

4 Population and disease

4.1 HS is a chronic inflammatory disease of hair follicles mainly in intertriginous (axilla, groin, perineal, perianal) skin. It is hypothesised that obstruction of follicles together

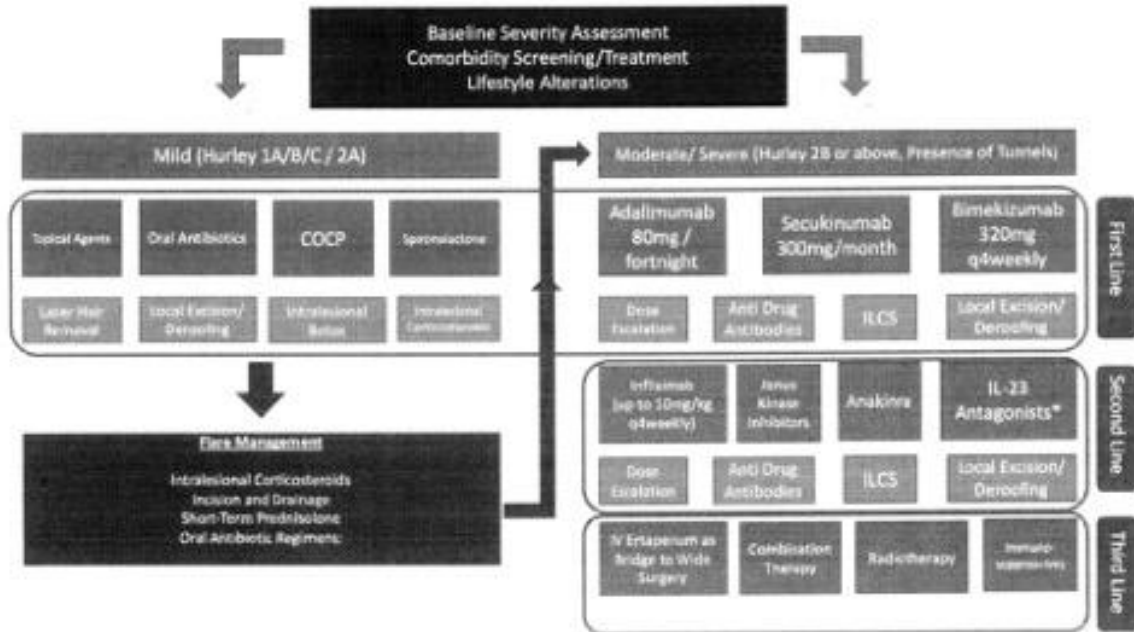
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with the mechanical stresses on intertriginous skin led to follicular rupture, peri-follicular inflammation and, in more severe cases, the formation of painful nodules, abscesses and sinus tracts or fistulae, often extensive and intercommunicating and referred to as skin tunnels. Obesity and smoking are strongly associated with HS, and there is a genetic component related to control of inflammation.

- 4.2 Prevalence is around 1% of the population. However, diagnosis is often delayed and many milder cases are never diagnosed. Women are more commonly affected than men.
- 4.3 Severity of HS is graded as Hurley Stage; Hurley Stage I = inflammatory nodules without skin tunnels or scarring; Stage II is recurrent nodules and abscesses with draining tunnels or scarring, but lesions are separated by normal skin; Stage III is nodules, abscesses and draining tunnels or scarring and no normal skin separating lesions. Most patients are Stage I.
- 4.4 HS is associated with impaired quality of life. The main symptoms that impair quality of life are pain from nodules and abscesses, and discharge and odour from draining abscesses and skin tunnels.
- 4.5 The treatment algorithm presented by the submission as representing current practice was taken from Vekic & Cairns, 2017. This guideline was prepared before secukinumab and bimekizumab were available. The submission refers to the "treatment algorithm proposed, based on EU guidelines, [...] presented below", but this was not included in the submission.
- 4.6 The most recent Australasian consensus guidelines were not referred to in the submission.¹ The treatment algorithm from these guidelines is shown in Figure 1. This guideline places adalimumab, secukinumab and bimekizumab as first-line treatments for severe HS, which appears to be what the submission proposes.

¹ Frew J, Fernandez Penas P, Foley P, et al. Australasian hidradenitis suppurativa management guidelines. *Australas J Dermatol* 2024; <https://doi.org/10.1111/ajd.14388>

Figure 1: Treatment algorithm from 2024 Australasian consensus guidelines for treatment of HS



Source: Frew et al, 2024, Figure 2. COCP = combined oral contraceptive pill; IL-23 = interleukin 23; ILCS = intra-lesional corticosteroids.

- 4.7 Bimekizumab is an antibody to IL-17A and IL-17F, members of a family of pro-inflammatory cytokines (A to F) produced by T helper 17 (Th17) cells.
- 4.8 IL-17 acts on target cells which express the IL-17 receptor (IL-17R) family on the cell surface. The IL-17R family consists of five subtypes: RA, RB, RC, RD, and RE.
- 4.9 The interactions of the IL-17 subtypes and the IL-17R subtypes in different tissues are not well understood but are likely to be complex. The ability of bimekizumab to bind IL-17A and IL-17F could, as the submission suggests, be an advantage, but it could also lead to different and/or worse long-term adverse effects.
- 4.10 Because of their mechanism of action, IL-17 inhibitors are contraindicated in active inflammatory bowel disease and in active, clinically significant infections, and are associated with an increase in infections, most often nasopharyngitis and mucocutaneous 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 primary comparator and adalimumab as the secondary comparator on the grounds that these two biologic disease-modifying anti-rheumatic drugs (bDMARDs) are listed on the PBS for HS. Secukinumab was chosen as the primary comparator as it has a similar pharmacological action, and the submission proposed that for this reason it was more likely to be replaced by bimekizumab. These comparators were appropriate, although the argument for secukinumab as the primary comparator was debatable, because the submission's

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argument was that the mechanism of action of bimekizumab is meaningfully different from that of secukinumab.

- 5.2 No near-market comparators were identified.
- 5.3 In the context of the cost-minimisation approach taken by the submission, a further consideration for PBAC is that, under Section 101(3B) of the *National Health Act 1953*, when the proposed medicine is substantially more costly than an alternative therapy, the committee cannot make a positive recommendation unless it is satisfied that, for some patients, the proposed medicine provides a significant improvement in efficacy and/or reduction of toxicity over the alternative therapy. If the committee is so satisfied, it must make a statement to this effect.
- 5.4 For the requested population, the following PBS-listed medicines may be considered alternative therapies because they could be replaced in practice: secukinumab and adalimumab.

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

6 Consideration of the evidence

Sponsor hearing

- 6.1 The sponsor requested a hearing for this item. The clinician discussed the high burden of disease, which manifests through painful flares of swollen, painful lesions, often in sensitive areas, which impacts people's ability to engage with employment, education, relationships and physical function. The clinician also discussed the effectiveness of non-biologic therapies such as antibiotics and biologic therapies and highlighted the effectiveness of bimekizumab for treating the symptoms of hidradenitis suppurativa, and cited case studies and anecdotal experiences of using bimekizumab in practice for this condition.

Consumer comments

- 6.2 The PBAC noted and welcomed the input from individuals (2), health care professionals (3) and professional organisations (1) and consumer organisations (2) via the Consumer Comments facility on the PBS website.
- 6.3 The PBAC welcomed the input from individuals that describe hidradenitis suppurativa as 'hell on earth', restricting the ability of those living with the condition to sit, walk, talk or move comfortably, and highlighted the limitations of current treatment options, which are painful, can cause fatigue, and require refrigeration. The PBAC also welcomed the input from health professionals who noted current treatments provide up to about a 50% improvement in inflammatory lesions in around 50-60% of patients, and described bimekizumab as being highly effective, including in patients who have failed other biologic therapies.
- 6.4 The Committee welcomed the input from the Australasian College of Dermatologists supporting the listing of bimekizumab, which highlighted the debilitating impact of

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hidradenitis suppurativa and stated an expanded listing for bimekizumab through new forms of the drug can help address existing gaps in care and improve health equity, particularly for patients in underserved communities.

- 6.5 The PBAC also welcomed the input from consumer organisations Hidradenitis Suppurativa Australia and the Global Healthy Living Foundation Australia, both also supporting the listing of bimekizumab. The Committee noted the input from Hidradenitis Suppurativa Australia discussed the debilitating symptoms and emphasised that the condition is often misunderstood and misdiagnosed, highlighting the need for greater awareness, education, early intervention and better access to dermatologists to achieve better patient outcomes. The input also emphasised the need for additional treatment options as many patients remain undertreated with current options, with surgery often the next step when existing treatment options are exhausted.
- 6.6 The PBAC noted the input from the Global Healthy Living Foundation Australia discussed misconceptions about hidradenitis suppurativa and highlighted the debilitating nature of the condition, the impacts on mental health, emotional impact and social isolation, as well as the financial impact of managing the disease. The input also highlighted the positive results of the pivotal bimekizumab BE HEARD trials and a 2023 systematic review and meta-analysis² that suggested bimekizumab is non-inferior to adalimumab and secukinumab, and reiterated the importance of having a third biologic option available to patients.

Clinical trials

- 6.7 The submission presented two randomised placebo-controlled trials of bimekizumab (BE HEARD I/II; also referred to as HS0003 and HS0004), and a Phase II randomised controlled three-arm trial of bimekizumab, placebo and adalimumab (HS0001). Two randomised placebo-controlled trials of secukinumab (SUNSHINE and SUNRISE) were submitted. Three placebo-controlled trials of adalimumab were submitted (PIONEER I/II and M10-467).
- 6.8 The submission proposed that bimekizumab be listed at a dose of 320 mg every 2 weeks for 16 weeks then 320 mg every 4 weeks. Only a minority of patients in the trials received this dose regimen: in BE HEARD I, 129/505 patients and in BE HEARD II, 131/509.
- 6.9 PBAC considered the SUNSHINE and SUNRISE trials, and PIONEER I/II and M10-467 in July 2023. At that meeting PBAC also considered SHARPS, a placebo-controlled trial of adalimumab as adjunctive therapy in patients having radical surgery for HS, but that trial was not included in the present submission because PBAC determined in

² Tsai YC, Hung CY, Tsai TF. Efficacy and Safety of Biologics and Small Molecules for Moderate-to-Severe Hidradenitis Suppurativa: A Systematic Review and Network Meta-Analysis. *Pharmaceutics*. 2023 Apr 28;15(5):1351. doi: 10.3390/pharmaceutics15051351. PMID: 37242593; PMCID: PMC10224469

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July 2023 that it was inappropriate to include it in an ITC with trials in a quite different clinical setting.

- 6.10 The submission claimed that HS0001 could not be used as a head-to-head comparison of adalimumab and bimekizumab because that comparison "was not part of the study's primary analysis". However, it was a pre-specified analysis (HS0001 CSR), and comparison of the HiSCR75 and HiSCR90 endpoints used in the post-hoc analyses of the PIONEER I/II, SUNSHINE and SUNRISE trials. The issue is of minor importance because the head-to-head bimekizumab vs adalimumab results from HS0001 were similar to those of the indirect treatment comparison and do not alter the therapeutic conclusions with respect to bimekizumab and adalimumab.
- 6.11 A key issue in trials of treatment of HS is the outcome measure used. The primary outcome measure used in the trials recently considered by PBAC is HiSCR, **H**idradenitis **S**uppurativa **C**linical **R**esponse. HiSCR was introduced for the PIONEER trials and then used in the SUNSHINE and SUNRISE and BE HEARD trials and several subsequent trials of various therapies for HS. Although HiSCR has been widely used in HS trials, it is noted that all the papers have the same first author (Kimball) and essentially the same investigators.
- 6.12 The HiSCR is biased towards acute inflammatory change and de-emphasises manifestations of chronic disease, so that it favours anti-inflammatory treatments - although, because it was devised for and validated using data from the adalimumab trials, it is not clear that it favours all anti-inflammatory treatments equally.
- 6.13 Most trials have used the outcome of HiSCR50, defined as a 50% reduction in inflammatory lesion count (abscesses + inflammatory nodules) and no increase in abscesses or draining fistulas compared to baseline.
- 6.14 The submission sought to include HiSCR75 and HiSCR90 (i.e., 75% and 90% reductions in the count of abscesses and nodules and no increases in abscesses or draining tunnels). These measures were introduced in HS0001 as exploratory outcomes.
- 6.15 The submission argued that HiSCR75 and HiSCR90 are "more stringent outcome measures" that are useful because "achieving a HiSCR50 response does not result in complete or near complete resolution of symptoms". However, HiSCR does not require any improvement in draining tunnels, and draining tunnels are a major cause of symptoms in HS, so HiSCR75 and 90 do not necessarily represent "complete or near complete resolution of symptoms".
- 6.16 NICE determined, in contrast, that based on quality-of-life data a 25% reduction in nodules and abscesses with no new draining tunnels (HiSCR25) would justify continuing treatment with adalimumab.³

³ NICE, Adalimumab for treating moderate to severe hidradenitis suppurativa, 2016; www.nice.org.uk/guidance/ta392 pp44-45.

