SMC2698

bimekizumab solution for injection in pre-filled syringe and pre-filled pen (Bimzelx®)

UCB Pharma Ltd

07 March 2025

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission

bimekizumab (Bimzelx®) is accepted for restricted use within NHSScotland.

Indication under review: for the treatment of active moderate to severe hidradenitis suppurativa (HS) (acne inversa) in adults with an inadequate response to conventional systemic HS therapy.

SMC restriction: for use in adult patients with active moderate to severe HS for whom adalimumab is contraindicated or otherwise unsuitable, including those who have failed to respond or have lost response to prior adalimumab treatment.

In two phase III studies in patients with moderate to severe HS, significantly more patients achieved a clinical response (defined as ≥50% decrease in abscess and inflammatory nodule [AN] count with no increase in the number of abscesses and/or in the number of draining fistulae) with bimekizumab (every two weeks) compared with placebo at week 16.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Bimekizumab is a recombinant, human immunoglobulin G1/κ (IgG1/κ) monoclonal antibody that binds and neutralises interleukin (IL)-17A, IL-17F, and IL-17AF. Their inhibition reduces the release of pro-inflammatory cytokines and other mediators of tissue damage; which contribute to hidradenitis suppurativa (HS).[1, 2]

The recommended dose of bimekizumab for HS in adults is 320 mg by subcutaneous (SC) injection every 2 weeks up to week 16; followed by 320 mg every 4 weeks thereafter. Consideration should be given to discontinuing treatment in patients who have shown no improvement by week 16 of treatment.[1]

1.2. Disease background

HS also known as 'acne inversa' or 'Verneuil's disease' is a chronic, inflammatory skin disease that usually presents with recurrent, deep-seated and painful lesions that can progress to become chronic with purulent discharge, scarring and sinus formation. These lesions mainly occur in areas like the armpits, groin and anogenital regions. HS has a highly negative impact on quality of life and devastating psychological effects, with an impact greater than for many other dermatologic diseases. The extent and severity of HS are often determined using the Hurley staging system; the focus of the licensed indication is moderate (Hurley stage 2) to severe (Hurley stage 3) HS.[2-4] It is estimated that approximately 45% of patients with HS have moderate to severe disease.[5] Onset of HS is typically after puberty, and affects women two to five times more commonly than men. The 1-year prevalence of HS is estimated to be around 1% in adults.[2, 6-8] People with HS have an unmet medical need because of diagnostic delays and a limited range of effective therapies.[9-11]

1.3. Company proposed position

The company has requested that SMC considers bimekizumab when positioned for use in adult patients with active moderate to severe HS for whom adalimumab is contraindicated or otherwise unsuitable, including those who have failed to respond or have lost response to prior adalimumab treatment.

1.4. Treatment pathway and relevant comparators

Symptoms of HS are managed in a stepwise approach dependent on disease severity. In mild to moderate settings, HS is initially treated with topical antiseptics and antibiotics, switching to systemic antibiotics if there is continued progression. Upon failure of systemic antibiotics other conventional therapies are trialled including retinoid therapy, intralesional steroid injections, dapsone, ciclosporin, metformin, and surgical procedures (for example incision and drainage or excision).[12] Once all conventional therapies are exhausted, then adalimumab is an option for patients with moderate to severe HS in NHS Scotland (SMC1143/16). Following this, secukinumab is available in patients with active moderate to severe HS for whom adalimumab is contraindicated or otherwise unsuitable, including those who have failed to respond or have lost response to prior adalimumab treatment (SMC2592).

For the proposed positioning, the submitting company considered the relevant comparators to be secukinumab and best supportive care (which includes surgical procedures, conventional therapies, as well as some continued use of adalimumab). Clinical experts contacted by SMC agreed with this but some noted that off-label biologics, such as infliximab, are used as a treatment option in this population; infliximab (off-label) is recommended as a treatment option in the British Association of Dermatologists guidelines for HS.[12]

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy and safety of bimekizumab for the treatment of patients with moderate to severe HS comes from the identical BE HEARD I and II studies. Details are summarised in Table 2.1.

