swissmedic

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Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report
Extension of therapeutic indication

Bimzelx

International non-proprietary name:	bimekizumab
Pharmaceutical form:	Solution for injection in pre-filled syringe Solution for injection in pre-filled pen
Dosage strength(s):	160 mg, 320 mg
Route(s) of administration:	subcutaneous
Marketing authorisation holder:	UCB-Pharma SA
Marketing authorisation no.:	68548
Decision and decision date:	approved on 13.01.2026

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

Table of contents

1 Terms, Definitions, Abbreviations

ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
ALT	Alanine aminotransferase
API	Active pharmaceutical ingredient
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical Classification System
AUC	Area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	Area under the plasma concentration-time curve for the 24-hour dosing interval
CI	Confidence interval
C_{max}	Maximum observed plasma/serum concentration of drug
CYP	Cytochrome P450
DDI	Drug-drug interaction
DLQI	Dermatology Life Quality Index
EMA	European Medicines Agency
ERA	Environmental risk assessment
FDA	Food and Drug Administration (USA)
GI	Gastrointestinal
GLP	Good Laboratory Practice
HiSCR	Hidradenitis Suppurativa Clinical Response
HPLC	High-performance liquid chromatography
HSSDD	Hidradenitis Suppurativa Symptom Daily Diary
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
Ig	Immunoglobulin
INN	International non-proprietary name
ITT	Intention-to-treat
LoQ	List of Questions
MAH	Marketing authorisation holder
Max	Maximum
Min	Minimum
MRHD	Maximum recommended human dose
N/A	Not applicable
NO(A)EL	No observed (adverse) effect level
PBPK	Physiology-based pharmacokinetics
PD	Pharmacodynamics
PIP	Paediatric investigation plan (EMA)
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PRO	Patient-Reported Outcome
PSP	Pediatric study plan (US FDA)
Q4W	Every 4 weeks
RMP	Risk management plan
SAE	Serious adverse event
SwissPAR	Swiss Public Assessment Report
TEAE	Treatment-emergent adverse event
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)

2 Background information on the procedure

2.1 Applicant's request(s) and information regarding procedure

Extension(s) of the therapeutic indication(s)
The applicant requested the addition of a new therapeutic indication or modification of an approved one in accordance with Article 23 TPO.

2.2 Indication and dosage

2.2.1 Requested indication

Bimzelx is indicated for the treatment of moderate to severe hidradenitis suppurativa (acne inversa) in adults.

2.2.2 Approved indication

Hidradenitis suppurativa (HS)
Bimzelx is indicated for the treatment of adults with active moderate to severe hidradenitis suppurativa (acne inversa) who have had an inadequate response to systemic antibiotic therapy.

2.2.3 Requested dosage

Summary of the requested standard dosage:
The recommended dose for adult patients with hidradenitis suppurativa is 320 mg (given as 2 subcutaneous injections of 160 mg each) every 2 weeks up to week 16 and every 4 weeks thereafter.

2.2.4 Approved dosage

(see appendix)

2.3 Regulatory history (milestones)

Application	31 July 2024
Formal objection	22 August 2024
Response to formal objection	4 September 2024
Formal control completed	4 October 2024
List of Questions (LoQ)	31 January 2025
Response to LoQ	30 March 2025
Preliminary decision	6 June 2025
Response to preliminary decision	24 August 2025
Labelling corrections and/or other aspects	14 October 2025
Response to labelling corrections and/or other aspects	6 November 2025
Final decision	13 January 2026
Decision	approval

3 Medical context

Hidradenitis suppurativa (HS), also known as acne inversa, is a chronic, inflammatory skin disease affecting hair follicles in areas with apocrine glands, such as the armpits, groin, and anogenital regions. It typically manifests after puberty, with a prevalence of about 1% in Europe, and significantly impacts patients' quality of life. HS is associated with conditions like obesity, metabolic syndrome, Crohn's disease, and smoking. The disease is characterised by painful, inflamed lesions caused by hair follicle occlusion and inflammation. The disease causes both physical and emotional distress, with pain and social stigma significantly affecting mental health. Stress and certain factors like tight clothing, wet shaving, and sweat can exacerbate the condition.

HS is classified into inflammatory and non-inflammatory forms, with severity assessed using the Hurley staging system. Hurley stage I involves single or multiple abscesses without scarring, stage II includes limited scarring and sinus tracts, and stage III involves extensive scarring and sinus tracts.

Treatment modalities according to different international guidelines include intralesional corticosteroids, topical clindamycin, oral tetracyclines, combination clindamycin and rifampicin therapy, adalimumab, and wide local excision. Oral tetracyclines are consistently recommended across several guidelines as first-line systemic therapy. A combination regimen of clindamycin and rifampicin is typically used as second-line treatment.

The following medicinal products are approved for HS in Switzerland: adalimumab and secukinumab. Both monoclonal antibodies are used in cases of active moderate to severe HS that have not responded sufficiently to treatment with systemic antibiotic therapy.

4 Nonclinical aspects

The applicant submitted new pharmacology studies to further support the requested new indication (hidradenitis suppurativa). No additional nonclinical safety studies were provided, which is considered acceptable. The new indication is unlikely to result in any significant risk to the environment. From the nonclinical point of view, there are no objections to the approval of the new indication applied for.

5 Clinical aspects

The assessment of the clinical data of this application has been carried out in reliance on previous regulatory decisions by EMA and FDA (US product label). The available assessment report (EMA only) and respective product information from EMA and FDA were used as an additional basis for the clinical assessment.

5.1 Clinical pharmacology

Sparse PK samples were collected in the HS population, and a dedicated PopPK analysis was conducted. Compared with the results from the population PK analysis for patients with diseases of the previously approved indications (PSO, PsA and axSpA), an increase in clearance is observed. This leads to a short half-life ($t_{1/2}$). In addition, the average bodyweight of the HS population included in the dataset was approx. 15 kg higher compared to the other indication, further affecting the exposure of bimekizumab in the HS population.

This results in a comparable C_{max} for the HS population at 320 mg after bi-weekly injections vs the other indications at 320 mg dosed every 4 weeks (44.0 µg/mL), whereas higher C_{trough} concentrations can be expected in the HS population.

The treatment-emergent ADA incidence, at approx. 50 % to 60%, was comparable to the ADA incidence rate observed in patients from previously submitted indications.

5.2 Dose Finding / Dose Recommendation

The HS0001 study was a phase 2 multicentre, randomised, investigator- and participant-blind, placebo-controlled trial with an active reference arm. It aimed to evaluate the efficacy, safety, and PK of bimekizumab in eligible adults with moderate to severe HS. Participants received a loading dose of 640 mg bimekizumab at baseline, followed by 320 mg every two weeks (Q2W) until week 10. Over the 12-week period, bimekizumab 320 mg Q2W demonstrated consistent and clinically meaningful efficacy in treating HS compared to placebo.
The decision to omit a loading dose for the phase 3 programme has been adequately justified based on PK and exposure/response data from patients enrolled in HS0001 and the dose regimens (no loading doses) for the PSO, PsA, and axSpA indications. Overall, the choice of the dosing regimen for the phase 3 HS studies can be followed based on Study HS0001.