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- 6.17 The use of a primary outcome measure focused on acute inflammatory processes, which does not measure all patient-relevant aspects of the disease, and which may not measure all effects of all inflammatory response modulators may make relative efficacy difficult to estimate.
- 6.18 The clinical claim was supported by two indirect treatment comparisons (ITCs), as shown in Figure 2.

Figure 2: The structure of the ITCs included in the submission.

BE HEARD I		
BE HEARD II		
HS0001		
Bimekizumab	Placebo	
	Placebo	Secukinumab
	SUNSHINE	
	SUNRISE	
	Placebo	Adalimumab
	HS0001	
	PIONEER I	
	PIONEER II	
	M10-467	

Source: Figure 2.4, p64 of the submission. ITC = indirect treatment comparison.

- 6.19 The trials and associated reports and publications are listed in Table 2.

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Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Bimekizumab		
BE HEARD I NCT04242446	Kimball A, et al. Efficacy and safety of bimekizumab in patients with moderate-to-severe hidradenitis suppurativa (BE HEARD I and BE HEARD II): two 48-week, randomised, double-blind, placebo-controlled, multicentre phase 3 trials.	<i>Lancet</i> , 2024; 403:2504-2519.
BE HEARD II NCT04242498		
HS0001 NCT03248531	Glatt S et al. Efficacy and Safety of Bimekizumab in Moderate-to-severe Hidradenitis Suppurativa: A Phase 2, Double-blind, Placebo-Controlled Randomized Clinical Trial.	<i>JAMA Dermatology</i> 2021; 157(11):1279-1288
Secukinumab		
SUNSHINE NCT03713619	Kimball A, et al. Secukinumab in moderate-to-severe hidradenitis suppurativa (SUNSHINE and SUNRISE): week 16 and week 52 results of two identical, multicentre, randomised, placebo-controlled, double-blind phase 3 trials.	<i>Lancet</i> , 2023; 401:747-761.
SUNRISE NCT03713632		
Adalimumab		
PIONEER I NCT01468207	Kimball A, et al. Two phase 3 trials of adalimumab for hidradenitis suppurativa.	<i>N Engl J Med</i> , 2016; 375:422-434.
PIONEER II NCT01468233		
M10-467 NCT00918255	Kimball A, et al. Adalimumab for the Treatment of Moderate to Severe Hidradenitis Suppurativa.	<i>Ann Intern Med</i> , 2012; 157:846-855.
	Kimball A, et al. HiSCR (Hidradenitis Suppurativa Clinical Response): a novel clinical endpoint to evaluate therapeutic outcomes in patients with hidradenitis suppurativa from the placebo-controlled portion of a phase 2 adalimumab study.	<i>J Eur Acad Dermatol Vener</i> , 2016; 30:989-994.

Source: Table 2.7, p58 of the submission.

- 6.20 The key features of the trials are summarised in Table 3. The submission made separate claims related to 16 weeks treatment and 48 weeks treatment: superiority to secukinumab at both time points, and of non-inferiority to adalimumab at 16 weeks but superiority at 48 weeks. Only the comparisons at 16 weeks are based on double-blind, placebo-controlled trials.
- 6.21 Although the BE HEARD I/II trials were double-blind and placebo-controlled in the first 16-week period, they were blinded only to bimekizumab every 2 weeks vs every 4 weeks from 16 to 48 weeks and the trials have been classified as open label. Patients receiving bimekizumab every 4 weeks throughout and patients switching to bimekizumab after completing the first 16 weeks on placebo were not included in the submission (Table 2.12 of the submission).
- 6.22 In SUNSHINE and SUNRISE there may have been blinding as to secukinumab dose (the published paper is unclear) but the treatment period beyond 16 weeks was not placebo-controlled and the extension phase has been classified as open label in this case also. Patients who completed the first 16 weeks on placebo were then

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randomised to secukinumab every 2 weeks vs every 4 weeks, and were not included in the submission (Table 2.14 of the submission).

- 6.23 Patients in PIONEER I and II randomised to placebo in period 1 (12 weeks) were "reassigned in a blinded fashion" for period 2 (24 weeks) to adalimumab 40 mg weekly (PIONEER I) or continued on placebo (PIONEER II). "To maintain blinding", there was a dummy re-randomisation process using an interactive voice-response system, which also instructed patients who had worsening symptoms or lack of improvement to discontinue the study and enter an open-label extension (Figures 1 and 2, Kimball 2016). Patients who did so were considered non-responders at 36 weeks (Kimball, 2016, p428). It is not obvious how informed consent to the dummy reassignment was obtained without compromising blinding in period 2.
- 6.24 In period 1, dropouts in both groups were 17/307 (5.5%) in PIONEER I and 20/326 (6%) in PIONEER II, while in period 2 dropouts in all groups were 120/290 (41%) in PIONEER I and 190/306 (62%) in PIONEER 2. Of the period 2 dropouts, 84/120 (70%) in PIONEER I and 151/190 (80%) in PIONEER II dropped out as instructed by the interactive voice response system. The very high dropout rate means a high risk of attrition bias and high overall risk of bias in period 2. Of patients enrolled in the second treatment period, only those receiving adalimumab 40 mg weekly in the second treatment period were included in the submission (Table 2.16 of the submission).

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Table 3: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)
BE HEARD I NCT04242446	505	R, DB, MC; placebo-controlled period = 16 weeks followed by 32 week OL; R 2:2:2:1 to BKZ 320mg q2wk for 48 weeks (N = 160); BKZ 320mg q4wk for 48 weeks (not included in submission); BKZ 320mg q2wk for 16 weeks then 320mg q4 weeks for 32 weeks (N = 129); placebo for 16 weeks then 320mg q 2 weeks for 32 weeks (72).	Low	≥18 years; HS for ≥6 months with at least two areas affected and at least one Hurley II or III and ≥5 nodules + abscesses; inadequate response or intolerance to antibiotics or relapse when antibiotic ceased; draining tunnel count <20	Primary: HiSCR with 50% reduction at 16wk; Secondary: HiSCR with 75% reduction at 16wk
BE HEARD II NCT04242498	509	R, DB, MC; placebo-controlled period = 16 weeks followed by 32 week OL; R 2:2:2:1 to BKZ 320mg q2wk for 48 weeks (N = 160); BKZ 320mg q4wk for 48 weeks (not included in submission); BKZ 320mg q2wk for 16 weeks then 320mg q4 weeks for 32 weeks (N = 131); placebo for 16 weeks then 320mg q 2 weeks for 32 weeks (N = 74).	Low	≥18 years; HS for ≥6 months with at least two areas affected and at least one Hurley II or III and ≥5 nodules + abscesses; inadequate response or intolerance to antibiotics or relapse when antibiotic ceased; draining tunnel count <20	Primary: HiSCR with 50% reduction at 16wk; Secondary: HiSCR with 75% reduction at 16wk
HS0001 NCT03248531	90	R, DB, 12 weeks; R 2:1:1 BKZ 320mg q2wk (N = 46), ADA 40mg weekly (N = 22) placebo (N = 22).	Low	18-70 years, HS for ≥1 year with at least two areas affected and at least one Hurley II or III and nodules + abscesses >3; inadequate response or intolerance to antibiotics	Primary: HiSCR with 50% reduction at 12wk.
SUNSHINE NCT03713619	541	R, DB, MC, placebo-controlled period 16 weeks with primary endpoint analysis then 36 weeks (?DB); R 1:1:1 SEC 300mg q2wk (N = 181), SEC 300mg q4wk (N = 180), placebo (N = 180); after 16 weeks placebo group re-randomised to SEC 300mg q2wk or SEC 300mg q4wk (not included in submission).	Unclear	≥18 years, HS for ≥1 year with at least two areas affected and at least one Hurley II or III and nodules + abscesses ≥3; draining tunnel count <20	Primary: HiSCR with 50% reduction at 16wk
SUNRISE NCT03713632	543	R, DB, MC, placebo-controlled period 16 weeks with primary endpoint analysis then 36 weeks (?DB); R 1:1:1 SEC 300mg q2wk (N = 180), SEC 300mg q4wk (N = 180), placebo (N = 183); after 16 weeks placebo group re-randomised to SEC 300mg q2wk or SEC 300mg q4wk (not included in submission).	Unclear	≥18 years, HS for ≥1 year with at least two areas affected and at least one Hurley II or III and nodules + abscesses ≥3; draining tunnel count <20	Primary: HiSCR with 50% reduction at 16wk

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Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)
PIONEER I NCT01468207	307	R, DB, MC; period 1 (12 weeks) 1:1 adalimumab 40mg weekly (N = 153), placebo (n = 154); period 2 (24 weeks) placebo completers switched DB to adalimumab 40mg weekly, adalimumab completers re-randomised DB to adalimumab 40mg weekly, adalimumab 40mg q2wk, or placebo (not included in submission).	High	HS for ≥ 1 year with at least two areas affected and at least one Hurley II or III and nodules + abscesses ≥ 3 ; inadequate response to oral antibiotics and no previous anti-TNF.	Primary: HiSCR with 50% reduction at 16wk
PIONEER II NCT01468233	326	R, DB, MC; period 1 (12 weeks) 1:1 adalimumab 40mg weekly (N = 163), placebo (N = 163); period 2 (24 weeks) placebo completers continued DB on placebo, adalimumab completers re-randomised DB to adalimumab 40mg weekly; adalimumab 40mg q2wk, placebo (not included in submission).	High	HS for ≥ 1 year with at least two areas affected and at least one Hurley II or III and nodules + abscesses ≥ 3 ; inadequate response to oral antibiotics and no previous anti-TNF.	Primary: HiSCR with 50% reduction at 16wk
M10-647 NCT00918255	154	R, DB, MC, placebo-controlled period 16 weeks, then 36 week OL; 1:1:1 ADA 40mg weekly (N = 51), ADA 40mg q2wk (N = 52), placebo (N = 51), after 16 weeks all patients continued on ADA 40 mg q2wk (not included in submission).	Low	≥ 18 years, moderate to severe HS (= HS-PGA score ≥ 3) in at least two areas and unresponsive or intolerant to oral antibiotics	Primary: HS-PGA score 0,1, or 2 with at least 2-grade improvement at 16wk

Source: Constructed during the evaluation from CSRs and published reports.

A = abscesses; ADA = adalimumab; BKZ = bimekizumab; CFB = change from baseline; DB = double blind; DLQI = dermatology life quality index; HiSCR = hidradenitis suppurativa clinical response; HS = hidradenitis suppurativa; HS-PGA = hidradenitis suppurativa physician's global assessment; MC = multi-centre; N = number; R = randomised; SEC = secukinumab; TNF = tumour necrosis factor; wk = weeks.