Table 2.1. Overview of relevant studies

Criteria	BE HEARD I and BE HEARD II.[2, 13]
Study Design	International, randomised, double-blind, parallel-group, phase III studies.
Eligible Patients	• 18 years or older with a diagnosis of HS ≥ 6 months prior to baseline. • Moderate to severe HS defined as at least five inflammatory lesions (that is abscesses and/or inflammatory nodules) that affect at least two distinct anatomic areas, one of which must be at least Hurley stage II or III at screening and baseline visits. • Documented history of inadequate response to systemic antibiotics for HS at screening. • No TNF-alpha inhibitors (for example adalimumab) within previous 12 weeks, and no IL-17 biological response modifier therapy (for example secukinumab) within previous 6 months.
Treatments & Randomisation	Patients were randomised in a 2:2:2:1 ratio to receive subcutaneous: • Bimekizumab 320 mg every two weeks (up to week 48) or • Bimekizumab 320 mg every four weeks (up to week 48) or • Bimekizumab 320 mg every two weeks (up to week 16) then every four weeks (up to week 48) or • Placebo every two weeks (up to week 16) then bimekizumab 320 mg every two weeks (up to week 48) Randomisation was stratified by Hurley stage at baseline (II or III) and baseline systemic antibiotic use (yes or no). Concomitant oral antibiotic use was permitted if the patient was on a stable dose regimen of a systemic tetracycline antibiotic for 28 days prior to baseline. The concomitant use of analgesia, and certain products for wound (for example dressings) and lesion (petroleum jelly) care were permitted.
Primary outcome	The proportion of patients with HiSCR50 at week 16; defined as ≥50% reduction in the total AN count with no increase, from baseline, in the number of abscesses and/or draining fistulae.
Key Secondary outcomes	• HiSCR75 at week 16; defined as ≥75% reduction in the total AN count with no increase, from baseline, in the number of abscesses and/or draining fistulae. • Flare by week 16[a] (BE HEARD II only). • Change from baseline in DLQI total score (at week 16). • Change from baseline in HSSDD worst skin pain score[b] (at week 16). • HSSDD worst skin pain response[c] (at week 16).
Statistical analysis	A hierarchical testing strategy was applied within each individual study. The primary and secondary outcomes were tested sequentially in the pre-specified order above, simultaneously for each bimekizumab dose. No further formal testing was carried out after the first non-significant outcome in the hierarchy.

[a] a flare was defined as a ≥25% increase in AN count with an increase of at least two abscess and inflammatory nodules relative to baseline.

[b] as assessed by the 'worst skin pain' item (11-point numeric rating scale) in the HSSDD.

[c] based on the threshold for within-patient clinically meaningful change (defined as ≥ 3-point decrease from baseline in HSSDD weekly worst skin pain score at week 16 among study participants with a score of ≥ 3 at baseline.

Abbreviations: AN = abscess and inflammatory nodule; DLQI = Dermatology Life Quality Index; HiSCR = hidradenitis suppurativa clinical response; HS= hidradenitis suppurativa; HSSDD = hidradenitis suppurativa symptoms daily diary.

In both studies, the predefined primary analysis method involved a stringent modified non-responder data imputation (mNRI) where patients were treated as non-responders at all subsequent visits (or treated as experiencing a HS flare for the HS flare endpoint) if they: took any systemic antibiotic (that is a new or increased dose); discontinued study treatment due to an adverse event; or had absence of efficacy (mNRI [All-ABX]). Other missing data were imputed via multiple imputation (primary, pre-specified analysis method). For the primary outcome (HiSCR50 response), treatment with bimekizumab 320 mg every 2 weeks (using data from two treatment groups that received this dose) resulted in a statistically significant improvements compared with placebo at week 16 (in both studies). Treatment with bimekizumab 320 mg every 4 weeks also resulted in a statistically significant improvements compared with placebo at week 16 (BE HEARD II only)[1, 2, 13]; however, these results are not shown in Table 2.2 since the 4-weekly dosing regimen (during the first 16 weeks of treatment) is unlicensed.[1]