5.3 Efficacy

HS0003 and HS0004 are nearly identically designed studies. HS0003 and HS0004 are Phase 3, randomised, double-blind, placebo-controlled, multicentre, pivotal studies evaluating the efficacy and safety of bimekizumab in study participants with moderate to severe HS.

The study design consisted of a Screening Period (≥14 days to ≤5 weeks), a double-blind, 48-week Treatment Period comprising a 16-week Initial Treatment Period, a 32-week Maintenance Treatment Period, and a 20-week Safety Follow-up Period following the final injection of investigational medicinal product if study participants did not enter a subsequent extension study (HS0005) or withdraw prematurely from treatment.

To be eligible to participate in the HS0003 or HS0004 studies, adult participants must have had a diagnosis of HS based on clinical history and physical examination for at least 6 months prior to the Baseline visit, HS lesions present in at least 2 distinct anatomic areas, 1 of which must be at least Hurley Stage II or Hurley Stage III, moderate to severe HS defined as a total of ≥5 inflammatory lesions, and history of inadequate response to a course of systemic antibiotics for treatment of HS.

Study participants were randomised in a 2:2:2:1 ratio (stratified by Hurley Stage and current antibiotic use) to 1 of 4 treatment sequences as follows:

- Bimekizumab 320 mg every 2 weeks (Q2W) from Weeks 0 to 48
- Bimekizumab 320 mg every 4 weeks (Q4W) from Weeks 0 to 48
- Bimekizumab 320 mg Q2W to Week 16, continuing with 320 mg Q4W from Weeks 16 to 48
- Placebo to Week 16, continuing with bimekizumab 320 mg Q2W from Weeks 16 to 48

Efficacy was evaluated using both clinician-reported outcome and PRO measures after the 16-week, double-blind, placebo-controlled Initial Treatment Period. The primary efficacy variable was $HiSCR_{50}$, defined as at least a 50% reduction from Baseline in the total abscess and inflammatory nodule count, with no increase from Baseline in antibiotic therapy or draining tunnel count.
Ranked secondary endpoints, such as $HiSCR_{75}$ and the HS-specific fit-for-purpose symptom outcome measure for worst skin pain (e.g. responder definition for threshold of within-patient clinically meaningful change), as well as the other endpoint, $HiSCR_{90}$, reflect more stringent efficacy assessments.

Study HS0003: Treatment with bimekizumab 320 mg Q2W demonstrated statistically superior improvements for the primary efficacy endpoint ($HiSCR_{50}$ response at Week 16) and the ranked secondary efficacy endpoints ($HiSCR_{75}$ response at Week 16, change from Baseline in DLQI Total Score at Week 16, and change from Baseline in HSSDD worst skin pain score at Week 16) in the testing procedure compared with placebo. The testing procedure stopped at the fifth ranked endpoint (worst skin pain response status at Week 16), as statistical significance for bimekizumab 320mg Q2W compared to placebo was not achieved.
Treatment with bimekizumab 320 mg Q4W did not demonstrate statistically superior improvements for the primary efficacy endpoint. Therefore, all subsequent endpoints in the hierarchy for the bimekizumab 320 mg Q4W dose were not evaluated for statistical significance.

Study HS0004: Treatment with bimekizumab 320 mg Q4W and bimekizumab 320 mg Q2W demonstrated clinically meaningful and statistically superior improvements for the primary efficacy endpoint ($HiSCR_{50}$ response at Week 16) and the first ranked secondary efficacy endpoint ($HiSCR_{75}$ response at Week 16) in the testing procedure compared with placebo. The testing procedure stopped at the second ranked secondary efficacy endpoint (flare by Week 16), as statistical significance for both bimekizumab 320 mg Q2W and bimekizumab 320 mg Q4W compared with placebo was not achieved.

Consistent efficacy in both pivotal studies for the primary endpoint $HiSCR_{50}$ response at Week 16 was shown only for bimekizumab 320mg Q2W. The same applies for the first ranked secondary endpoint for bimekizumab 320mg Q2W. Thus, only bimekizumab 320 mg Q2W showed robust results. Although bimekizumab 320 mg Q2W showed further significant results for additional ranked secondary endpoints in study HS0003, the same could not be demonstrated in study HS0004.

As the mandatory inclusion criterion of “history of inadequate response to a course of systemic antibiotics for treatment of HS” applied in both pivotal studies, Bimzelx can only be approved as a second-line treatment in active HS, like other approved biological products in Switzerland. This was accepted accordingly by the applicant in its answer to the LoQ.

5.4 Safety

The safety profile of bimekizumab is well-known from different indications. However, the studies in HS (HS0003 and HS0004) had a doubling or quadrupling of the dose compared to other indications.

The median duration of exposure in Studies HS0003 and HS0004 during the Initial Treatment Period was 112 days for all treatment groups; during the Maintenance Treatment Period, it ranged from 223 to 224 days across all treatment groups; and during the Overall Period, it ranged from 333 to 336 days across all treatment groups.

In the HS0003 study, the incidence of treatment-emergent adverse events (TEAEs) during the Initial Treatment Period was the same between the bimekizumab total group and the placebo group (66.7% each). TEAEs were reported at comparable rates in the bimekizumab 320 mg Q4W group (65.7%) and the 320 mg Q2W group (67.1%). During the Overall Period, TEAEs were slightly lower in the Q4W/Q4W group (85.3%) compared to the Q2W/Q2W group (89.4%).
During the Initial Treatment Period, the most commonly reported TEAEs, by PT, in the bimekizumab total group were hidradenitis (7.2%), headache (7.0%), and diarrhoea (7.0%) and, in the placebo group, hidradenitis (13.9%), back pain (8.3%), and headache (4.2%)

During the Overall Period, the most reported TEAEs were hidradenitis (19.4%), coronavirus infection (14.4%), and diarrhoea (9.9%). Hidradenitis and psychiatric evaluation abnormalities were more frequent in the Q4W/Q4W group, while coronavirus infection was more frequent in the Q2W/Q2W group.

A small number of serious TEAEs were reported during the Initial Treatment Period (2.3% in the bimekizumab group, none in the placebo group), with similar incidences between the Q4W (2.8%) and Q2W (2.1%) groups. During the Overall Period, serious TEAEs occurred in 8.1% of the bimekizumab group, with hidradenitis, suicidal ideation, cellulitis, and nephrolithiasis being the most common. Serious TEAE rates were comparable between the Q4W/Q4W (9.1%) and Q2W/Q2W (9.2%) groups. One death due to cardiac failure occurred in the Q2W/Q2W group and was deemed unrelated to the investigational product.

In the HS0004 study, during the Initial Treatment Period, TEAEs were slightly more frequent in the bimekizumab group (60.2%) compared to placebo (56.8%). TEAEs were lower in the bimekizumab 320 mg Q4W group (51.4%) than in the 320 mg Q2W group (64.5%). During the Overall Period, TEAEs were slightly lower in the Q4W/Q4W group (79.6%) compared to the Q2W/Q2W group (84.7%).

The most common TEAEs during the Initial Treatment Period were hidradenitis (8.8%), oral candidiasis (6.7%), and headache (5.8%), while in the placebo group they were headache (9.5%), diarrhoea (8.1%), and hidradenitis (6.8%).