- 6.25 Although BE HEARD I and II and HS0001 had an overall low risk of bias, there was a risk of unblinding in all three trials because bimekizumab and placebo syringes were distinguishable (the placebo syringes were clear and bimekizumab syringes were opalescent and pale yellowish-brown) and required different preparation and handling, so that all treatment was administered by unblinded staff (BE HEARD I CSR; BE HEARD II CSR; HS0001 CSR).
- 6.26 SUNSHINE and SUNRISE were considered by the PBAC to have an unclear overall risk of bias, because of concerns over the handling of missing data (paragraph 6.10, secukinumab PSD, March 2023 PBAC Meeting).
- 6.27 M10-467 was completed in April 2011, and the results were published in December 2012. The first publication reporting the validation of HiSCR using the M10-467 data was in December 2014 (Kimball, 2014). PIONEER I and II began in November 2011; PIONEER I was completed in January 2014 and PIONEER II in April 2014. For both trials no version of the protocol on ClinicalTrials.gov up to trial completion specified a primary outcome measure (the primary outcome was "Proportion of subjects achieving clinical response at Week 12; Subjects improvement

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in hidradenitis suppurativa severity" but "response" and "severity" were not defined). HiSCR was not mentioned until October 2015, when it was defined as the primary outcome measure.⁴

- 6.28 Because it appears that the primary outcome measure of the PIONEER trials was defined only after the end of the trials, they have been classified as having a high overall risk of bias, which differs from the risk of bias assessment previously made by PBAC (Table 3, paragraph 6.9, secukinumab PSD, July 2023 PBAC Meeting).
- 6.29 Details are provided for the bimekizumab trials (BE HEARD I/II and HS0001). Summary baseline and outcome data are provided for the secukinumab and adalimumab trials previously considered by PBAC in the presentation of the indirect treatment comparisons.
- 6.30 Chronic or recurrent infection of any aetiology, active inflammatory bowel disease, sarcoidosis, systemic lupus erythematosus, Hepatitis B and C, HIV infection, and depression required exclusion. Tuberculosis was carefully excluded, and any patient with evidence of exposure to tuberculosis had to receive preventative treatment before enrolment. The risk of adverse events related to these conditions may be higher in routine clinical use where screening may be less consistent.
- 6.31 Patients in HS0001 had more severe disease, with higher draining tunnel counts and IHS4 scores than in the BE HEARD trials,⁵ and more patients in Hurley Stage III (about 50%) than in BE HEARD I (about 45%), which had more patients in Hurley Stage III than BE HEARD II (about 36%).
- 6.32 Discontinuation due to adverse events was more common among bimekizumab patients in both BE HEARD I and II (7/289, 2.4% vs 1/72, 1.4% and 9/291, 3.1% vs 1/74, 1.4%).

Comparative effectiveness

- 6.33 The presentation of response data in BE HEARD I/II is complicated by the treatment of missing data, and of patients who received rescue antibiotics during the trials.
- 6.34 Receipt of rescue antibiotics for HS lesions was added to discontinuation for adverse events or lack of efficacy to form the category of "intercurrent event". Patients with an intercurrent event were to be classified as non-responders in the primary outcome

⁴ <https://clinicaltrials.gov/study/NCT01468207?term=NCT01468207&rank=1&tab=history&a=17#version-content-panel> accessed 18 January 2025.

⁵ IHS4 = International Hidradenitis Suppurativa Severity Score System; the score is the nodule count plus the abscess count x 2 plus the draining tunnel count x 4 (i.e., it emphasises manifestations of chronic disease compared to HiSCR). The IHS4 can be recorded as a continuous variable, or as a categorical variable (3 or less = mild, 4-10 = moderate, 11 or above = severe), or as a binary, called IHS4-55, a 55% reduction of the score from baseline. The submission reports continuous values but uses IHS4-55 in the indirect treatment comparisons.

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(BE HEARD I CSR, BE HEARD II CSR). That is, the primary outcome was achieving HiSCR at 16 weeks and not having received rescue antibiotics.

- 6.35 Treatment of an acute abscess with incision and drainage or intra-lesional corticosteroids was not an "intercurrent event" and did not require patients to be classified as non-responders; if there were more than two such interventions in the 16 week treatment period the patient "should have been discontinued" (BE HEARD I CSR), but numbers appear to have been much smaller than the numbers receiving rescue antibiotics (the reason for withdrawal under which these patients were counted, or whether this was counted as "lack of efficacy", was not stated in the CSR; BE HEARD I CSR, BE HEARD II CSR).
- 6.36 Rescue antibiotics accounted for most intercurrent events. Use of rescue antibiotics was less common among bimekizumab-treated patients in BE HEARD I (47/289, 16.3% vs 15/72, 20.8%), but more common among bimekizumab-treated patients in BE HEARD II (45/291 (15.5% vs 6/74, 8.1%).
- 6.37 In SUNSHINE and SUNRISE and PIONEER I/II rescue antibiotics were permitted and patients receiving them were not automatically classified as non-responders.
- 6.38 Missing data for the primary outcome in BE HEARD I/II at week 16 not preceded by an intercurrent event was imputed, and missing data from patients receiving rescue antibiotics was imputed for secondary outcomes. The amount of missing data was not stated.
- 6.39 The effect of various methods of data imputation for HiSCR were assessed. The results for P values, but not effect sizes, are provided in the submission (Table 2-33). In some cases, changing the method for handling missing data was associated with marked changes in the primary outcome.
- 6.40 Results for primary and selected secondary outcomes in BE HEARD I and II in the first 16 weeks are shown in Table 4. The statistical analysis plan for HS0001 was different to that for BE HEARDI/II, using Bayesian rather than frequentist methods. For this reason, the efficacy outcomes for HS0001 are shown separately, in Table 5.

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Table 4: Efficacy outcomes in BE HEARD I and II

	BE HEARD I		BE HEARD II	
	BKZ 320mg every 2 weeks N = 289	Placebo N = 72	BKZ 320mg every 2 weeks N = 291	Placebo N = 74
HiSCR50 at week 16, n % 95% CI	138 47.8% 41.8, 53.7	21 28.7% 18.1, 39.3	151 52.0% 46.1, 57.8	24 32.2% 21.4, 42.9
Difference (95% CI)	18.1 (6.3, 30.0)		19.6 (7.5, 31.7)	
IHS4, CFB, mean (SE)	-15.6 (1.4)	-4.9 (2.6)	-17.7 (1.3)	-6.8 (1.9)
Baseline Abscess + nodule count, mean (SD)	15.3 (13.5)	15.0 (11.9)	16.7 (15.5)	13.9 (7.8)
Abscess + nodule count, CFB, mean (SE)	-7.5 (0.6)	-3.9 (1.1)	-8.9 (0.6)	-4.4 (0.9)
Baseline Draining tunnel count, mean (SD)	4.0 (0.3)	3.2 (0.5)	3.6 (0.2)	3.5 (0.4)
Draining tunnel count, CFB, mean (SE)	-1.5 (0.2)	-0.3 (0.4)	-1.7 (0.2)	-0.4 (0.3)
Flares, n (%) ¹	82 (28.5%)	34 (47.8%)	NR	NR
DLQI, CFB				
Median	-4.0	-2.0	-3.0	-3.0
IQR	-8.0, -1.0	-6.0, 1.0	-8.0, 0.0	-6.5, 0.0
Range	-26.0, 11.0	-20.0, 18	-25.0, 10.0	-17.0, 9.0
LS Mean (95% CI)	-5.2 (-6.1, -4.3)	-2.5 (-4.1, -1.0)	-4.7 (-5.5, -3.9)	-2.4 (-3.6, -1.1)
Difference (95% CI)	-2.7 (-4.2, -1.2)		-2.3 (-3.5, -1.1)	
% with DLQI 0 or 1 at 16 weeks (95% CI)	32.6 (27.0, 38.2)	21.1 (11.6, 30.6)	16.6 (12.3, 21.0)	6.8 (NE)
Baseline HSSDD Worst Skin Pain Score, mean (SD)	5.5 (2.5)	6.0 (2.5)	5.3 (2.4)	5.0 (2.4)
CFB to 16 weeks HSSDD Worst skin Pain score, mean (SD)	-1.9 (2.6)	-1.1 (2.0)	-1.9 (2.4)	-0.4 (2.1)
LS mean difference at 16 weeks Worst Skin Pain BKZ-PBO (95% CI)	-1.2 (-1.9, -0.4)		-1.3 (-1.9, -0.6)	

Source: Kimball, 20204, Table 2; BE HEARD I CSR, Table 7-8, pp152-154, Table 8-15, p218, Table 8-19, pp235-236, Table 8-25, p252; BE HEARD II CSR, Table 7-8, pp148-151, Table 8-9, p193, Table 8-16, p218, Table 8-19, pp228-230, Table 8-26, p252; Table 2.40, p131 of the submission. Statistically significant results are in **bold**.

¹ A disease flare was defined as a 25% increase from baseline abscess + nodule count with a minimum absolute increase of 2. BKZ = bimekizumab; CFB = change from baseline; CI = confidence interval; DLQI = dermatology life quality index; HiSCR50 = 50% reduction in hidradenitis suppurativa clinical response; HSSDD = hidradenitis suppurativa symptom daily diary (each symptom scored on an 11-point scale); IHS4 = international hidradenitis suppurativa severity score system; IQR = inter-quartile range; LS = least squares; NE = not evaluable; SE = standard error.

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Table 5: Efficacy outcomes in HS0001

	Bimekizumab N = 46	Adalimumab N = 21	Placebo N = 21
Posterior response rate at 12 weeks, %			
Mean (SD)	57.3 (7.4)	59.5 (7.7)	26.1 (6.8)
Median	57.4	59.7	25.7
95% credible interval	42.4, 71.4	44.2, 73.9	13.8, 40.5
BKZ - ADA			
Posterior Difference, mean (SD)		-2.2 (10.6)	
95% credible interval		-11.2, 6.6	
Probability Difference > 0%, %		42.1%	
BKZ - PBO			
Posterior Difference, mean (SD)		31.2 (10.1)	
95% credible interval		11.0, 50.4	
Probability Difference > 0%, %		99.8%	
Frequentist analysis of HiSCR at 12 weeks			
Response rate (%) 95% CI	56.0 (41.4, 71.2)	NR	23.7 (10.2, 45.8)
Baseline Abscess + nodule count, mean (SD)	14.5 (11.9)	NR	22.1 (21.2)
CFB at 12 weeks in abscesses + nodules count, mean (SD)	-9.4 (11.8)	NR	-4.8 (15.8)
mean % change (SD)	-54.1% (67.3)		-2.3% (89.4)
Baseline draining tunnel count, mean (SD)	5.3 (5.1)	NR	5.5 (5.3)
CFB at 12 weeks in draining tunnels count, mean (SD)	-3.1 (4.2)	NR	-0.9 (4.1)
mean % change (SD)	-54.6% (54.4)		6.8% (71.4)
CFB DLQI, mean (SD)	-5.4 (6.8)	-7.5 (6.0)	-0.8 (6.6)

Source: HS0001 CSR, Table 8-1, p115; Table 8-2, p117; Table 8-7, pp128-129; Table 8-11, p137.

ADA = adalimumab; BKZ = bimekizumab; CFB = change from baseline; DLQI = dermatology life quality index; HiSCR = hidradenitis suppurativa clinical response; PBO = placebo; SD = standard deviation.

- 6.41 The HiSCR50 primary outcome was more often achieved in bimekizumab-treated patients. Bimekizumab was superior on all other outcomes, although the effect size was generally less than with HiSCR and some of the differences were not statistically significant.
- 6.42 A disease flare was defined as a 25% increase in abscesses + nodules count with a minimum absolute increase from baseline of 2, and a flare could occur, but a patient could still achieve a HiSCR response at 16 weeks. The flare rate was somewhat lower with bimekizumab in BE HEARD I but was not reported for BE HEARD II. However, time to disease flare was reported in BE HEARD II and clearly did not differ between bimekizumab-treated and placebo-treated patients (BE HEARD II CSR, Figure 8-7).
- 6.43 DLQI scores fell (i.e., quality of life was less impaired) in both treatment groups. The minimum clinically important difference (MCID) for DLQI has been reported to be

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between 3 and 5 in inflammatory conditions, with 4 a commonly used MCID.⁶ On that basis, the mean changes from baseline in DLQI with bimekizumab in BE HEARD I/II were just clinically significant, and the differences between bimekizumab and placebo were not clinically significant.