Table 2.2: Primary and selected secondary outcomes from the BE HEARD I and II studies at week 16 (using the mNRI [All-ABX] primary analysis method for data imputation).[2, 13]

	BE HEARD I		BE HEARD II	
	Bimekizumab 320 mg every 2 weeks (n=289)[a]	**Placebo (n=72)**	**Bimekizumab 320 mg every 2 weeks (n=291)[a]**	**Placebo (n=74)**
Primary outcome: HiSCR50 response at week 16				
HiSCR50 response	48%	29%	52%	32%
OR versus placebo (95% CI)	2.2 (1.2 to 4.3)	-	2.3 (1.2 to 4.3)	-
p-value	0.006[b]	-	0.003[b]	-
Secondary outcome: HiSCR75 response at week 16				
HiSCR75 response	33%	18%	36%	16%
OR versus placebo (95% CI)	2.2 (1.0 to 4.6)	-	3.0 (1.4 to 6.6)	-
p-value	0.021[b]	-	0.002[b]	-
Secondary outcome: Flare by week 16				
Proportion with flares	NA	NA	29%	28%
OR versus placebo (95% CI)	NA	-	1.1 (0.5 to 2.0)	-
p-value	NA	-	NSS	-
Secondary outcome: Change from baseline in DLQI Total Score (at week 16)[c]				
Change from baseline, mean (SE)	-5.0 (0.4)	-2.7 (0.9)	-4.5 (0.3)	-3.1 (0.6)
OR versus placebo[d] (95% CI)	-2.7 (-4.4 to -1.0)	-	-2.3 (-3.7 to -0.9)	-
p-value	<0.001[b]	-	NSS	-
Secondary outcome: Change from baseline in HSSDD worst skin pain score (at week 16)[c]				
Change from baseline, mean (SE)	-1.9 (0.2)	-1.1 (0.2)	-1.9 (0.1)	-0.4 (0.3)
OR versus placebo (95% CI)	-1.2 (-2.1 to -0.3)	-	-1.3 (-2.0 to -0.6)	-
p-value	0.002[b]	-	NSS	-
Secondary outcome: HSSDD worst skin pain response (at week 16).				
Responder rate	32%	15%	32%	11%

OR versus placebo (95% CI)	2.8 (1.0 to 7.3)	-	3.8 (1.4 to 10.3)	-
p-value	NSS	-	NSS	-

[a] This includes patients assigned to the two bimekizumab treatment groups that received 320 mg every 2 weeks up to week 16.
[b] Statistically significant based on the pre-defined testing hierarchy.
[c] Negative values indicate an improvement in symptoms.
[d] ORs are presented for binary variables and least-squares-mean difference presented for continuous variables.

AN = abscess and inflammatory nodule; CI = confidence interval; DLQI = Dermatology Life Quality Index; HiSCR = hidradenitis suppurativa clinical response; HS = hidradenitis suppurativa; HSSDD = hidradenitis suppurativa symptoms daily diary; LS = least squares; NA = not applicable; NSS = not statistically significant; OR = odds ratio; SE = standard error.

The submitting company used the more stringent primary analysis method (mNRI [All-ABX]) in the BE HEARD studies, based on the results from the adalimumab phase 3 programme, where markedly better results were observed in the study which included concomitant systemic antibiotic treatment. The submitting company presented results of a supportive post-hoc analysis in which: discontinuation due to an adverse event or absence of response, or systemic antibiotic use considered by the investigator to be rescue treatment for HS resulted in imputation of nonresponse (mNRI [HS-ABX]); this approach led to more numerically favourable outcomes (HiSCR50 and HiSCR75 response) for both bimekizumab dosing regimens compared to placebo.[1, 2, 13] The submitting company used results using this method of imputation (mNRI [HS-ABX]) to inform the economic analyses.

In both studies, the onset of action of bimekizumab occurred as early as week 2, and the efficacy of bimekizumab was demonstrated regardless of systemic antibiotic use at baseline.[1, 2, 13] In both studies, responder rates for HiSCR50, HiSCR75, and HiSCR90 were generally sustained from week 16 to week 48.[2, 13] In both studies, bimekizumab HiSCR90 and HiSCR100 response rates increased from week 16 to week 48[13]; HiSCR90 also informed the economic analyses.