During the Overall Period, the most common TEAEs in the bimekizumab group were hidradenitis (18.0%), oral candidiasis (12.8%), and headache (8.6%). The Q4W/Q4W group had slightly higher incidences of vulvovaginal candidiasis but lower rates of oral candidiasis and nasopharyngitis compared to the Q2W/Q2W group.

A small number of serious TEAEs were reported, with 2.8% in the bimekizumab group and none in the placebo group during the Initial Treatment Period. During the Overall Period, serious TEAEs occurred in 4.8% of the bimekizumab group, with hidradenitis and skin pain being the most common. Serious TEAE rates were comparable between the Q4W/Q4W (4.9%) and Q2W/Q2W (6.9%) groups. No deaths occurred during the Initial or Maintenance Periods.

Tinea infections occurred in the bimekizumab 320 mg Q2W/Q2W group in up to 5.0% (HS0003) and 5.6% (HS0004). However, this adverse drug reaction is already covered in the Information for healthcare professionals.

In addition, slight imbalances were noted for suicidal ideation and behaviour in both studies. However, the numbers and imbalances were so small that no causal relationship between bimekizumab and suicidality could be established. The safety topic on suicidal ideation and behaviour will continue to be closely monitored in future PSURs.

5.5 Final benefit-risk assessment

Bimzelx demonstrated significant and meaningful improvements in moderate to severe HS in two placebo-controlled, randomised Phase 3 trials (HS0003 and HS0004). These trials included adult patients with a history of inadequate response to systemic antibiotics for HS treatment. While the

results of the two well-designed pivotal studies were not entirely identical, the higher dose of bimekizumab (320 mg every two weeks) consistently showed greater efficacy compared to the lower dose (320 mg every four weeks).

The safety profile observed in these trials aligns with the known safety data from previous studies in other approved indications.

As a result, the benefit-risk profile of Bimzelx 320 mg Q2W as a second-line treatment for active HS, following the failure of antibiotic therapy, is considered positive.

6 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

7 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for Bimzelx was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected new or serious adverse reactions. See the "Undesirable effects" section for advice on the reporting of adverse reactions.

BIMZELX

Composition

Active substances

Bimekizumab, manufactured from genetically modified CHO (Chinese Hamster Ovary) cells.

Excipients

Glycine, Sodium acetate trihydrate (E262), Glacial acetic acid, Polysorbate 80, Water for injection q.s. in a solution of 1 ml or 2 ml.
Each pre-filled pen (1ml) contains 0.45 mg sodium.
Each pre-filled pen (2 ml) contains 0.90 mg sodium.
Each pre-filled syringe (1ml) contains 0.45 mg sodium.
Each pre-filled syringe (2 ml) contains 0.90 mg sodium.

Pharmaceutical form and active substance quantity per unit

Solution for injection, in a pre-filled pen or in a pre-filled syringe for subcutaneous use.
Each pre-filled pen of 1 ml or pre-filled syringe of 1 ml contains 160 mg bimekizumab.
Each pre-filled pen of 2 ml or pre-filled syringe of 2 ml contains 320 mg bimekizumab.

Appearance
The solution is clear to slightly opalescent and, colourless to pale brownish-yellow.

Indications/Uses

Plaque psoriasis
Bimzelx is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy.

Psoriatic arthritis
Bimzelx, alone or in combination with methotrexate, is indicated for the treatment of active psoriatic arthritis in adults who have had an inadequate response or who have been intolerant to one or more disease-modifying antirheumatic drugs (DMARDs).

Axial spondyloarthritis

Non-radiographic axial spondyloarthritis (nr-axSpA)

Bimzelx is indicated for the treatment of adults with severe active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and magnetic resonance imaging (MRI) who have responded inadequately or are intolerant to non-steroidal anti-inflammatory drugs (NSAIDs).

Ankylosing spondylitis (AS, radiographic axial spondyloarthritis)

Bimzelx is indicated for the treatment of adults with severe active ankylosing spondylitis who have responded inadequately or are intolerant to conventional therapy.

Hidradenitis suppurativa (HS)

Bimzelx is indicated for the treatment of adults with active moderate to severe hidradenitis suppurativa (acne inversa) who have had an inadequate response to systemic antibiotic therapy.

Dosage/Administration

Bimzelx is intended for use under the guidance and supervision of a doctor experienced in diagnosing and treating conditions for which Bimzelx is indicated.

To ensure traceability of biotechnological medicinal products, it is recommended that the trade name and batch number should be documented for each treatment.

Plaque psoriasis

The recommended dose of Bimzelx for adult patients with plaque psoriasis is 320 mg (given as 2 subcutaneous injections of 160 mg or 1 subcutaneous injection of 320 mg) at Week 0, 4, 8, 12, 16 and every 8 weeks thereafter.

Psoriatic arthritis

The recommended dose for adult patients with active psoriatic arthritis is 160 mg (given as 1 subcutaneous injection of 160 mg) every 4 weeks.

For psoriatic arthritis patients with coexistent moderate to severe plaque psoriasis, the recommended dose is the same as for plaque psoriasis [320 mg (given as 2 subcutaneous injections of 160 mg or 1 subcutaneous injection of 320 mg) at Week 0, 4, 8, 12, 16 and every 8 weeks thereafter]. After 16 weeks, regular assessment of efficacy is recommended and if a sufficient clinical response in joints cannot be maintained, a switch to 160 mg every 4 weeks can be considered.

Axial spondyloarthritis (nr-axSpA and AS)

The recommended dose for adult patients with axial spondyloarthritis is 160 mg (given as 1 subcutaneous injection of 160 mg) every 4 weeks.

Hidradenitis suppurativa
The recommended dose 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 2 weeks up to Week 16 and every 4 weeks thereafter.

For above indications, consideration should be given to discontinuing treatment in patients who have shown no improvement by 16 weeks of treatment.

Special dosage instructions

Overweight patients with plaque psoriasis
For some patients with plaque psoriasis (including psoriatic arthritis with coexistent moderate to severe psoriasis) and a body weight ≥ 120 kg who did not achieve complete skin clearance at Week 16, 320 mg every 4 weeks after Week 16 may further improve treatment response (see *Clinical efficacy)****Fehler! Textmarke nicht definiert.****.*

Patients with hepatic disorders

Bimzelx has not been studied in these patient populations. Dose adjustments are not considered necessary based on pharmacokinetics (see *Pharmacokinetics*).

Patients with renal disorders

Bimzelx has not been studied in these patient populations. Dose adjustments are not considered necessary based on pharmacokinetics (see *Pharmacokinetics*).

Elderly patients

No dose adjustment is required (see *Pharmacokinetics*).

Children and adolescents

Bimzelx is not authorised for use in the paediatric population.

Mode of administration

Bimzelx is administered by subcutaneous injection. A 320 mg dose can be given as 2 subcutaneous injections of 160 mg or 1 subcutaneous injection of 320 mg.
Suitable areas for injection include thigh, abdomen and upper arm. Injection sites should be rotated, and injections should not be given into psoriasis plaques or areas where the skin is tender, bruised, erythematous, or indurated. Administration in the upper arm may only be performed by a healthcare professional or caregiver.