- 6.44 The proportions of patients with DLQI of 0 or 1 (i.e., no or minimal impairment) were higher with bimekizumab, but the rates in BE HEARD I were higher in both treatment groups than in either treatment group in BE HEARD II.
- 6.45 A threshold for clinically meaningful change in pain scores was also defined. The average of daily worst pain scores for the week preceding each study visit was calculated, and a clinically significant change was a three-point or greater fall in this weekly mean from baseline. Patients with a weekly average score of less than three at baseline were, therefore, excluded.
- 6.46 The least squares mean difference in pain scores at 16 weeks was less than the clinically significant change: -1.2 in BE HEARD I and -1.3 in BE HEARD II. In BE HEARD I the percentage (95% CI) of patients with a clinically significant response in pain score was 15.0% (3.6, 26.5) among placebo-treated patients and 32.3% (25.1, 39.5) among bimekizumab-treated patients. In BE HEARD II the percentage (95% CI) of patients with a clinically significant response in pain was 10.9% (1.7, 20.1) among placebo-treated patients and 31.8% (25.1, 38.4) among bimekizumab-treated patients.
- 6.47 Analysis of subgroups was reported in Table 2.34 of the submission.
- 6.48 The most important of these sub-group results for the purpose of the submission was that HiSCR50 response rates were higher for bimekizumab-treated patients with Hurley Stage II than for patients with Hurley Stage III (53.1% vs 42.1% respectively in BE HEARD I and 58.1% vs 42.4% respectively in BE HEARD II). Differences in the proportions of patients with Hurley Stages II and III among trials may be an important transitivity issue, because trials with fewer Hurley Stage III patients would likely report better results.

Indirect Treatment Comparisons for Efficacy to 16 weeks

- 6.49 Baseline characteristics of patients and the placebo response rates for HiSCR50 in the trials used in the indirect treatment comparison (ITCs) are shown in Table 6.

⁶ NICE, Adalimumab for treating moderate to severe hidradenitis suppurativa, 2016, www.nice.org.uk/guidance/ta392 p44.

Basra MK, Salek MS, Camilleri L, Sturkey R, Finlay AY. Determining the minimal clinically important difference and responsiveness of the Dermatology Life Quality Index (DLQI): further data. *Dermatology* 2015; 230:27-33.

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Table 6: Transitivity considerations in the trials used in ITCs

	HS0001	BE HEARD I	BE HEARD II	SUNRISE	SUNSHINE	PIONEER I	PIONEER II	M10-467
	BKZ vs ADA vs PBO	BKZ vs PBO	BKZ vs PBO	SEC vs PBO	SEC vs PBO	ADA vs PBO	ADA vs PBO	ADA vs PBO
BMI, kg/m ² , mean (SD)	34.8 (8.4)	33.8 (8.2)	32.3 (8.0)	31.8 (7.6)	32.5 (7.6)	33.8 (7.8)	32.1 (7.7)	NR
A + N count, mean (SD)	17.7 (14.8)	16.0 (17.5)	16.5 (14.6)	13.3 (9.1)	12.8 (8.8)	14.4 (13.4)	11.3 (9.7)	NR
DT count, mean (SD)	5.1 (4.9)	3.8 (4.8)	3.4 (3.7)	2.7 (3.4)	2.6 (3.4)	4.2 (4.8)	3.4 (4.7)	4.5 (NR)
HS Duration, years, mean (SD)	9.0 (8.0)	9.0 (8.3)	7.0 (7.1)	7.4 (7.4)	7.2 (7.3)	NR	NR	12.4 (9.8)
US Region, %	50.0	40.8	22.2	15.2	15.2	50.5	27.3	74.5
DLQI, mean (SD)	12.6 (7.5)	12.0 (7.1)	10.8 (6.6)	14.9 (7.1)	13.8 (6.7)	16.1 (6.9)	14.5 (7.5)	15.9 (7.6)
Current Smokers, %	NR	43.0	48.1	54.0	54.0	56.4	65.6	57.8
Hurley III, %	51.0	49.7	38.9	40.5	34.0	47.6	46.3	29.4
Placebo HiSCR50 response at end of treatment period, % (95 % CI)	23.7 (10.2, 45.8)	28.7 (18.1, 39.3)	32.2 (21.4, 42.9)	31 (NR)	34 (NR)	26.0 (NR)	27.6 (NR)	25.5 (NR)

Source: Table 2.71, p172, Table 2.72, p172 of the submission; BE HEARD I CSR, Table 8-4, p185; BE HEARD II CSR, Table 8-4, p183. A + N = abscesses + nodules; ADA = adalimumab; BKZ = bimekizumab; BMI = body mass index; DLQI = dermatology life quality index; DT = draining tunnels; HS = hidradenitis suppurativa; PBO = placebo.

¹ A flare was defined as a 25% increase in abscess + nodule count and an absolute increase from baseline of at least 2.

6.50 Comparability of baseline severity was difficult to assess because relativities differed by severity metric. Patients in BE HEARD I/II had higher abscess + nodule counts than patients in SUNRISE and SUNSHINE or PIONEER I/II, and higher draining tunnel counts than patients in SUNSHINE and SUNRISE but not patients in PIONEER I/II, but less impairment of quality of life than patients in either SUNRISE/SUNSHINE or PIONEER I/II. Current smoking was associated with worse outcomes in HS, and BE HEARD I/II had a lower proportion of current smokers than SUNSHINE and SUNRISE, which had a lower proportion of current smokers than PIONEER I/II.

6.51 Placebo response rates using HiSCR50 were similar in all the trials. The results of the ITC for HiSCR50 are shown in Table 7.

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Table 7: Indirect treatment comparisons for HiSCR50 using NRI

	Relative Risk (95% CI)	Risk Difference (95% CI)
Adalimumab vs Placebo		
M10-672	2.1 (1.2, 3.8)	29.0 (9.3, 48.6)
HS0001	2.4 (1.02, 5.7)	31.8 (4.6, 59.0)
PIONEER I	1.61 (1.2, 2.2)	15.9 (5.4, 26.3)
PIONEER II	2.1 (1.6, 2.8)	31.3 (21.1, 41.5)
Meta-analysis, fixed effects	1.9 (1.6, 2.4)	24.8 (18.2, 31.5)
Bimekizumab vs Placebo		
HS-0001	2.4 (1.1, 5.4)	31.6 (9.0, 54.3)
BE HEARD I	1.6 (1.1, 2.2)	18.9 (6.6, 31.2)
BE HEARD II	1.7 (1.2, 2.4)	23.9 (11.8, 36.0)
Meta-analysis, fixed effects	1.7 (1.4, 2.2)	22.6 (14.5, 30.7)
Secukinumab vs Placebo		
SUNSHINE	1.3 (1.03, 1.7)	11.1 (1.2, 21.0)
SUNRISE	1.4 (1.03, 1.8)	11.3 (1.3, 21.3)
Meta-analysis, fixed effects	1.35 (1.1, 1.6)	11.2 (4.2, 18.2)
Bimekizumab vs Adalimumab		
Fixed effects	0.9 (0.6, 1.2)	-2.2 (-12.7, 8.2)
Bimekizumab vs Secukinumab		
Fixed effects	1.32 (0.98, 1.8)	13.5 (2.8, 24.2)

Source: Attachment 4.3 of the submission. CI = confidence interval; HiSCR50 = hidradenitis suppurativa clinical response as 50% reduction in abscess + nodule count with no increase in abscesses or draining tunnels; NRI = non-response imputation.

- 6.52 A similar pattern of results was seen with HiSCR75, HiSCR90 and IHS4-55 (response defined as 55% reduction in IHS4 score). However, on the IHS4-55 outcome the difference between bimekizumab and secukinumab was statistically significant in favour of bimekizumab: relative risk (95% CI) was 1.6 (1.1, 2.2) and risk difference was 15.8 (5.5, 26.2).
- 6.53 The Pre-Sub-Committee Response provided additional indirect treatment comparisons at 12-16 weeks based on BKZ treatment regimen (Q2W/Q4W and Q4W only) for the outcomes of HiSCR50, 75 and 90 response and change in IHS4 (international hidradenitis suppurativa severity score system). For the primary outcome of HiSCR50, the results found a statistically significant difference for the Q2W/Q4W regimen over secukinumab Q2W and Q4W based on the odds ratio statistic, with no significant difference found versus adalimumab or for the bimekizumab Q4W only regimen. The ESC considered the additional analyses provided in the PSCR at 12-16 weeks were difficult to interpret as the subgroup analyses were presented as odds ratios, whilst the original submission analyses were presented based on relative risk and risk difference. The Pre-PBAC Response clarified that analyses based on odds ratio were also presented in the original submission.

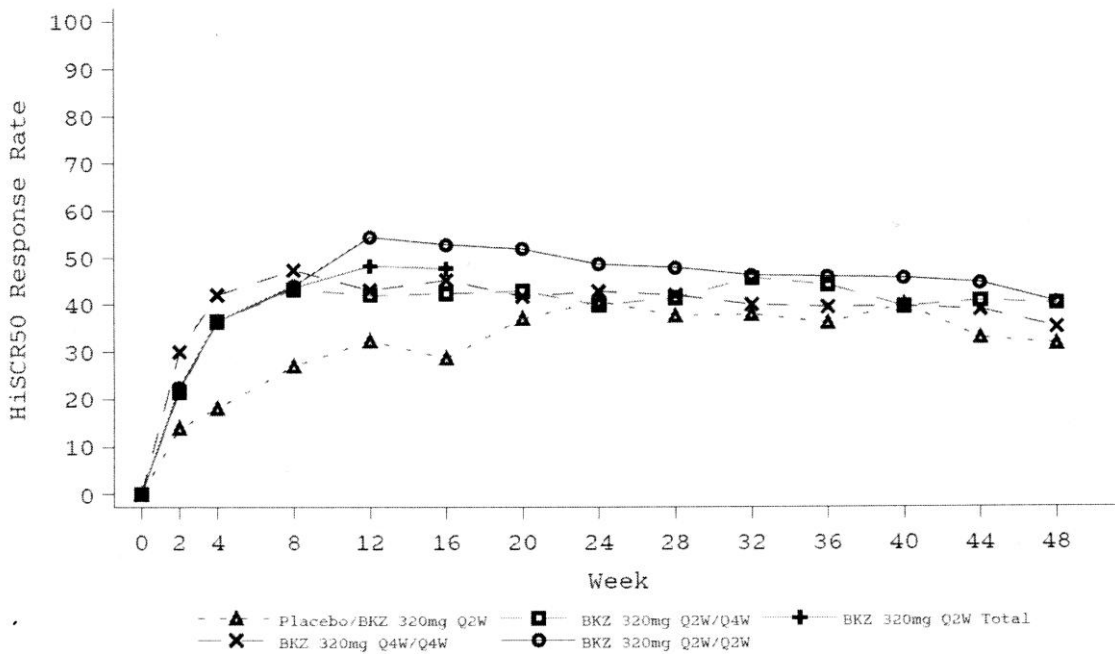
Efficacy during extended treatment periods

- 6.54 Response rates in BE HEARD I and II at 16 weeks and at 48 weeks are shown in Figure 3 and Figure 4. Placebo patients (triangles) switched to open label bimekizumab every 2 weeks after the 16 week double-blind period.
- 6.55 There was a trend, somewhat more marked in BE HEARD I, for response rates at 48 weeks to be lower, but most patients in BE HEARD I and II who had achieved a

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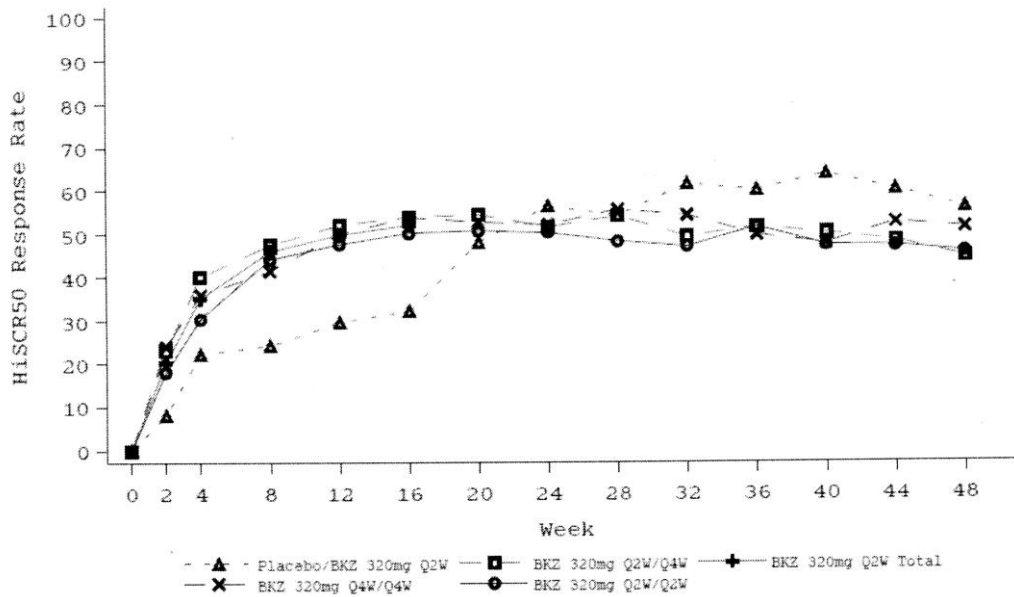
HiSCR50 response at 16 weeks sustained their response to 48 weeks. However, the proportion of patients who had a HiSCR50 response at week 16 and at week 48 was relatively low. In BE HEARD I, a HiSCR50 response was achieved at 16 and 48 weeks in 29/146 (19.9%) of patients treated with bimekizumab 320 mg every 2 weeks during the first 16 weeks and bimekizumab 320 mg every 4 weeks in the second 32 weeks (BE HEARD I CSR, Table 8-12). In BE HEARD II a HiSCR50 response was achieved at 16 and 48 weeks in 38/146 (26.0%) of patients treated with bimekizumab 320 mg every 2 weeks during the first 16 weeks and bimekizumab 320 mg every 4 weeks in the second 32 weeks. (BE HEARD II CSR, Table 8-13).