It is also worth highlighting that the economic model primarily utilised data from the licensed bimekizumab dose (320 mg every 2 weeks for 16 weeks followed by 320 mg every 4 weeks).[1]

2.2. Evidence to support the positioning proposed by the submitting company

The submitting company has positioned bimekizumab for use in adult patients whom adalimumab is contraindicated or otherwise unsuitable, including those who have failed to respond or have lost response to prior adalimumab treatment; however, only 25% (BE HEARD I) and 14% (BE HEARD II) of patients from the studies had previous biologic use (mostly with adalimumab).[2, 13] Subgroup analysis (which pooled all 1,014 patients from both studies) of the primary outcome showed the efficacy of bimekizumab (compared to placebo) was demonstrated regardless of prior biologic use at baseline.[1] HiSCR50 response rates were numerically lower in the group with prior biologic use (n=191).[14]

2.3. Health-related quality of life (HRQoL) outcomes

HRQoL was assessed using the DLQI as a secondary outcome, a skin disease specific questionnaire that evaluates the effect symptoms and treatments have on an individual's HRQoL. The DLQI Total score ranges from 0 to 30 with higher scores indicating a lower HRQoL.[2, 13] Across both studies, patients treated with bimekizumab experienced statistically significant improvements compared

to placebo in DLQI at week 16 (see table 2.2) and improvements were sustained through Week 48.[1, 2, 13]

Bimekizumab was also associated with numerically favourable differences over placebo for other outcomes (IHS4, HS-PGA, AN50, AN75, and AN90, HSSDD, and HSSQ) for the initial 16 weeks. Responses were maintained or further improved across these outcomes for all treatment groups through Week 48.[2]

2.4. Supportive studies

Patients that completed the entire 48-week study period in BE HEARD I and II were allowed to enter the planned two-year multicentre, open-label, parallel-group, phase III extensions study (BE HEARD EXT).[15] Patients were assigned to bimekizumab 320 mg every 2 or 4 weeks depending on their HiSCR90 response status, where patients on 320 mg every 4 weeks were switched to 320 mg every 2 weeks if they did not have HiSCR90 over a consecutive 8-week period on average.[2] The submitting company provided data suggesting that after 96 weeks of bimekizumab, HiSCR response scores were generally maintained with some numerical increases, in addition to consistent benefit in International Hidradenitis Severity Score System (IHS4).

Additional evidence is also available from a multicentre, randomised, double-blind, phase II study (HS0001) which compared bimekizumab with placebo and included an adalimumab reference arm.[16] However, the study was not powered to compare bimekizumab with adalimumab and used different bimekizumab doses from the licensed dose; therefore, the results were only used in the indirect evidence.

2.5. Indirect evidence to support clinical and cost-effectiveness comparisons

In the absence of direct evidence against the relevant comparator secukinumab, a Bayesian network meta-analysis (NMA) was conducted to compare the relative efficacy of bimekizumab with secukinumab through the common placebo groups at week 12 to 16 of their respective studies. Studies which had adalimumab as an intervention were also included in the NMA. In addition, due to a lack of placebo group after Week 16, an unanchored matching adjusted indirect comparison (MAIC) was conducted to compare the efficacy of bimekizumab with secukinumab at weeks 48 to 52.

The submitting company concluded that bimekizumab 320 mg every 2 weeks consistently resulted in better clinical outcomes than secukinumab 300 mg every 2 or 4 weeks after the initial treatment period (16 weeks). In addition, the licensed bimekizumab dose is more likely to be associated with the maintenance of treatment responses up to week 48, when compared with either secukinumab 300 mg every 2 or 4 weeks.