After proper training in subcutaneous injection technique, patients may self-inject if their physician determines that it is appropriate and with medical follow-up as necessary. Patients should be instructed to inject the full amount of Bimzelx according to the instructions for handling (see *Patient information*).

Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section “Composition”.
Clinically important active infections (e.g., active tuberculosis).

Warnings and precautions

Infections
Bimzelx may increase the risk of infections such as upper respiratory tract infections and oral candidiasis (see *Undesirable Effects*).
Caution should be exercised when considering the use of Bimzelx in patients with a chronic infection or a history of recurrent infection. Treatment with Bimzelx should not be initiated in patients with any clinically important active infection (particularly HIV, HBV, or HCV infections) until the infection resolves or is adequately treated. Patients treated with Bimzelx should be instructed to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops an infection, the patient should be carefully monitored. If the infection becomes serious or is not responding to standard therapy, treatment should be discontinued until the infection resolves.

Pre-treatment evaluation for tuberculosis (TB)
In clinical studies, patients with latent TB receiving Bimzelx and an anti-TB therapy did not develop active TB. Prior to initiating treatment with Bimzelx, patients should be evaluated for TB infection. Bimzelx should not be given in patients with active TB. Patients receiving Bimzelx should be monitored for signs and symptoms of active TB. Anti-TB therapy should be considered prior to initiating Bimzelx in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed.

Malignancies
No increased risk of malignancy was observed with Bimzelx treatment in clinical studies up to one year. Results of long-term safety studies are not yet available.
As psoriasis patients are an at-risk population, patients should be evaluated for skin tumours before and during treatment with Bimzelx.

Inflammatory bowel disease

Cases of new or exacerbations of inflammatory bowel disease have been reported with Bimzelx. Bimzelx is not recommended in patients with inflammatory bowel disease. If a patient develops signs and symptoms of inflammatory bowel disease, or experiences an exacerbation of pre-existing inflammatory bowel disease, Bimzelx should be discontinued and appropriate medical management should be initiated.

Hypersensitivity reactions
Serious hypersensitivity reactions including anaphylactic reactions have been observed with interleukin-17 (IL-17) inhibitors. If a serious hypersensitivity reaction occurs, administration of Bimzelx should be discontinued immediately and appropriate therapy initiated.

Vaccinations
Prior to initiating therapy with Bimzelx, completion of all age-appropriate immunizations according to current immunization guidelines is recommended. Live vaccines should not be given in patients treated with Bimzelx. Patients treated with Bimzelx may receive inactivated or non-live vaccinations. Healthy individuals who received a single 320 mg dose of Bimzelx two weeks prior to vaccination with an inactivated seasonal influenza vaccine had similar antibody responses compared to individuals who did not receive Bimzelx prior to vaccination.

Excipients
This medicinal product contains 0.4 mg of polysorbate 80 in each 1 ml solution. Polysorbates may cause allergic reactions.
This medicinal product contains less than 1 mmol sodium (23 mg) per pre-filled pen (160 mg and 320 mg), that is to say essentially ‘sodium-free’.
This medicinal product contains less than 1 mmol sodium (23 mg) per pre-filled syringe (160 mg and 320 mg), that is to say essentially ‘sodium-free’.

Interactions

No CYP450 interaction studies have been performed in humans. There is no direct evidence for the role of IL-17A or IL-17F in the expression of CYP450 enzymes. The formation of some CYP450 enzymes is suppressed by increased levels of cytokines during chronic inflammation. Thus, anti-inflammatory treatments, such as with the IL-17A and IL-17F inhibitor Bimzelx, may result in normalisation of CYP450 levels with accompanying lower exposure of CYP450-metabolised co-medications. Therefore, a clinically relevant effect on CYP450 substrates with a narrow therapeutic index, in which the dose is individually adjusted (e.g. warfarin) cannot be excluded. On initiation of Bimzelx therapy in patients being treated with these types of medicinal products, therapeutic monitoring should be considered.

Population pharmacokinetic (PK) data analyses indicated that concomitant administration of conventional disease modifying antirheumatic drugs (cDMARDs) including methotrexate or prior exposure to biologics have no clinically relevant impact on the clearance of bimekizumab.

Pregnancy, lactation

Pregnancy

There is a limited amount of data on the use of Bimzelx in pregnant women. Women of childbearing potential should use an effective method of contraception during treatment and for at least 17 weeks after treatment. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition or postnatal development (see *Preclinical Data*). Bimzelx should only be used during pregnancy if the benefit to the mother clearly outweighs the potential risk to the foetus.

Lactation

It is not known whether Bimzelx is excreted in human milk or absorbed systemically by the infant. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Bimzelx and any potential adverse effects on the breastfed infant from Bimzelx or from the underlying maternal condition.

Fertility

The effect of Bimzelx on human fertility has not been evaluated. Animal trials do not indicate direct or indirect harmful effects on fertility (see *Preclinical Data*).

Effects on ability to drive and use machines

The influence of Bimzelx on the ability to drive and use machines has not been specifically studied.

Undesirable effects

Summary of the safety profile

Clinical studies

Overview

A total of 5862 patients have been treated with bimekizumab in blinded and open-label clinical studies in plaque psoriasis (PSO), psoriatic arthritis (PsA), axial spondyloarthritis (nr-axSpA and AS) and hidradenitis suppurativa (HS) representing 11468.6 patient-years of exposure. Of these, over 4660 patients were exposed to bimekizumab for at least one year. Overall, the safety profile of bimekizumab is consistent across all indications.

The most frequently reported adverse drug reactions (ADRs) were upper respiratory tract infections (14.5%, 14.6%, 16.3% and 8.8% in plaque psoriasis , psoriatic arthritis , axial spondyloarthritis (axSpA) and hidradenitis suppurativa respectively) and oral candidiasis (7.3%, 2.3%, 3.7%, and 5.6% in PSO, PsA, axSpA and HS respectively).

List of adverse reactions

The adverse reactions for bimekizumab are classified by MedDRA System Organ Class and frequency, using the following convention: very common (≥ 1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1,000), very rare (<1/10,000), not known (frequency cannot be estimated from the available data).

Table 1: List of adverse reactions in clinical studies

System Organ Class	Frequency	Adverse effects
Infections and infestations	Very common	Upper respiratory tract infections
	Common	Oral candidiasis, Tinea infections, Ear infections, Herpes simplex infections, Oropharyngeal candidiasis, Gastroenteritis, Folliculitis, Vulvovaginal fungal infection (including vulvovaginal candidiasis)
	Uncommon	Conjunctivitis, Mucosal and cutaneous candidiasis (including oesophageal candidiasis)
Blood and lymphatic system disorders	Uncommon	Neutropenia
Nervous System disorders	Common	Headache
Gastrointestinal disorders	Uncommon	Inflammatory bowel disease
Skin and subcutaneous tissue disorders	Common	Dermatitis and eczema, Acne, Rash
General disorders and administration site conditions	Common	Injection site reactions[a], Fatigue
[a)] Includes: injection site erythema, reaction, oedema, pain, swelling and haematoma.		