Figure 3: HiSCR50 response rates to 48 weeks in BE HEARD I



Source: BE HEARD I CSR, Figure 8-4, p203. BKZ = bimekizumab.

Figure 4: HiSCR50 response rates to 48 weeks in BE HEARD II



Source: BE HEARD II CSR, Figure 8-4, p204. BKZ = bimekizumab.

- 6.56 The submission presented a figure from Kimball 2024 for response rates over 48 weeks showing a marked rise in response rates in all groups between 16 and 48 weeks (Figures 2.12 and 2.13 of the submission). This graph was prepared using the observed cases method of handling missing data, which was pre-specified only as a sensitivity analysis (BE HEARD I CSR, Table 6-1; BE HEARD II CSR, Table 6-1).
- 6.57 The graphs of HiSCR responses to 48 weeks reproduced above from the CSR were prepared using the multiple imputation Markov-Chain Monte Carlo method used generally in the CSR. For patients treated with bimekizumab 320 mg every 2 weeks to week 16, HiSCR50 response rate was 61.9% by the observed case method and 50% by the protocol-defined method of handling missing data. The response rate for patients treated with bimekizumab 320 mg every 2 weeks to week 16 then 320 mg every 4 weeks to week 48 was 81.3% at week 48 by the observed case method and about 42% by the multiple imputation Markov-Chain Monte Carlo method. This degree of sensitivity of outcomes to the method of handling missing data raises concerns about the generalisability of the results.
- 6.58 The HiSCR response rate at 52 weeks for pooled SUNSHINE and SUNRISE (secukinumab) data was 155/254 (61%) for patients receiving secukinumab 300 mg every 2 weeks and 151/255 (59.2%) for patients receiving secukinumab 300 mg every 4 weeks (Table 2.49 of the submission). These rates were higher than those achieved at 48 weeks with bimekizumab.
- 6.59 However, data for HiSCR50 response rates at 52 weeks in SUNSHINE and SUNRISE were difficult to compare with data from BE HEARD I/II, because of the method of dealing with missing data. The method used in SUNSHINE and SUNRISE was not clearly

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defined in the published paper, but appears to have been similar to the observed case method in BE HEARD I/II and may have resulted in higher estimated response rates for secukinumab (Figures 2.22 and 2.23 of the submission).

- 6.60 In PIONEER I and II loss of response with continued treatment was common. Of 21 patients in PIONEER I treated with adalimumab 40 mg weekly for the first 12 weeks who had a HiSCR50 response at 12 weeks and who continued adalimumab 40 mg weekly, 11/21 (52.4%) had a response at week 36. In the same group of patients in PIONEER II, 14/31 (45.2%) had a response at week 36.
- 6.61 In PIONEER I/II more new responses between weeks 12 and 36 were reported among patients who had not achieved a HiSCR50 response at 12 weeks than in BE HEARD I/II and SUNSHINE/SUNRISE. In PIONEER I of 27 subjects who received adalimumab 40 mg weekly to week 12 but had not had a response at week 12 and then continued on adalimumab 40 mg weekly, 10/27 (37%) had a response at week 36. In the same group of patients in PIONEER II, 8/20 (40%) had a response at week 36.
- 6.62 Overall, during the extended treatment periods (48 or 52 weeks), there were no large differences between bimekizumab and secukinumab using HiSCR50 as the response. However, comparison is difficult because of differences in methods of handling missing data, and the decision to make patients receiving rescue antibiotics non-responders in BE HEARD I/II but not in SUNSHINE and SUNRISE.
- 6.63 Comparison with longer-term data in PIONEER I/II is very difficult because of the very high drop-out rates in PIONEER I/II between week 12 and week 36, and the small numbers of patients completing 36 weeks.
- 6.64 The PSCR presented a group of Matching-Adjusted Indirect Comparisons (MAIC) at 48 weeks for the bimekizumab Q2W/Q4W and Q4W regimens versus secukinumab Q2W, Q4W and adalimumab, matched on sex, race, smoking status and HS severity status, with scenario analyses exploring different methods of handling missing data. Analyses for bimekizumab Q4W only versus secukinumab using a non-responder imputation approach also found statistically significant differences favouring bimekizumab over both secukinumab regimens for HiSCR50, 75 and 90 response. Analyses for bimekizumab Q2W/Q4W and Q4W versus adalimumab generally found no difference between bimekizumab and adalimumab for HiSCR50, 75 or 90, with the exception of bimekizumab Q2W/Q4W versus adalimumab, which favoured bimekizumab. The ESC also considered the Matching-Adjusted Indirect Comparison (MAIC) at 48 weeks to be uncertain, as issues such as handling of missing data in the statistical comparison and large dropout rates in the adalimumab trials were not clearly addressed. Furthermore, the ESC also considered the available data for adalimumab to be unreliable to inform comparisons at 48 weeks, due to the large number of dropouts in the adalimumab trials. The Pre-PBAC Response reiterated these analyses represent the best available evidence and argued bimekizumab should not be disadvantaged due to the unreliability of the adalimumab data due to the high withdrawal rate in those trials.

Comparative harms

- 6.65 A summary of adverse events in BE HEARD I and II and HS0001 are shown in Table 8.
- 6.66 The increased rate of abnormalities of liver function seen in BE HEARD I but not BE HEARD II was noted in the TGA Delegate's overview (Table 43, 44). Also noted by the Delegate was that in BE HEARD I there were only 2/140 (1.4%) patients randomised to bimekizumab 320 mg every 4 weeks throughout who had at least one abnormal liver function test result.

Table 8: Summary of key adverse events in BE HEARD I and II and HS0001

	BE HEARD I		BE HEARD II		HS0001		
	BKZ 320mg q2wk N = 286	Placebo N = 72	BKZ 320mg q2wk N = 290	Placebo N = 74	BKZ N = 46	ADA N = 21	Placebo N = 21
Treatment Period 0 to 16 weeks							
Patients with TEAE, n (%)	192 (67.1%)	48 (66.7%)	187 (64.5%)	42 (56.8%)	32 (70%)	15 (71%)	13 (62%)
Patients with TESAEs, n (%)	6 (2.1%)	0	9 (3.1%)	0	2 (4%)	1 (5%)	2 (10%)
Patients discontinuing due to AE, n (%)	10 (3.5%)	1 (1.4%)	12 (4.1%)	0	1 (2%)	0	0
Patients with Infections and infestation, n (%)	98 (34.3%)	18 (25.0%)	95 (32.8%)	12 (16.2%)	20 (44%)	9 (43%)	4 (19%)
Number of infections and infestations	154	26	154	15	41	19	4
Patients with oral candidiasis, n (%)	17 (5.9%)	0	24 (8.3%)	0	3 (7%)	1 (5%)	0
Number of events of oral candidiasis	18	0	26	0	4	1	0
Patients with at least one abnormal liver test, n (%)	10 (3.5%)	0	3 (1.0%)	1 (1.4%)	NR		
AST or ALT >3x ULN, n (%)	8 (2.8%)	0	0	0			

Source: Table 2.61, p153, Table 2.62, pp154-155, Table 2.65, p160 of the submission; BE HEARD I CSR, Table 11-6, p301, Table 11-7, pp305-308; BE HEARD II CSR, Table 11-6, p308, Table 11-7, p313; Bimekizumab Delegate's Overview e005979 – (0026) Table 43, 44, pp66-67. ADA = adalimumab; AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BKZ = bimekizumab; TEAE = treatment-emergent adverse event; TESAE = treatment-emergent serious adverse event; ULN = upper limit of normal.

- 6.67 Overall, the adverse event profiles of bimekizumab, secukinumab and adalimumab were similar. Oral candidiasis was more common with bimekizumab than with secukinumab, but total infections were similar. Total infections were more common with bimekizumab than with adalimumab. Discontinuations due to adverse events

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were more common with bimekizumab than with placebo, and the rate with bimekizumab may have been higher than with secukinumab and adalimumab. There was one death in all eight trials, considered not to be treatment related.

Extended Assessment of Safety (Bimekizumab only)

- 6.68 Safety data from an open label extension study of BE HEARD I/II, BE HEARD EXT (also referred to as HS0005), were included in the submission. Patients entering BE HEARD EXT who had achieved HiSCR90 response were treated with bimekizumab 320 mg every 4 weeks, and those who had not achieved HiSCR90 response were treated with bimekizumab 320 mg every 2 weeks. Patients could switch from every 4 weeks to every 2 weeks based on prespecified criteria (Zouboulis, 2024, slide 3). The numbers receiving each dose were not reported. A total of 556 patients entered BE HEARD EXT, but "96 week" data were presented for 995 patients - i.e., patients who had received only 48 week treatment were included. For this reason, these data are not included in the evaluation.
- 6.69 Bimekizumab has been in clinical use since 2021 and the Periodic Safety Update Report (PSUR) from August 2024 was provided. The dose of bimekizumab for HS is twice that for other indications (for plaque psoriasis the dose is 320 mg every 4 weeks for 16 weeks then 8th weekly; for psoriatic arthritis and axial spondyloarthritis the dose is 160 mg every 4 weeks). Since most use has been in conditions requiring lower doses, the data from post-marketing experience may not reflect adverse event risk in HS. This is especially relevant in relation to the increased incidence of abnormal liver function tests seen in bimekizumab-treated patients in BE HEARD I.
- 6.70 Hypersensitivity reactions and serious infections have been identified by regulatory agencies as risks of bimekizumab. No new safety signals were identified in post-marketing data for these risks.
- 6.71 Other issues identified as requiring post-marketing monitoring were adverse events for pre-filled pen vs pre-filled syringe preparations and suicidal ideation or behaviour; bimekizumab clinical trials excluded patients thought to be at higher risk of suicide.
- 6.72 Rates of adverse events were roughly twice as high with pre-filled pen than with pre-filled syringe (47.82 per 100 patient-years vs 26.41) (Attachment 5.2, Table 15-1 of the submission). Events likely to be related to the injection method were consistently more common with the pre-filled pen (e.g., injection site pain 2.60 per 100 patient-years vs 1.01) (Attachment 5.2, Table 15-3 of the submission). However, similar differences were seen for nearly all adverse event classes, including some with no obvious connection to the injection device, which may indicate reporting bias.
- 6.73 Suicidal ideation or behaviour was reported in 22 patients, with no reported events of suicide attempts or completed suicide (one case of suicidal ideation was reported from Australia). The reported rate was not clearly higher than in the community at large, but it appears to have increased recently: using data up to 19 February 2024 it

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was 0.17 per 100 patient years and using data from then until 19 August 2024 it was 0.26 (Attachment 5.2, Table 15-7 of the submission).

Benefits/harms

- 6.74 A benefits and harms table is not presented as the submission made a claim of non-inferiority in relation to adalimumab and no evidence was presented from which benefits and harms could be calculated versus secukinumab.