Table 2.3: Summary of indirect treatment comparison

Criteria	Overview
Design	A Bayesian NMA for comparison up to week 12 to 16, and an unanchored MAIC for comparison up to Week 48 to 52.
Population	Adult patients with moderate to severe HS; this included patients who did not have prior biologic use.
Comparators (studies included)	Bimekizumab (HS0001[16], BE HEARD I & BE HEARD II[13]), using the mNRI for HS-ABX imputation method, compared with secukinumab (SUNRISE and SUNSHINE[17]) through the placebo groups (BE HEARD I, BE HEARD II, SUNRISE, SUNSHINE, PIONEER I[a], PIONEER II[a], NCT00918225[a], and SHARPS).[13, 17-20]
Outcomes	HiSCR50, HiSCR75, HiSCR90, HiSCR100, IHS4, change from baseline in AN count, change from baseline in draining tunnel count, and skin pain response (NRS30).
Results	For the primary outcome (HiSCR50) for the NMA (up to week 16): bimekizumab 320 mg every 2 weeks is likely more effective than placebo, secukinumab 300 mg every 2 weeks (OR: 1.70 [95% CrI: 1.16 to 2.45]) and secukinumab 300 mg every 4 weeks (OR: 1.69 [95% CrI: 1.14 to 2.43]). In the biologic experienced subgroup, treatment with bimekizumab 320 mg every 2 weeks had a more numerically favourable HiSCR50 than secukinumab 300 mg every 2 weeks and secukinumab 300 mg every 4 weeks; however, the 95% CrIs were wide and included 1.0. For the primary outcome (HiSCR50) for the MAIC (up to week 48 to 52): Comparing bimekizumab (320 mg every 2- and 4-weeks data pooled) to secukinumab 300 mg every 2 and 4 weeks, bimekizumab was more favourable compared to secukinumab 300 mg every 2 weeks (OR: 2.00 [CI: 1.42 to 2.80]) and 300 mg every 4 weeks (OR: 2.06 [CI: 1.45 to 2.92]). These results were consistent for the HiSCR75 and HiSCR90 outcomes.

[a]These studies included adalimumab as an intervention.

Abbreviations: AN = abscess and inflammatory nodule; CI = confidence interval; CrI = credible interval; HiSCR = hidradenitis suppurativa clinical response; IHS4 = International Hidradenitis Severity Score; MAIC = matching adjusted indirect comparison; NMA = network meta analysis; OR = odds ratio.

3. Summary of Safety Evidence

The overall safety profile of bimekizumab for patients with moderate to severe HS was deemed to be consistent with the known safety profile of this medicine for other indications; this conclusion applied to both the short-term (up to 16 weeks) and long-term (up to 48 weeks) safety data.[2]

A pooled safety set was analysed by pooling the two bimekizumab dosing groups (320 mg every 2 weeks, n=576; 320 mg every 4 weeks, n=285), and those who received placebo (n=146), from the BE HEARD I and BE HEARD II studies together. During the initial 16-week treatment period most adverse events (AEs) were non-serious, mild to moderate in severity, and did not usually lead to discontinuation of bimekizumab (≤4% in all treatment groups).[2, 13]

For the licensed bimekizumab dosing groups (320 mg every 2 weeks for 16 weeks followed by 320 mg every 4 weeks) in BE HEARD I (n=145) and BE HEARD II (n=146) respectively, during the 48-week period, similar rates of: serious treatment-emergent AEs (TEAEs) (5.5% and 3.4%), TEAEs leading to discontinuation (6.9% and 6.8%), and severe TEAEs (4.8% and 5.5%) were reported.[2, 13]

The only serious TEAEs reported by >1% of participants who received any dose of bimekizumab in both studies (n=995) was hidradenitis (1.4%).[2]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- In BE HEARD I and BE HEARD II, the licensed bimekizumab dose (320 mg every 2 weeks for 16 weeks) for HS resulted in a statistically significant improvement in HiSCR50 response at week 16 (primary outcome) compared with placebo and in the more stringent secondary outcome HISCR75 response. These observed treatment effects were clinically meaningful.[1, 2, 13]
- Compared with placebo at week 16, the licensed bimekizumab dose resulted in statistically and clinically significant improvements in the secondary outcomes, change from baseline in DLQI total score and change from baseline in HSSDD worst skin pain score (BE HEARD I only).[1, 2, 13]
- No new safety signals were identified in patients with moderate to severe HS compared to the established safety profile of bimekizumab in other indications. The proportion of patients suffering from a serious AE was low.[1, 2, 13]