Description of specific adverse reactions and additional information

Infections

In the placebo-controlled period of Phase III clinical studies in plaque psoriasis, infections were reported in 36.0% of patients treated with bimekizumab for up to 16 weeks compared with 22.5% of patients treated with placebo. The majority of infections consisted of non-serious mild to moderate upper respiratory tract infections such as nasopharyngitis. Serious infections occurred in 0.3% of patients treated with bimekizumab and 0% treated with placebo.
There were higher rates of oral and oropharyngeal candidiasis in patients treated with bimekizumab consistent with the mechanism of action (7.3% and 1.2% respectively compared to 0% for placebo-treated patients). The vast majority of cases were non-serious, mild or moderate in severity, and did not require treatment discontinuation.
Over the entire treatment period of Phase III studies in plaque psoriasis, infections were reported in 63.2% of patients treated with bimekizumab (120.4 per 100 patient-years). Serious infections were reported in 1.5% of patients treated with bimekizumab (1.6 per 100 patient-years) (see *Warnings and Precautions*).
Infection rates observed in PsA and axSpA (nr-axSpA and AS) Phase III clinical studies were similar to those observed in plaque psoriasis apart from oral and oropharyngeal candidiasis rates in patients treated with bimekizumab, which were lower at 2.3% and 0% respectively in PsA and 3.7% and 0.3% respectively in axSpA compared to 0% with placebo.

Infection rates observed in HS Phase III clinical studies were similar to those observed in other indications.
In the placebo-controlled period, oral and oropharyngeal candidiasis rates in patients treated with bimekizumab were 7.1% and 0% respectively, compared to 0% with placebo.

Neutropenia
Neutropenia was observed with bimekizumab in phase III clinical studies in plaque psoriasis. In the 16 weeks placebo-controlled period neutropenia grade 3/4 were observed at the same frequency of 0.6% in patients receiving bimekizumab or placebo. Over the entire treatment period of Phase III studies, neutropenia grade 3/4 were observed in 1% of patients treated with bimekizumab.
The frequency of neutropenia in PsA, axSpA (nr-axSpA and AS) and HS clinical studies was similar to that observed in plaque psoriasis studies.
Most cases were transient and did not require treatment discontinuation. No serious infections were associated with neutropenia.

Liver value increases
During the placebo-controlled period of Trials HS0003 and HS0004, liver serum transaminase elevations (> 3 times the upper limit of normal [ULN]) occurred in 1.2% (10/854) of subjects treated

with BIMZELX versus 0% (0/144) of subjects receiving placebo. Elevated liver serum transaminases resolved during continued treatment or after discontinuation of BIMZELX.

Immunogenicity

As with all therapeutic proteins, there is the potential for immunogenicity with bimekizumab. The detection of anti-drug antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of anti-drug antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to bimekizumab with the incidence of antibodies to other products may be misleading.

Plaque psoriasis

Approximately 45% of plaque psoriasis patients treated with bimekizumab up to 56 weeks at the recommended dosing regimen (320 mg every 4 weeks up to Week 16 and 320 mg every 8 weeks thereafter) developed anti-drug antibodies. Of the patients who developed anti-drug antibodies, approximately 34% (16% of all patients treated with bimekizumab) had antibodies that were classified as neutralizing.

Psoriatic arthritis

Approximately 31% of patients with psoriatic arthritis treated with bimekizumab at the recommended dosing regimen (160 mg every 4 weeks) up to 16 weeks had anti-drug antibodies. Of the patients with anti-drug antibodies, about 33% (10% of all patients treated with bimekizumab) had antibodies that were classified as neutralizing. By week 52, approximately 47% of biologic disease-modifying anti-rheumatic drug (bDMARD) treatment naïve patients with psoriatic arthritis in the BE OPTIMAL study treated with bimekizumab at the recommended dosing regimen (160 mg every 4 weeks) had anti-drug antibodies. Of the patients with anti-drug antibodies, about 38% (18% of all patients in the BE OPTIMAL study treated with bimekizumab) had antibodies that were classified as neutralizing.

Axial spondyloarthritis (nr-axSpA and AS)

Approximately 57% of patients with nr-axSpA treated with bimekizumab up to 52 weeks at the recommended dosing regimen (160 mg every 4 weeks) had anti-drug antibodies. Of the patients with anti-drug antibodies, approximately 44% (25% of all patients treated with bimekizumab) had antibodies that were classified as neutralizing.

Approximately 44% of patients with AS treated with bimekizumab up to 52 weeks at the recommended dosing regimen (160 mg every 4 weeks) had anti-drug antibodies. Of the patients with

anti-drug antibodies, approximately 44% (20% of all patients treated with bimekizumab) had antibodies that were classified as neutralizing.

Hidradenitis suppurativa
Approximately 59% of HS patients treated with bimekizumab up to 48 weeks at the recommended dosing regimen (320 mg every 2 weeks up to Week 16 and 320 mg every 4 weeks thereafter) developed anti-drug antibodies. Of the patients who developed anti-drug antibodies, approximately 63% (37% of all patients treated with bimekizumab) had antibodies that were classified as neutralizing.

Across indications, no clinically meaningful impact on clinical response was associated with anti-bimekizumab antibodies development and an association between immunogenicity and treatment emergent adverse events has not been clearly established.

Hypersensitivity reactions:
Serious hypersensitivity reactions, including anaphylactic reactions, have been observed during treatment with IL-17 inhibitors.

Elderly (≥ 65 years of age)
Limited data are available regarding this age group. In the placebo-controlled period of the Phase III clinical trials in patients with plaque psoriasis, oral candidiasis was observed in 18.2% of patients ≥ 65 years of age versus 6.3% in patients <65 years of age. Dermatitis and eczema affected 7.3% of patients ≥ 65 years of age compared to 2.8% of patients < 65 years of age.

Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the ElViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

Overdose

Single doses of 640 mg intravenously or 640 mg subcutaneously, followed by 320 mg subcutaneously every two weeks for five doses have been administered in clinical studies without dose-limiting toxicity. In the event of overdose, it is recommended that the patient be monitored for any signs and symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

Properties/Effects

ATC code

L04AC21

Mechanism of action

Bimekizumab is a humanized IgG1/κ monoclonal antibody that selectively binds with high affinity to IL-17A, IL-17F and IL-17AF cytokines, blocking their interaction with the IL-17RA/IL-17RC receptor complex. Elevated concentrations of IL-17A and IL-17F have been implicated in the pathogenesis of several immune-mediated inflammatory diseases including plaque psoriasis, psoriatic arthritis, axial spondyloarthritis and hidradenitis suppurativa. IL-17A and IL-17F cooperate and/or synergize with other inflammatory cytokines to induce inflammation. IL17-F is produced in significant amount by innate immune cells. This production can be independent of IL-23. Bimekizumab inhibits the proinflammatory cytokines, resulting in the normalization of skin inflammation and substantial decrease of local and systemic inflammation, and as a consequence improvement in clinical signs and symptoms associated with psoriasis, psoriatic arthritis, axial spondyloarthritis and hidradenitis suppurativa. From *in vitro* models, bimekizumab was shown to inhibit psoriasis-related gene expression, cytokine production, the migration of inflammatory cells and pathological osteogenesis to a greater extent than inhibition of IL-17A alone.

Pharmacodynamics

No formal pharmacodynamic studies have been conducted with bimekizumab.