Clinical claim

- 6.75 The submission described bimekizumab as superior in efficacy to secukinumab after both 16 weeks and 48 weeks treatment, and non-inferior in efficacy to adalimumab after 16 weeks treatment and superior after 48 weeks treatment (Table 1.1 of the submission).
- 6.76 The evaluation and ESC considered the claim of superiority to secukinumab in relation to 16 weeks treatment was not adequately supported. The results of the indirect treatment comparison were marginally statistically significant, and there were issues with the treatment of missing data that compromised the reliability of the comparisons.
- 6.77 The evaluation and ESC considered that the superiority claims at 48 weeks treatment (against both secukinumab and adalimumab) were not adequately supported due to the lack of interpretable comparative data capable of justifying these claims being presented (versus secukinumab) and due to the large dropouts in adalimumab (versus adalimumab). The ESC acknowledged the PSCR statement that the presented data represents the best available data, however considered the comparisons were associated with inherent substantial uncertainty, for the purposes of establishing superiority; however, considered a claim of non-inferiority may be reasonable.
- 6.78 The evaluation considered the claim of non-inferior efficacy versus adalimumab in 16 weeks treatment was not adequately supported based on the RCT evidence alone because of the high risk of bias in the key trials of adalimumab and the issues with the handling of missing data in the bimekizumab trials; but the evaluation and ESC considered that, taking into account the totality of the evidence, the claim is probably reasonable.
- 6.79 The evaluation and ESC considered the claims of non-inferior safety relative to adalimumab and secukinumab were adequately justified.
- 6.80 The PBAC considered that the claim of superior comparative effectiveness to secukinumab at 16 weeks and 48 weeks was overall likely not supported by the available data. The PBAC considered the claim of non-inferiority to adalimumab at 16 weeks was overall reasonable, however the claim of superiority beyond 48 weeks was not adequately supported due to difficulties interpreting the available data. Overall, the PBAC considered a claim of non-inferior comparative effectiveness across both 16

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and 48 weeks of treatment to both secukinumab and adalimumab was likely supported by the data.

6.81 The PBAC considered that the claim of non-inferior comparative safety to secukinumab and adalimumab was reasonable.

Economic analysis

6.82 The submission presented a cost minimisation approach for the economic analysis. The key components in the analysis 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 Section 2, effectiveness of bimekizumab is assumed to be superior to secukinumab and non-inferior to adalimumab
Therapeutic claim: safety	Based on evidence presented in Section 2, safety is assumed to be non-inferior to secukinumab and adalimumab with potential benefits compared to adalimumab due to reduced injection frequency.
Evidence base	Indirect comparison of randomised placebo-controlled trials.
Equi-effective doses	The equi-effective doses are based on the PIs and PBAC recommendation for SEC (Nov 2023): BKZ 320 mg every 2 weeks up to Week 16 and every 4 weeks thereafter (30.25 x 320 mg doses over two years) SEC 300 mg weekly for 5 doses then SEC 300 mg every 4 weeks (80%) or SEC 300 mg every 2 weeks (20%) (29.25 x 300 mg doses over two years OR 5 x 300 mg doses plus 49.5 x 150 mg doses over two years). Using an 80:20 split from PBAC recommendation equals on average 34.3 x 300 mg doses of SEC over two years ADA 160 mg initially at Day 1 followed by 80 mg two weeks later at Day 15 two weeks later continue with a dose of 40 mg every week or 80 mg fortnightly (53.5 x 80 mg doses over two years).
Direct medicine costs	Cost minimisation of BKZ and SEC is based on the dosage recommendations in the PIs and PBAC recommendation over a 2-year period, which captures the loading and maintenance doses. Total costs of treatment are calculated over the 2-year period and the AEMP is calculated for BKZ based on the required number of packs. The total two-year cost (AEMP) of SEC is \$45,158.01 using published prices. The proposed AEMP of BKZ 320 mg using the SEC visible price is calculated to be \$1,492.83 (\$45,158.01/30.25), which is a DPMQ of \$1,632.78 for 2 x 160 mg syringes
Other costs or cost offsets	None

Source: Table 3.1.1, pp197-198 of the submission. ADA = adalimumab, AEMP = approved ex-manufacture price, BKZ = bimekizumab, DPMQ = dispensed price max quantity, EED = equi-effective dose, mg = milligram, PBS = Pharmaceutical Benefits Scheme, PI = Product Information, SEC = secukinumab

6.83 The equi-effective doses were based on the PBAC recommendation for secukinumab from November 2023 and were estimated as:

- BKZ 320 mg every 2 weeks up to Week 16 and every 4 weeks thereafter (30.25 x 320 mg doses over two years);
- SEC 300 mg weekly for 5 doses (weeks 0, 1, 2, 3, 4) then SEC 300 mg every 4 weeks (80%) or SEC 300 mg every 2 weeks (20%) (29.25 x 300 mg doses over two years)

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OR 5 x 300 mg doses plus 49.5 x 150 mg doses over two years). Using an 80:20 split from the PBAC recommendation equals on average 34.3 x 300 mg doses of SEC over two years; and

- ADA 160 mg initially at Day 1 followed by 80 mg two weeks later at Day 15 then two weeks later continue with a dose of 40 mg every week or 80 mg fortnightly (53.5 x 80 mg doses over two years).

These doses were consistent with the Product Information documents, including the draft PI for bimekizumab although the dose of secukinumab described in the text for the 2 weekly regimen should be 300 mg, not 150 mg; 300 mg was used in the calculations in the submission. The Pre-PBAC Response proposed a weighting of bimekizumab initial dose regimens based on 20% Q2W/Q4W use and 80% Q4W use.

6.84 The use of a quarter-cycle correction to account for the 104th week is unnecessary, as the standard approach for 2-year cost minimisation approaches for therapies of this type are calculated to the end of week 103. The calculations below removes the additional dose allowance for the 104th week, and accounts for the bimekizumab induction dose weighting proposed in the Pre-PBAC Response. The results of the cost minimisation calculations using the published prices are shown in Table 10. As the price versus adalimumab was not presented in the submission it has been added, based on AEMP of \$618.80/80 mg injection as of 1 February 2025 data.

Table 10: Results of the cost minimisation approach, over 2 years, published prices.

Name	Doses over two years*	AEMP per dose	Two-year AEMP
Secukinumab 300 mg Q4W	29	\$1,316.56	\$38,180.24
Secukinumab 300 mg Q2W	54	\$1,316.56	\$71,094.24
Weighted 2-year cost (80% Q4W, 20% Q2W)			\$44,763.04
Adalimumab 80mg	53	\$618.90	\$32,801.70
Bimekizumab 320 mg Q2W/Q4W	30	\$1,093.39	\$32,801.70
Bimekizumab 320 mg Q4W	26	\$1,261.60	\$32,801.70

Source: Tables 3.4.1 and 3.4.2, p202 of the submission. Abbreviations: AEMP = approved ex-manufacturer price, mg = milligram

*Updated based on Pre-PBAC Response based on regimens outlined in the TGA Delegate’s Overview. The AEMP per dose is taken from the September 2024 PBS pricing spreadsheets

6.85 Should the PBAC accept the clinical claim of overall non-inferior effectiveness and safety (versus secukinumab or adalimumab), the cost-minimisation approach must establish that the cost per patient for treatment with bimekizumab would be no more than the cost per patient treated with secukinumab or adalimumab. 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. No compelling evidence was provided that bimekizumab provides a significant improvement in efficacy and/or safety over secukinumab or adalimumab.

6.86 The PSCR noted that based on the ACM advice that supported both Q2W and Q4W dosing in initial treatment, that a re-specified cost minimisation approach that included a proportion of Q4W use in initial treatment would result in fewer doses over

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two years and an increase in the price of bimekizumab. The Pre-PBAC Response noted the TGA had registered the Q2W dosing regimen for initial treatment (16 weeks) and proposed an 80:20 weighting (80% Q4W, 20% Q2W) dosing for initial treatment, based on the dosing regimen split the PBAC recommended for secukinumab in November 2023 (paragraph 5.8, secukinumab PSD, November 2023 PBAC).

Drug cost/patient/ year

6.87 Based on the cost minimisation approach using the published price of secukinumab, the cost per patient over 2 years would be \$45,158.01.

Estimated PBS usage & financial implications

6.88 This submission was not considered by DUSC. The submission appropriately used a market share approach to estimate the use and financial impact of listing bimekizumab for HS. The key inputs for the financial estimates are shown in Table 11.

Table 11: Key inputs for financial estimates

Parameter	Value applied and source	Comment		
Current market for HS	PBS Statistics for adalimumab and secukinumab, authority codes	Reasonable		
Uptake rate from existing treatments		Estimates based on sponsor assumptions.		
	Year 1 (2025)		adalimumab %	secukinumab %
	Year 2 (2026)		%	%
	Year 3 (2027)		%	%
	Year 4 (2028)		%	%
	Year 5 (2029)		%	%
	Year 6 (2030)		%	%
Growth rate	Year 1 (2025)	%	Assumes market growth will flatten over time. *Growth rate not needed for this year of the model.	
	Year 2 (2026)	%		
	Year 3 (2027)	%		
	Year 4 (2028)	%		
	Year 5 (2029)	%		
	Year 6 (2030)	%*		
Grandfathered patients	Not included – claims it would be double counting	May be reasonable		
Dose/duration	Calculated over 2 years as for economic evaluation	Reasonable		
Script equivalence	12.2 = 13.0 Derived from PI documents and weighted according to secukinumab PBAC recommendation for usage- 20% Q2W: 80%Q4W.	reasonable		
MBS items	None	Appropriate		

Source: compiled from Section 4 of the submission

6.89 The net cost to the PBS using the published price of secukinumab to calculate the cost minimised price of bimekizumab is shown in Table 12. The submission also presented estimates of the cost based on the proposed published price of bimekizumab.

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Table 12: Estimated use and financial implications, DPMQ, published prices.

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of scripts dispensed	█ ¹	█ ¹	█ ¹	█ ²	█ ²	█ ²
Estimated financial implications of bimekizumab.						
Cost to PBS/RPBS less copayments	\$█ ³	\$█ ³	\$█ ³	\$█ ⁴	\$█ ⁴	\$█ ⁴
Estimated financial implications for other medicines)						
Cost to PBS/RPBS less copayments	-\$█ ⁵	-\$█ ⁵	-\$█ ⁵	-\$█ ⁵	-\$█ ⁵	-\$█ ⁵
Net financial implications						
Net cost to PBS/RPBS	\$█ ³	\$█ ³	\$█ ³	\$█ ³	\$█ ³	\$█ ³

Source: Tables 4.6, 4.7, 4.10, pp208-210 of the submission.

The redacted values correspond to the following ranges:

- ¹ 500 to < 5,000
- ² 5,000 to < 10,000
- ³ \$0 to < \$10 million
- ⁴ \$10 million to < \$20 million
- ⁵ net cost saving

6.90 The submission presented sensitivity analyses varying population growth and therefore market growth rates as well as uptake rates. These are shown in Table 13, based on the published prices.

Table 13: Results of the sensitivity analysis – proposed effective price of BKZ using published SEC price, and published prices of substituted products

	2025	2026	2027	2028	2029	2030	% Change
Base case	\$█ ¹	\$█ ¹	\$█ ¹	\$█ ¹	\$█ ¹	\$█ ¹	-
Population growth (-20%)	\$█ ¹	\$█ ¹	\$█ ¹	\$█ ¹	\$█ ¹	\$█ ¹	-█%
Population growth (+20%)	\$█ ¹	\$█ ¹	\$█ ¹	\$█ ¹	\$█ ¹	\$█ ¹	█%
Uptake reduced by 20%	\$█ ¹	\$█ ¹	\$█ ¹	\$█ ¹	\$█ ¹	\$█ ¹	-█%
Uptake increased by 20%	\$█ ¹	\$█ ¹	\$█ ¹	\$█ ¹	\$█ ¹	\$█ ¹	█%

Source: Table 4.15, p214 of the submission. Italics – corrected during the evaluation to refer to difference versus base case estimate.

The redacted values correspond to the following ranges:

- ¹ \$0 to < \$10 million

Financial Management – Risk Sharing Arrangements

6.91 The submission did not propose a risk sharing arrangement.

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

7 PBAC Outcome

7.1 The PBAC recommended the General Schedule, Authority Required (in writing) listing of bimekizumab for the treatment of moderate to severe hidradenitis suppurativa (HS). The PBAC's recommendation was based on, among other matters, its assessment that the cost effectiveness of bimekizumab would be acceptable if it were cost

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minimised to the least costly alternative therapy of either secukinumab or adalimumab.