4.2. Key uncertainties

- There are uncertainties around the generalisability of the population included in the direct and indirect evidence as it is broader than the positioning proposed by the submitting company. In BE HEARD I and BE HEARD II, ≤25% of patients had prior biologic use. In the bimekizumab and secukinumab studies included in the indirect evidence, only small numbers of patients were biologic experienced. However, results from subgroup (for example prior biologics therapy) and sensitivity (for example assessing different data imputation methods) analyses were consistent with the primary analysis.[1, 2]
- There is a lack of direct data for the licensed bimekizumab regimen against active comparators, specifically secukinumab, which is most relevant comparator for this submission. The key limitations of the network meta-analysis relate to the generalisability of the population to the proposed population, and clinical and methodological differences between the bimekizumab and secukinumab studies. In both studies, the efficacy of bimekizumab over placebo was only assessed up to 16 weeks.
- After week 16, all patients were treated with bimekizumab and there is no comparative efficacy or safety data. Data for weeks 16 to 48 are presented as observed with no control group. HEARD EXT provides uncontrolled data up to 96 weeks, however there is limited data on longer term use, treatment breaks and maintenance of effect following withdrawal. This raises some uncertainty about bimekizumab effect in the longer term given HS is a chronic, recurrent condition.[2, 13]

4.3. Clinical expert input

Clinical experts consulted by SMC considered bimekizumab to be a therapeutic advancement and would fulfil an unmet need in this therapeutic area where patients have limited treatment options following adalimumab treatment.

4.4. Service implications

Clinical experts consulted by SMC indicated that there would be no major service implications, as biologic treatments (for example secukinumab) are already in use.

5. Summary of Patient and Carer Involvement

The following information reflects the views of the specified Patient Group.

- We received a patient group submission from Hidradenitis Suppurativa UK, which is a patient support group in the process of registering as a charity.
- Hidradenitis Suppurativa UK has not received any pharmaceutical company funding in the past two years.
- The delay in diagnosis often means that patients are experiencing moderate or severe HS which is difficult to manage. HS can cause pain and fatigue which will impact on patients' ability to work, socialise and enjoy an active life. This often leads to mental health issues such as anxiety and depression. The economic impacts of HS can also have a significant effect on the lives of patients. As well as the issues with finding or keeping work, or perhaps not being able to work full time hours, time off for appointments and treatments, and the cost of getting to appointments - as dermatology appointments are often some distance away.
- HS is treated with a number of medicines, which have varying success rates. The biologics which are currently available tend to have a limited period of efficacy for the patients who can tolerate them. Experiences with treatments vary vastly between patients.
- This medicine is one that most HS patients would see as a positive addition to a very small pool of available treatments. It would mean that there is another option available, one which may be more successful, or more suitable for some patients than the existing treatments.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

A summary of the economic evaluation is provided below.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost utility analysis
Time horizon	A time horizon of 60 years was used, with an assumed average starting age of 36.6 years.
Population	The population in the model were adults with active moderate to severe HS with an inadequate response to conventional systemic treatments and for whom adalimumab is either contraindicated or otherwise unsuitable, or patients have failed to respond or lost response to prior adalimumab treatment.
Comparators	Comparators for the economic analysis were: secukinumab and best supportive care (BSC) (defined as biologics, topical antibiotics, oral antibiotics, dapsone, retinoids, ciclosporin and anti-androgens).
Model description	The economic analysis used a 6-state Markov model. The included states were: • Very high response was defined as at least 90% of total AN count reduction from baseline with no increase in abscesses or DTs. • High response was defined as at least 75% but <90% total AN reduction from baseline with no increase in abscesses or DTs. • Response was defined as at least 50% but <75% total AN reduction from baseline with no increase in abscesses or DTs.