Clinical efficacy

Plaque psoriasis

The safety and efficacy of bimekizumab was evaluated in 1480 patients with moderate to severe plaque psoriasis in three Phase III multicenter, randomized, placebo and/or active comparator-controlled studies. Patients were at least 18 years of age, had a Psoriasis Area and Severity Index (PASI) score ≥12 and Body Surface Area (BSA) affected by PSO ≥10%, an Investigators Global Assessment (IGA) score ≥3 on a 5-point scale and were candidates for systemic psoriasis therapy and/or phototherapy. The efficacy and safety of bimekizumab were evaluated versus placebo and ustekinumab (BE VIVID – PS0009), versus placebo (BE READY – PS0013) and versus adalimumab (BE SURE - PS0008).

The BE VIVID study evaluated 567 patients for 52 weeks where patients were randomized to receive either bimekizumab 320 mg every 4 weeks, ustekinumab (45 mg or 90 mg, depending on patient weight, at baseline and Week 4 and then every 12 weeks), or placebo for an initial 16 weeks followed by bimekizumab 320 mg every 4 weeks.

The BE READY study evaluated 435 patients for 56 weeks. Patients were randomized to receive bimekizumab 320 mg every 4 weeks or placebo. At Week 16, patients who achieved a PASI 90

response entered the 40-week randomized withdrawal period. Patients initially randomized to bimekizumab 320 mg every 4 weeks were re-randomized to either bimekizumab 320 mg every 4 weeks or bimekizumab 320 mg every 8 weeks or placebo (i.e. withdrawal of bimekizumab). Patients initially randomized to placebo continued to receive placebo provided they were PASI 90 responders. Patients who did not achieve a PASI 90 response at Week 16 entered an open-label escape arm and received bimekizumab 320 mg every 4 weeks for 12 weeks. Patients who relapsed (did not achieve PASI 75 response) during the randomized withdrawal period also entered the 12-week escape arm.

The BE SURE study evaluated 478 patients for 56 weeks. Patients were randomized to receive either bimekizumab 320 mg every 4 weeks through Week 56, bimekizumab 320 mg every 4 weeks through Week 16 followed by bimekizumab 320 mg every 8 weeks through Week 56 or adalimumab as per labeling recommendation through Week 24 followed by bimekizumab 320 mg every 4 weeks through Week 56.

Baseline characteristics were consistent across all 3 studies. Among those, the median baseline BSA was 20%, the median baseline PASI score was 18 and the baseline IGA score was severe in 33% of patients. The median baseline scores for Patient Symptoms Diary (PSD) pain, itch and scaling items ranged between 6 and 7 on a 0-10 points scale and the median baseline Dermatology Life Quality Index (DLQI) total score was 9.

Across all 3 studies, 38% of patients had received a prior biologic therapy; 23% had received at least one anti-IL17 agent and 13% had received at least one TNF-antagonist. Twenty-two percent were naïve to any systemic therapy (including non-biologic and biologic) and 39% of patients had received prior phototherapy or photochemotherapy.

The efficacy of bimekizumab was evaluated with respect to impact on skin disease overall, specific body locations (scalp, nails and hand and foot), patient reported symptoms and impact on quality of life. The two co-primary end-points in all 3 studies were the proportion of patients who achieved 1) a PASI 90 response and 2) an IGA “clear or almost clear” (IGA 0/1 with at least two points improvement from baseline) response at Week 16. PASI 100, IGA 0 response at Week 16 and PASI 75 response at Week 4 were key secondary endpoints in all 3 studies.

<u>Skin disease overall</u>

Treatment with bimekizumab resulted in significant improvement in the measures of disease activity compared to placebo, ustekinumab or adalimumab at Week 16. The key efficacy results are shown in Table 2.

Table 2: Summary of clinical responses in BE VIVID, BE READY and BE SURE

	BE VIVID			BE READY		BE SURE	
	Placebo (N= 83) n (%)	**BKZ 320 mg Q4W (N= 321) n (%)**	**Ustekinumab (N=163) n (%)**	**Placebo (N= 86) n (%)**	**BKZ 320 mg Q4W (N= 349) n (%)**	**BKZ 320 mg Q4W (N= 319) n (%)**	**Adalimumab (N= 159) n (%)**
PASI 100 Week 16	0 (0.0)	188 (58.6) [a]	34 (20.9)	1 (1.2)	238 (68.2) [a]	194 (60.8) [a]	38 (23.9)
PASI 90 Week 16	4 (4.8)	273 (85.0) [a, b]	81 (49.7)	1 (1.2)	317 (90.8) [a]	275 (86.2) [a]	75 (47.2)
PASI 75 Week 4 Week 16	2 (2.4) 6 (7.2)	247 (76.9) [a, b] 296 (92.2)	25 (15.3) 119 (73.0)	1 (1.2) 2 (2.3)	265 (75.9) [a] 333 (95.4)	244 (76.5) [a] 295 (92.5)	50 (31.4) 110 (69.2)
IGA 0 Week 16	0 (0.0)	188 (58.6) [a]	36 (22.1)	1 (1.2)	243 (69.6) [a]	-	-
IGA 0/1 Week 16	4 (4.8)	270 (84.1) [a, b]	87 (53.4)	1 (1.2)	323 (92.6) [a]	272 (85.3) [a]	91 (57.2)
Absolute PASI ≤ 2 Week 16	3 (3.6)	273 (85.0)	84 (51.5)	1 (1.2)	315 (90.3)	280 (87.8)	86 (54.1)
PSD Pain (N) Week 16	(N=54) 9 (16.7)	(N=229) 177 (77.3) [a]	(N=107) 73 (68.2)	(N=67) 6 (9.0)	(N=255) 201 (78.8) [a]	-	-
PSD Itch (N) Week 16	(N=61) 8 (13.1)	(N=244) 187 (76.6) [a]	(N=117) 77 (65.8)	(N=72) 4 (5.6)	(N=278) 210 (75.5) [a]	-	-
PSD Scaling (N) Week 16	(N=63) 8 (12.7)	(N=246) 193 (78.5) [a]	(N=116) 69 (59.5)	(N=70) 4 (5.7)	(N=286) 223 (78.0) [a]	-	-

BKZ 320 mg Q4W= bimekizumab every 4 weeks. Non-Responder Imputation (NRI) is used.