- 7.2 The PBAC considered the equi-effective doses were:
- Bimekizumab 320 mg given either once every 2 weeks or once every 4 weeks for 16 weeks, and 320 mg every four weeks thereafter (total 26 or 30 doses over 2 years);
 - Secukinumab 300 mg given at weeks 0, 1, 2, 3, 4, followed by 300 mg given every 2 or 4 weeks; and
 - Adalimumab 80 mg given every 2 weeks, with an additional dose at initiation.
- 7.3 The PBAC acknowledged HS is a severe and debilitating condition that has a significant impact on quality of life and considered there remained a moderate to high clinical need for additional effective therapies. The Committee welcomed the input from individuals, health professionals and organisations that described HS as 'hell on earth' and highlighted the pain, anxiety and isolating nature of the condition, the stigma arising from wounds and repeat surgeries and the impacts of disease flares, as well as reiterating that current treatments are only partially effective, and not all patients respond. The PBAC acknowledged that additional treatment options would be beneficial to patients with HS.
- 7.4 With respect to the requested listing and restriction, the PBAC considered the listing should be aligned with that of adalimumab and secukinumab, including prior antibiotics, abscess and nodule counts, remain age agnostic, with quantities and repeats to achieve the last dose in the initial treatment phase at 16 weeks (at either the 2-weekly or 4-weekly dosing schedule), with the continuing listing to provide for up to 6 months treatment based on maintenance dosing at 4-weekly intervals (a.k.a. Q2W/Q4W or Q4W). The Committee noted the TGA registration included the Q2W dosing option for the first 16 weeks for patients who require rapid symptom control and therefore considered it was appropriate to permit this dosing option in the initial treatment phase. The PBAC also considered it reasonable for the assessment of response timeframe to occur after a minimum of 12 weeks, to provide patients with 4 weeks of treatment (i.e., up until Week 16) before their response is assessed. Noting the addition of bimekizumab to the PBS would mean a third biological medicine for the treatment of HS, the PBAC found it appropriate for patients to trial and fail, or cease to respond to each biologic once within the same treatment cycle. As such, a new treatment cycle reset date upon PBS listing was also considered to be reasonable.
- 7.5 The PBAC considered the nominated comparators of secukinumab (primary) and adalimumab (secondary) were appropriate.
- 7.6 The PBAC noted the submission was supported by three randomised controlled trials, BE-HEARD I and II, and HS0001, and the comparator trials for secukinumab (SUNSHINE/SUNRISE) and adalimumab (PIONEER I/II and M10-467) having been previously seen in support of those submissions. The Committee noted the primary

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outcome for most of these trials was a 50% improvement in hidradenitis suppurativa clinical response (HiSCR50). The PBAC noted some of the adalimumab trials may have occurred whilst the HiSCR scale was being devised (paragraphs 6.28-6.29 refer) and considered that whilst this introduced some uncertainty, it would likely not preclude an assessment of the comparative effectiveness of bimekizumab and adalimumab. The PBAC also noted the clinical effectiveness claims were supported primarily by indirect treatment comparisons using the available evidence.

- 7.7 With respect to comparative effectiveness, the PBAC noted the submission and subsequent responses discussed the effectiveness of bimekizumab (versus placebo) and described it as superior to secukinumab in both induction and maintenance therapy, and non-inferior to adalimumab in initial treatment but superior after 48 weeks' treatment. The PBAC considered the available data suggests HS is a difficult condition to treat, with HiSCR50 response rates to treatment of about 50% in BE HEARD I/II but also noted the relatively high placebo response rates (~20-30%) observed in the BE HEARD trials out to week 16 before patients switched to bimekizumab treatment.
- 7.8 Overall, the Committee noted the results of the BE HEARD trials supported a conclusion that bimekizumab is effective for the treatment of moderate to severe HS (Bayesian difference (95% CI) for BE HEARD I of 18.1 (6.3, 30.0) and BE HEARD II of 19.6 (7.5, 31.7)). The PBAC noted the results of the analyses for difference in dermatology quality of life (DLQI) and least squares mean difference for worst skin pain at 16 weeks favoured bimekizumab (Table 4). With respect to longer term outcomes, the PBAC also noted the results of the open label extension phases of BE HEARD I and II from week 16-48 supported a conclusion that the effectiveness of bimekizumab is likely maintained over this period.
- 7.9 The PBAC noted the results of the indirect treatment comparisons in the submission and PSCR responses produced mixed results based on outcome, statistical method and time of measurement. For the comparisons at 16 weeks, the PBAC noted the results of the analyses in the submission based on relative risk (RR) and risk difference (RD) for the Q4W regimen did not find a statistically significant difference between bimekizumab and either secukinumab (RR 1.32, 95% CI 0.98, 1.8) or adalimumab (RR 0.9, 95% CI 0.6, 1.2), and also noted the risk difference did favour bimekizumab over secukinumab but not adalimumab (Table 7). The Committee noted the analyses presented in the PSCR were based on odds ratio (OR) and also noted the variability in the results, with the Q2W/Q4W regimen finding a statistically significant improvement in HiSCR50 over secukinumab Q2W and Q4W (but no difference versus adalimumab), but no statistically significant differences for the bimekizumab Q4W regimen versus secukinumab (either regimen) or adalimumab (paragraph 6.53). With respect to the longer-term analyses out to 48 weeks, the PBAC agreed with the evaluation and ESC that the results of the analyses (including the matching-adjusted analyses) were difficult to interpret due to the nature of the informing data (paragraphs 6.77-6.78 refer). The PBAC considered that while some of the results tended to favour

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bimekizumab, the analyses had substantial inherent uncertainty and were therefore likely not sufficient for the purposes of establishing superiority over secukinumab or adalimumab. Overall, the Committee considered on balance, taking into account the totality of the available evidence, that a claim of non-inferior comparative effectiveness to both secukinumab and adalimumab at both 16 and 48 weeks was likely to be reasonable.

- 7.10 In terms of comparative safety, the PBAC noted the submission did not present a formal statistical comparison of bimekizumab, secukinumab and adalimumab, however considered the available data suggested the adverse event profiles were similar, and the extended assessment of safety that included additional open label extension data did not raise additional significant concerns. Overall, the PBAC was satisfied that the claim of non-inferior comparative safety to secukinumab and adalimumab was likely supported.
- 7.11 The PBAC noted the submission requested listing on a cost minimisation basis. Given its view on the clinical claims that bimekizumab is likely non-inferior to both secukinumab and adalimumab, the Committee considered that the cost minimisation approach (CMA) presented in the submission was generally methodologically consistent with the standard two-year approach for bDMARDs. Furthermore, the PBAC noted the TGA registered two dosing regimens for bimekizumab (Q2W/Q4W and Q4W) after the submission was lodged, and the CMA required adjustment to account for this. The PBAC noted the Q2W/Q4W regimen was only recommended for patients in whom rapid symptom control is required. Given this, the Committee noted the Pre-PBAC Response proposed a weighting of 20% Q2W/Q4W and 80% Q4W dosing, based on a similar weighting being accepted for secukinumab for HS in November 2023 (paragraph 5.8, secukinumab PSD, November 2023 PBAC) and considered that in the absence of any other evidentiary basis for determining the weighting this was reasonable.
- 7.12 The PBAC noted the financial estimates in the submission were based on published prices and considered that if bimekizumab were listed on a cost minimisation basis with the least costly alternative, the listing would 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.
- 7.13 The PBAC advised, under Section 101 (4AACD) of the *National Health Act 1953*, that bimekizumab 320 mg syringe and bimekizumab 320 mg pen; as well as bimekizumab 160 mg syringe and 160 mg pen, should be considered equivalent for the purposes of substitution (i.e., 'a' flagged in the Schedule with a NOTE stating PBS of one form and PBS of another form of the relevant strength are equivalent for the purposes of substitution).
- 7.14 The PBAC also noted the flow-ons to secukinumab and adalimumab to include bimekizumab in the list of eligible therapies for moderate to severe HS, and considered that a grandfather listing was appropriate, which should be removed after

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12 months per standard practice, in the absence of any other reason for an alternative period to apply.

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

Outcome:

Recommended

8 Recommended listing

8.1 Add new item:

Initial

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	2	4	3	Bimzalex
bimekizumab 160 mg/mL injection, 2 x 1 mL syringe	NEW	2	4	3	
bimekizumab 320 mg/2mL injection, 1 x 2 mL pen devices	NEW	2	2	3	
bimekizumab 320 mg/2mL injection, 1 x 2 mL syringe	NEW	2	2	3	
Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required (in writing only via OPA/post/HPOS upload)					
Prescribing rule level:					
Administrative Advice: Overarching administrative note.					
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.					
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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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 authorisation under this restriction should be made using the Online PBS Authorities system (see www.servicesaustralia.gov.au/hpos)

Alternatively, applications for authority to prescribe can 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 [new1] / Treatment of Concept: [new1A]

Indication: Moderate to severe hidradenitis suppurativa

Treatment Phase: Initial treatment – Initial 1 (new patient)

Clinical criteria:

Patient must have, at the time of application, a Hurley stage II or III grading with an abscess and inflammatory nodule (AN) count greater than or equal to 3

AND

Clinical criteria:

Patient must have failed to achieve an adequate response to 2 courses of different antibiotics each for 3 months prior to initiation of PBS subsidised treatment with this drug for this condition; or

Patient must have had an adverse reaction to an antibiotic of a severity necessitating permanent treatment withdrawal resulting in the patient being unable to complete treatment with 2 different courses of antibiotics each for 3 months prior to initiation of PBS-subsidised treatment with this drug for this condition; or

Patient must be contraindicated to treatment with an antibiotic due to an allergic reaction of a severity necessitating permanent treatment withdrawal resulting in the patient being unable to complete treatment with 2 different courses of antibiotics each for 3 months prior to initiation of PBS-subsidised treatment with this drug for this condition

AND

Clinical criteria:

Patient must not have received PBS-subsidised treatment with a biological medicine for this condition

AND

Clinical criteria:

Patient must not receive more than 16 weeks of treatment under this restriction

Treatment criteria:

Must be treated by a dermatologist

Prescribing Instructions:

Assessment of disease severity must be no more than 4 weeks old at the time of application.

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.

Prescribing Instructions:

Where a response assessment is not conducted within the required timeframe, the patient will be deemed to have failed to respond to treatment with this drug, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.

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<p>Prescribing Instructions: The authority application must be made via the Online PBS Authorities System, or in writing via HPOS form upload or mail and must include: (i) the Hurley stage grading; and (ii) the AN count; and (iii) the name of the antibiotic/s received for two separate courses each of three months; or (iv) confirmation that the adverse reaction or allergy to an antibiotic necessitated permanent treatment withdrawal resulting in the patient being unable to complete a three month course of antibiotics. The name of the one course of antibiotics of three months duration must be provided. Where the patient is unable to be treated with any courses of antibiotics the prescriber must confirm that the patient has a history of adverse reaction or allergy necessitating permanent treatment withdrawal to two different antibiotics.</p> <p>If the application is submitted through HPOS form upload or mail, it must include: (i) details of the proposed prescription(s); and (ii) 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)</p>
<p>Administrative Advice: 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>Restriction Summary [new2] / Treatment of Concept: [new2A]</p>
<p>Indication: Moderate to severe hidradenitis suppurativa</p>
<p>Treatment Phase: Initial treatment – Initial 2 (Change or re-commencement of treatment after a break in biological medicine of less than 5 years)</p>
<p>Clinical criteria: Patient must have received prior PBS-subsidised treatment with a biological medicine for this condition in this treatment cycle</p>
<p>AND</p>
<p>Clinical criteria: Patient must not have already failed, or ceased to respond to, PBS-subsidised treatment with 3 biological medicines for this condition within this treatment cycle</p>
<p>AND</p>
<p>Clinical criteria: Patient must not have already failed, or ceased to respond to, PBS-subsidised treatment with this drug for this condition during the current treatment cycle.</p>
<p>AND</p>
<p>Clinical criteria: Patient must not receive more than 16 weeks of treatment under this restriction</p>
<p>Treatment criteria: Must be treated by a dermatologist</p>
<p>Prescribing Instructions: Assessment of disease severity must be no more than 4 weeks old at the time of application.</p>
<p>Prescribing Instructions: A response to treatment is defined as, Achieving Hidradenitis Suppurativa Clinical Response (HiSCR) of a 50% reduction in AN count compared to baseline with no increase in abscesses or draining fistulae.</p>
<p>Prescribing Instructions: An application for a patient who has received PBS-subsidised treatment with this drug, has not experienced treatment failure, and wishes to re-commence therapy with this drug, must be accompanied by evidence of a response to the patient's most recent course of PBS-subsidised treatment with this drug, within the timeframes specified below.</p>