	• Partial response was defined as at least 25% but <50% total AN reduction from baseline with no increase in abscesses or DTs. • Non-response to treatment. • Death (absorbing state). Patients did not stop bimekizumab or secukinumab therapy for any reason except death before week 16. Following this, they discontinued treatment if they entered the non-response state in any cycle. In addition, an adverse event rate for discontinuation was applied, based on discontinuation for adverse events in the BE HEARD I and BE HEARD II studies. When discontinuing bimekizumab or secukinumab, patients were then assumed to receive BSC. Patients had elevated mortality in the non-response state because it was assumed they may be more likely to have severe HS and have surgical procedures further along the care pathway. A constant risk of discontinuation was applied, regardless of response state.
Clinical data	Clinical data came from the BE HEARD I and BE HEARD II studies which compare bimekizumab and placebo. Three doses of bimekizumab were explored in the clinical data, but the model used data from patients receiving 320 mg every 2 weeks to inform the model up to week 16. Beyond this, for the maintenance phase the model was informed by data for bimekizumab 320mg every 4 weeks. For most of the response thresholds, the data showed a higher proportion of patients in the bimekizumab group reached the threshold compared to patients in the placebo group, for the 16-week data.
Extrapolation	Beyond 16 weeks the model uses an NMA. The company submission focuses on the HS-ABX definition of efficacy because this matches the previous SUNSHINE and SUNRISE secukinumab study definitions, which allows the NMA to be conducted more easily given that these studies are also placebo-controlled. The transition probabilities for the model maintenance period (week 16 to 48) for secukinumab were based on the relative risk for secukinumab in the NMA compared to bimekizumab at week 12 to 16. For BSC, a gradual deterioration of response was assumed based on advice provided to the previous NICE submission for secukinumab. This was tested in scenario analysis, whereby the data used the NMA-derived relative risk for placebo versus bimekizumab prior to week 16, and separately a scenario where a literature value from the PIONEER II study for adalimumab was used, meaning 9.61% of BSC patients would move to the non-response state. For BSC the transition probabilities used a stable response in the long-term, as this approach was used in the adalimumab submission to NICE.
Quality of life	Health benefits were measured using the EQ-5D-3L data from the BE HEARD I and BE HEARD II studies. These utilities were applied to specific response states and used for bimekizumab and secukinumab. For BSC, the placebo data from these studies were used but adjusted using literature values based on the previous adalimumab submission. Treatment-specific utilities were used. The submitting company found evidence of statistical differences in utility between the arms, and also noted this has been done in evaluations of secukinumab. Disutilities for adverse events were not included in the base case as these were expected to be incorporated by the health state utility scores. Flares (reported as a secondary outcome in the clinical case whereby AN and DT increase) are not included in the economics, but the submitting company provided clarification that these would be expected to be incorporated by the health state utility scores. Surgical costs were incurred in the model, but utilities associated with surgery and disutilities from the procedure were not included.
Costs and resource use	Medicines costs included acquisition costs and administration costs. No adverse events costs were included in the base case, having been assumed included in wider health state costs Wider health care costs included in the model included monitoring, surgery, hospitalisation, A&E attendance and outpatient appointments.
PAS	A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount

	was offered on the list price. A PAS discount is in place for secukinumab and this was included in the results used for decision-making by using estimates of the comparator PAS price.

6.2. Results

In the base case economic analysis bimekizumab was dominant compared to BSC meaning it was estimated as resulting in lower costs and better health outcomes for patients. SMC considered results for decision-making that took into account all relevant PAS. For the comparison with secukinumab, SMC is unable to present these results due to competition law issues.

*Other data were also assessed but remain confidential.**

6.3. Sensitivity analyses

A range of sensitivity and scenario analyses were considered and results of these key scenarios are provided in Table 6.3 below for the comparison with BSC.