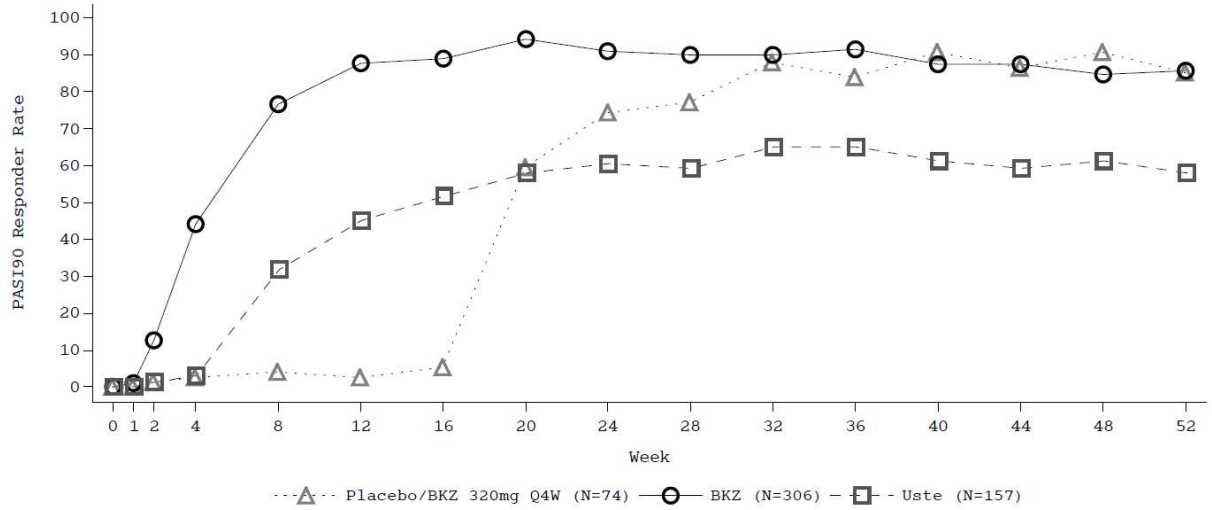
IGA 0/1 response was defined as Clear (0) or Almost Clear (1) with at least a 2-category improvement from Baseline at Week 16. IGA 0 response was defined as Clear (0) with at least a 2-category improvement from Baseline at Week 16. PSD is Patient Symptoms Diary. PSD response is defined as a change from baseline to Week 16 ≥ to a pre-specified threshold (1.98, 2.39, and 2.86 respectively for pain itch and scaling).

a) p<0.001 versus placebo (BE VIVID and BE READY), versus adalimumab (BE SURE), adjusted for multiplicity.

b) p<0.001 versus ustekinumab (BE VIVID), adjusted for multiplicity.

Bimekizumab was associated with a rapid onset of efficacy. In BE VIVID, at week 2 and week 4, PASI 90 response rates were higher for bimekizumab-treated patients (12.1% and 43.6% respectively) compared to placebo (1.2% and 2.4% respectively) and ustekinumab (1.2% and 3.1% respectively).

Figure 1: PASI 90 responder rates over time in BE VIVID

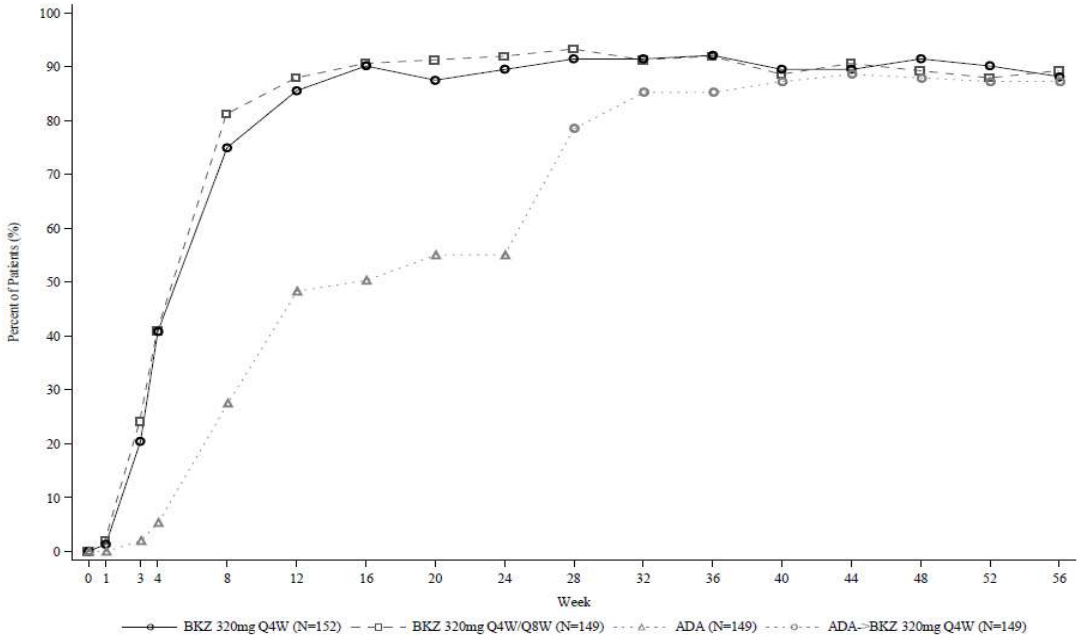


BKZ=bimekizumab; Uste=ustekinumab. NRI is used. Note: Patients in the Placebo/BKZ group switched from Placebo to BKZ in the Maintenance Treatment Period starting at Week 16.

In the BE VIVID study, at Week 52, bimekizumab-treated patients achieved higher response rates than the ustekinumab-treated patients on the endpoints of PASI 90 (81.6% bimekizumab vs 55.8% ustekinumab, p<0.001), IGA 0/1 (77.9% bimekizumab vs 60.7% ustekinumab, p<0.001) and PASI 100 (64.2% bimekizumab vs 38.0% ustekinumab).

In the BE SURE study at Week 24, a higher percentage of patients treated with bimekizumab achieved a PASI 90 and an IGA 0/1 responses as compared with adalimumab (85.6% and 86.5% respectively vs 51.6% and 57.9% respectively, p<0.001). Among the 65 adalimumab non-responders at Week 24 (< PASI 90), 78.5% achieved a PASI 90 response after 16 weeks of treatment with bimekizumab. No new safety findings were observed in patients who switched from adalimumab to bimekizumab. At Week 56, 70.2% of bimekizumab-treated patients achieved a PASI 100 response.

Figure 2: PASI 90 responder rates over time in BE SURE



BKZ 320 mg Q4W = bimekizumab every 4 weeks; BKZ 320 mg Q8W = bimekizumab every 8 weeks; ADA = adalimumab.
Note: Only patients who received bimekizumab at Week 24 or later are included. Patients in the BKZ Q4W/Q8W group switched from Q4W to Q8W dosing at Week 16. Patients in the ADA/BKZ 320 mg Q4W group switched from ADA to BKZ Q4W at Week 24. NRI is used.

The efficacy of bimekizumab was demonstrated regardless of age, gender, race, disease duration, body weight, PASI baseline severity and previous treatment with a biologic. Bimekizumab was efficacious in prior biologic exposed patients, including anti-TNF / anti IL-17 and in systemic treatment-naïve patients. Based on population PK / PD analysis and supported by clinical data, patients with higher body weight (≥120 kg) who did not achieve complete skin clearance at week 16 benefited from continued bimekizumab 320 mg every four weeks (Q4W) after the initial 16 weeks of treatment. In the BE SURE study, patients received bimekizumab 320 mg Q4W through week 16, followed by either Q4W or every eight weeks (Q8W) dosing through week 56, regardless of responder status at week 16. Patients in the ≥120 kg group (N=37) on the Q4W maintenance regimen showed greater improvement in PASI100 between week 16 (23.5%) and week 56 (70.6%) compared to those on the Q8W maintenance regimen (week 16: 45.0% vs week 56: 60.0%).