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<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 the required timeframe, the patient will be deemed to have failed to respond to treatment with this drug, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.</p>
<p>Prescribing Instructions: The authority application must be made via the Online PBS Authorities System, or in writing via HPOS form upload or mail and must include: (i) the Hurley stage grading; and (ii) the AN count. If the application is submitted through HPOS form upload or mail, it must include: (i) details of the proposed prescription(s); and (ii) 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)</p>
<p>Prescribing Instructions: If a patient fails to demonstrate a response to treatment with this drug under this restriction they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition within this treatment cycle.</p>
<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>Restriction Summary [new3] / Treatment of Concept: [new3A]</p>
<p>Indication: Moderate to severe hidradenitis suppurativa</p>
<p>Treatment Phase: Initial treatment - Initial 3 (re-commencement of treatment after a break in biological medicine of more than 5 years)</p>
<p>Clinical criteria: Patient must have, at the time of application, a Hurley stage II or III grading with an abscess and inflammatory nodule (AN) count greater than or equal to 3</p>
<p>AND</p>
<p>Clinical criteria: Patient must have previously received PBS-subsidised treatment with a biological medicine for this condition</p>
<p>AND</p>
<p>Clinical criteria: Patient must have a break in treatment of 5 years or more from the most recently approved PBS-subsidised biological medicine for this condition</p>
<p>AND</p>
<p>Clinical criteria: Patient must not receive more than 16 weeks of treatment under this restriction</p>
<p>Treatment criteria: Must be treated by a dermatologist</p>
<p>Prescribing Instructions: Assessment of disease severity must be no more than 4 weeks old at the time of application.</p>

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<p>Prescribing Instructions: A response to treatment is defined as, Achieving Hidradenitis Suppurativa Clinical Response (HiSCR) of a 50% reduction in AN count compared to baseline with no increase in abscesses or draining fistulae.</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 the required timeframe, the patient will be deemed to have failed to respond to treatment with this drug, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.</p>
<p>Prescribing Instructions: The authority application must be made via the Online PBS Authorities System, or in writing via HPOS form upload or mail and must include: (i) the Hurley stage grading; and (ii) the AN count.</p> <p>If the application is submitted through HPOS form upload or mail, it must include: (i) details of the proposed prescription(s); and (ii) 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)</p>
<p>Prescribing Instructions: If a patient fails to demonstrate a response to treatment with this drug under this restriction they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition within this treatment cycle.</p>

Balance of supply

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
BIMEKIZUMAB					
bimekizumab 160 mg/mL injection, 2 x 1 mL pen devices	NEW	2	4	3	Bimzelx
bimekizumab 160 mg/mL injection, 2 x 1 mL syringe	NEW	2	4	3	
bimekizumab 320 mg/2mL injection, 1 x 2 mL pen devices	NEW	2	2	3	
bimekizumab 320 mg/2mL injection, 1 x 2 mL syringe	NEW	2	2	3	
Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/electronic)					
Prescribing rule level:					
Administrative Advice: Overarching administrative note.					
Administrative Advice: Special Pricing Arrangements apply.					
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.					

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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 [new4] / Treatment of Concept: [new4A]
Indication: Moderate to severe hidradenitis suppurativa
Treatment Phase: Initial 1 (new patient), Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 5 years), or Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years) - balance of supply
Clinical criteria:
Patient must have received insufficient therapy with this drug for this condition under the Initial 1 (new patient) restriction to complete 16 weeks treatment; or
Patient must have received insufficient therapy with this drug for this condition under the Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 5 years) restriction to complete 16 weeks treatment; or
Patient must have received insufficient therapy with this drug for this condition under the Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years) restriction to complete 16 weeks treatment.
AND
Clinical criteria:
The treatment must provide no more than the balance of up to 16 weeks treatment.
AND
Treatment criteria:
Must be treated by a dermatologist

Continuing and Grandfather

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty unit	No. of Rpts	Available brands
BIMEKIZUMAB					
bimekizumab 160 mg/mL injection, 2 x 1 mL pen devices	NEW	1	2	5	Bimzelx
bimekizumab 160 mg/mL injection, 2 x 1 mL syringe	NEW	1	2	5	
bimekizumab 320 mg/2mL injection, 1 x 2 mL pen devices	NEW	1	1	5	
bimekizumab 320 mg/2mL injection, 1 x 2 mL syringe	NEW	1	1	5	
Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required (in writing only via OPA/post/HPOS upload)					
Prescribing rule level:					
Administrative Advice: Overarching administrative note.					
Administrative Advice: Special Pricing Arrangements apply.					
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:					

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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 authorisation under this restriction should be made using the Online PBS Authorities system (see www.servicesaustralia.gov.au/hpos)

Alternatively, applications for authority to prescribe can 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 [new5] / Treatment of Concept: [new5A]

Indication: Moderate to severe hidradenitis suppurativa

Treatment Phase: Continuing treatment

Clinical criteria:

Patient must have previously received PBS-subsidised treatment with this drug for this condition

AND

Clinical criteria:

Patient must have demonstrated a response to treatment with this drug for this condition

AND

Treatment criteria:

Must be treated by a dermatologist

Prescribing Instructions:

A response to treatment is defined as, Achieving Hidradenitis Suppurativa Clinical Response (HiSCR) of a 50% reduction in AN count compared to baseline with no increase in abscesses or draining fistulae.

Prescribing Instructions:

An application for the continuing treatment must be accompanied with the assessment of response conducted following a minimum of 12 weeks of therapy and no later than 4 weeks from cessation of the most recent course of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment.

Prescribing Instructions:

Where a response assessment is not conducted within the required timeframe, the patient will be deemed to have failed to respond to treatment with this drug, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.

Prescribing Instructions:

A maximum of 24 weeks treatment will be authorised under this restriction per continuing treatment.

Prescribing Instructions:

If the application is submitted through HPOS form upload or mail, it must include: (i) details of the proposed prescription; and,
 (ii) 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) which includes the Hidradenitis Suppurativa Clinical Response (HiSCR) result.

Restriction Summary [new6] / Treatment of Concept: [new6A]

Indication: Moderate to severe hidradenitis suppurativa

Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply – ‘Grandfather arrangements’

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Clinical criteria:
Patient must have received non-PBS-subsidised treatment with this drug for this PBS indication prior to [listing date],
AND
Clinical criteria:
Patient must have had a Hurley stage II or III with an abscess and inflammatory nodule (AN) count greater than or equal to 3 prior to starting treatment with this drug for this condition
AND
Clinical criteria:
Patient must have demonstrated a response to treatment by achieving Hidradenitis Suppurativa Clinical Response (HiSCR) after 12 weeks of treatment if the patient has been treated with this drug for this condition for 12 weeks or longer,
AND
Clinical criteria:
Patient must have failed to achieve an adequate response to 2 courses of different antibiotics each for 3 months prior to initiation of non-PBS-subsidised treatment with this drug for this condition; or
Patient must have had an adverse reaction to an antibiotic of a severity necessitating permanent treatment withdrawal resulting in the patient being unable to complete treatment with 2 different courses of antibiotics each for 3 months prior to initiation of non-PBS-subsidised treatment with this drug for this condition; or
Patient must be contraindicated to treatment with an antibiotic due to an allergic reaction of a severity necessitating permanent treatment withdrawal resulting in the patient being unable to complete treatment with 2 different courses of antibiotics each for 3 months prior to initiation of non-PBS-subsidised treatment with this drug for this condition
AND
Clinical criteria:
Patient must not receive more than 24 weeks of treatment under this restriction
Treatment criteria:
Must be treated by a dermatologist
Prescribing Instructions:
A response to treatment is defined as: Achieving Hidradenitis Suppurativa Clinical Response (HiSCR) of a 50% reduction in AN count compared to baseline with no increase in abscesses or draining fistulae.
Prescribing Instructions:
An application for the continuing treatment must be accompanied with the assessment of response conducted following a minimum of 12 weeks of therapy and no later than 4 weeks from cessation of the most recent course of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment.
Prescribing Instructions:
Where a response assessment is not conducted within the required timeframe, the patient will be deemed to have failed to respond to treatment with this drug, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.
Prescribing Instructions:
Assessment of disease severity must not have been more than 4 weeks old at the time treatment with this drug was initiated

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Prescribing Instructions:

The authority application must be made via the Online PBS Authorities System, or in writing via HPOS form upload or mail and must include:

- (i) the Hurley stage grading; and
- (ii) the AN count; and
- (iii) the name of the antibiotic/s received; or
- (iv) confirmation that the adverse reaction or allergy to an antibiotic necessitated permanent treatment withdrawal. The name of the one course of antibiotics must be provided. Where the patient is unable to be treated with any courses of antibiotics the prescriber must confirm that the patient has a history of adverse reaction or allergy necessitating permanent treatment withdrawal.
- (v) the Hidradenitis Suppurativa Clinical Response (HiSCR) result if the patient has received 12 weeks or more of treatment

If the application is submitted through HPOS form upload or mail, it must include:

- (i) details of the proposed prescription(s); and
- (ii) 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:

A patient may only qualify for PBS-subsidised treatment under this restriction once only.

Prescribing Instructions:

For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria.

Administrative Advice:

This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.

Overarching administrative advice note:

Amend 32635 Add New AA

Administrative Advice:

TREATMENT OF PATIENTS WITH MODERATE TO SEVERE HIDRADENITIS SUPPURATIVA

The following information applies to Pharmaceutical Benefits Scheme (PBS) benefits listed for patient with the indication of moderate to severe hidradenitis suppurativa.

Where the term 'biological medicine' appears in notes and restrictions, it refers to any PBS benefit where the PBS indication specifies: Moderate to Severe Hidradenitis Suppurativa.

Treatment cycles:

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 or secukinumab prior to [LISTING DATE] is considered to start their first cycle as of [LISTING DATE].

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.

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 'moderate to severe hidradenitis suppurativa' before starting a new treatment cycle.

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 *with another biological medicine* may be commenced within the same treatment cycle.

There is no limit to the number of treatment cycles a patient may undertake in their lifetime.

Prescribing under the correct 'Treatment phase' listing for the authority application:

- (1) Initial treatment.

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Apply under the 'Initial 1' treatment listing where the patient has never received a biological medicine for moderate to severe hidradenitis suppurativa.

(2) Grandfather patients (secukinumab and *bimekizumab* only).

A patient who commenced treatment with secukinumab *or bimekizumab* for moderate to severe hidradenitis suppurativa prior to 1 June 2024 and [bimekizumab LISTING DATE] respectively and who continues to receive treatment at the time of application, may qualify for treatment under the 'Grandfather' treatment restriction.

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 restriction. 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.

For the second and subsequent cycles, a 'grandfather' patient must qualify for continuing treatment under the criteria that apply to a continuing patient.

(3) Continuing treatment.

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.

(4) Changing/swapping therapy.

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 antibiotic use. 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 as defined in the restriction within the same treatment cycle. A response assessment to the preceding supply of biological medicine must accompany this initial 2 treatment authority application.

(5) Baseline measurements to determine response.

A response to treatment is to be determined by comparison of current disease activity measurements relative to the baseline measurement of abscess and inflammatory nodule (AN) count 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 baselines 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.

(6) Recommencement of treatment after a 5-year break in PBS-subsidised therapy.

Apply under the 'Initial 3' treatment listing. Prior antibiotic courses need not be re-trialled.

Flow-on changes

Amend the overarching administrative advice note (as above) that currently exists for the following biologic PBS listings for moderate to severe hidradenitis suppurativa (HS):

- Adalimumab (14587R, 14622N, 12450G, 12449F, 12395J, 12448E, 12408C, 12356H, 12385W, 12369B, 12330Y, 12383R, 12414J, 12454L, 12524E, 13221W)
- Secukinumab (14154Y, 14161H, 14146M)

These restrictions 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.