Table 6.3: Scenario analysis (Inclusive of PAS discount on bimekizumab and secukinumab)

	Parameter	Base case	Scenario	ICER - BSC	ICER - Secukinumab
	Base case			Dominant*	CiC
1	Time horizon	60 years	40 years	Dominant*	CiC
2	Model structure	Include separate "high" and "very high" response states	Remove "very high" response state	Dominant*	CiC
3	Long term response (48+ weeks) for secukinumab	NMA analysis	MAIC analysis	N/A	CiC
4	Long term response (48+ weeks) for BSC	Stable response (matched to approach in NICE TA392)	Continued use of NMA risk ratio	£9,503	CiC
5	Adverse event costs and disutilities	Excluded	Include	Dominant*	CiC
6	Mortality	Increased mortality risk for non-response patients only. All other patients have mortality equal to the general population	Increase mortality risk for non- and partial response patients	Dominant*	CiC
7			Use general population mortality for all patients	Dominant*	CiC
8	Biologic use in BSC patients	20.8% of patients receive biologic	No patients receive biologic use on	Dominant*	CiC
9	Treatment waning	Separate long term transition probabilities for bimekizumab and secukinumab	Long term transition probabilities for bimekizumab equal to secukinumab	Dominant*	CiC
10	Combined scenario	• Removal of very high response state (scenario 2) • MAIC analysis (Scenario 3) • No biologics in BSC (Scenario 8)		Dominant*	CiC

Abbreviations: BSC – ICER – incremental cost-effectiveness ratio; best supportive care; NMA – network meta analysis; MAIC – matched indirect treatment comparison; NICE – National Institute for Health and Care Excellence; CiC – commercial in confidence

*Dominant: The assessed medicine was estimated as having lower costs and greater health outcomes than the comparator.

6.4. Key strengths

- Two studies were available (BE HEARD I and BE HEARD II) that specifically compare bimekizumab and placebo.
- The available post-hoc data matched previous data definitions used in the SUNSHINE and SUNRISE trials for secukinumab versus placebo. This allowed for an NMA which compared bimekizumab and secukinumab.
- The model structure is similar to previous SMC submissions for this indication.

6.5. Key uncertainties

- The extrapolation of the model was considerable. Direct evidence, comparing bimekizumab against placebo, was only available up to 16 weeks. This was shorter than the 60-year time horizon of the model, which means that the long-term projections were seen as a source of uncertainty.
- The modelling of the BSC arm was broken into three stages. After 16 weeks, that modelling relied on assumptions. While these assumptions matched previous HTA submissions in similar indications, they remained a source of uncertainty and scenario analysis showed them to be a key driver of the economic results. As an extreme case, a scenario was run which maintained the transition probabilities for BSC from the first 16 weeks over the full duration of the model (see Scenario 4 in Table 6.3). This generated a large change in the economic results, although the company argued that this was implausible as it would maintain a placebo effect across the full treatment lifespan of patients.
- There was no direct evidence comparing bimekizumab against secukinumab, necessitating the use of an NMA. This was seen as introducing some uncertainty into the model, particularly given that the credible intervals were wide. That NMA compared the efficacy of bimekizumab and secukinumab at 12 to 16 weeks, however, those results informed the relative efficacy of the two treatments across the full lifespan of the model, which may have been a source of uncertainty. As a scenario a MAIC which compared bimekizumab and secukinumab up to week 48 to 52 was used for long term transition (Scenario 3). This only had a small impact on the economic results.

7. Conclusion

After considering all the available evidence, the Committee accepted bimekizumab for restricted use in NHSScotland.

8. Guidelines and Protocols

In 2018, the British Association of Dermatologists (BAD) published guidelines: British Association of Dermatologists guidelines for the management of hidradenitis suppurativa (acne inversa) 2018.[12]

9. Additional Information

9.1. Product availability date

07 June 2024

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per course (£)
Bimekizumab (Bimzelx®)	**320 mg by subcutaneous injection every two weeks up to week 16; followed by 320 mg every four weeks thereafter.** **Consideration should be given to discontinuing treatment in patients who have shown no improvement by week 16 of treatment.**	**First year: £43,974** **Subsequent years: £31,759**

Costs from BNF online on 22 July 2024. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

The submitting company estimated there would be 221 patients eligible for treatment in each year from year 1 to year 5.

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines or PAS associated with medicines used in a combination regimen.

*Other data were also assessed but remain confidential.**

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This assessment is based on data submitted by the applicant company up to and including 13 September 2024**.**

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.