Maintenance of response

Table 3: Maintenance of responses at Week 52 in responders at Week 16*

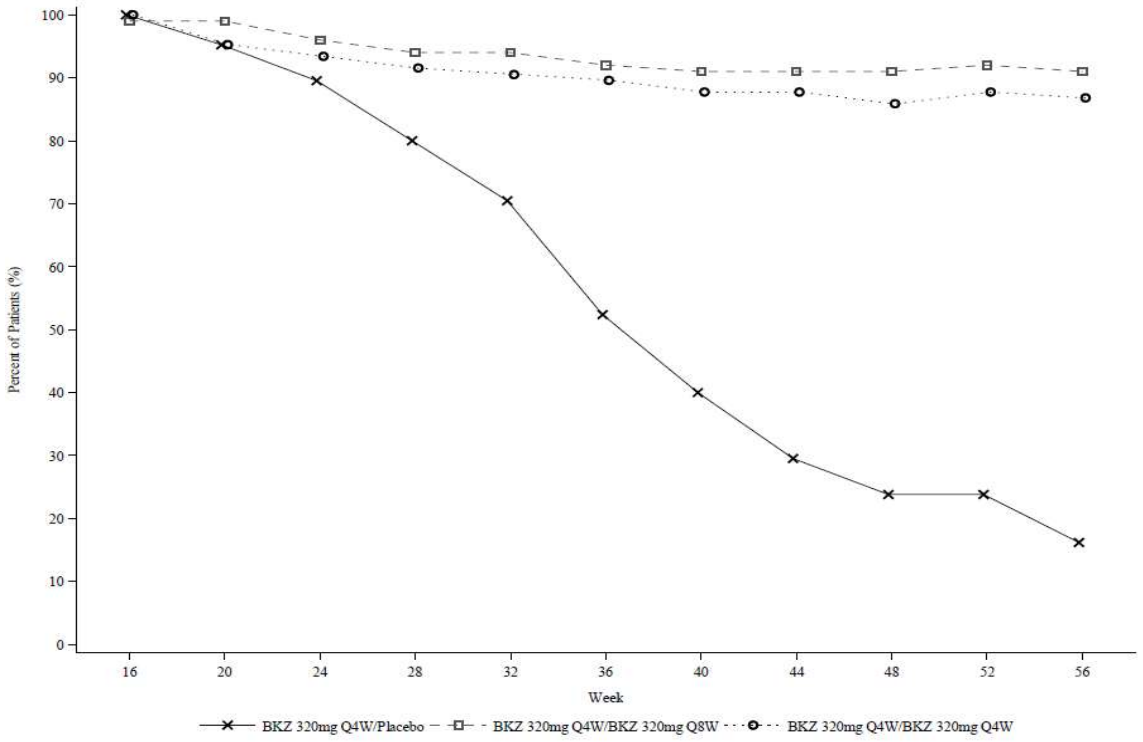
PASI 100		**PASI 90**		**IGA 0/1**		**Absolute PASI ≤ 2**	
BKZ 320mg Q4W/Q4W (N=355) n (%)	**BKZ 320mg Q4W/Q8W (N=182) n (%)**	**BKZ 320mg Q4W/Q4W (N=516) n (%)**	**BKZ 320mg Q4W/Q8W (N=237) n (%)**	**BKZ 320mg Q4W/Q4W (N=511) n (%)**	**BKZ 320mg Q4W/Q8W (N=234) n (%)**	**BKZ 320mg Q4W/Q4W (N=511) n (%)**	**BKZ 320mg Q4W/Q8W (N= 238) n (%)**
295 (83.1)	161 (88.5)	464 (89.9)	214 (90.3)	447 (87.5)	214 (91.5)	460 (90.0)	215 (90.3)

* Integrated analysis of BE VIVID, BE READY and BE SURE. NRI is used.

BKZ 320 mg Q4W/Q4W: bimekizumab 320 mg every 4 weeks followed by bimekizumab 320mg every 4 weeks from Week 16.
BKZ 320 mg Q4W/Q8W: bimekizumab 320 mg every 4 weeks followed by bimekizumab 320mg every 8 weeks from Week 16.

Durability of PASI 90 response (after bimekizumab discontinuation)

Figure 3: PASI 90 responder rates over time – Randomized withdrawal period in BE READY



NRI is used.

In BE READY, for PASI 90 responders at Week 16 who were re-randomized to placebo and withdrawn from bimekizumab, the median time to relapse, defined as loss of PASI 75, was approximately 28 weeks (32 weeks after the last bimekizumab dose). Among these patients, 88.1% regained a PASI 90 response within 12 weeks of restarting treatment with bimekizumab 320 mg every 4 weeks.

Specific body locations

Significant improvements were observed in psoriasis involving the scalp, nails and hands and feet in patients treated with bimekizumab at Week 16 in the studies BE VIVID and BE READY versus placebo (see Table 4).

Table 4: Specific body location responses in BE VIVID and BE READY at Week 16

	BE VIVID			BE READY	
	Placebo	**BKZ 320 mg Q4W**	**Ustekinumab**	**Placebo**	**BKZ 320 mg Q4W**
Scalp IGA (N)[a] Scalp IGA 0/1, n (%)	(72) 11 (15.3)	(285) 240 (84.2) [b]	(146) 103 (70.5)	(74) 5 (6.8)	(310) 286 (92.3) [b]
pp-IGA (N)[a] pp-IGA 0/1, n (%)	(29) 7 (24.1)	(105) 85 (81.0)	(47) 39 (83.0)	(31) 10 (32.3)	(97) 91 (93.8)
mNAPSI 100 (N)[a]	(51)	(194)	(109)	(50)	(210)

	BE VIVID			BE READY	
	Placebo	**BKZ 320 mg Q4W**	**Ustekinumab**	**Placebo**	**BKZ 320 mg Q4W**
mNAPSI 100, n (%)	4 (7.8)	57 (29.4)	15 (13.8)	3 (6.0)	73 (34.8)

NRI is used

a) Includes only patients with a scalp Investigator Global Assessment (IGA) of 2 or greater, a palmoplantar IGA of 2 or greater and a modified Nail Psoriasis and Severity Index (mNAPSI) score > 0 at baseline. Scalp IGA 0/1 and pp-IGA 0/1 responses were defined as Clear (0) or Almost Clear (1) with ≥2 category improvement relative to Baseline.

b) p<0.001 versus placebo, adjusted for multiplicity.

Scalp IGA and palmoplantar IGA responses were maintained through Week 52/56. Nail psoriasis continued to improve beyond Week 16. In BE VIVID, at Week 52, a higher proportion of patients treated with bimekizumab achieved a complete nail clearance (mNAPSI 100) compared to patients treated with ustekinumab (60.3% vs 40.4% respectively). In BE READY, at Week 56, 67.7% and 69.8% of Week 16 PASI 90 responders achieved complete nail clearance with bimekizumab 320 mg every 8 weeks and bimekizumab 320 mg every 4 weeks respectively.

Health-related Quality of Life / Patient reported outcomes

Across all 3 studies, a greater proportion of patients treated with bimekizumab experienced no impact of psoriasis on their quality of life as measured by the Dermatology Life Quality Index (DLQI) compared to placebo and active comparator-treated patients at Week 16.

In BE READY, the percentage of patients with Dermatology Life Quality Index (DLQI) of 0/1 (no impact of psoriasis on health-related quality of life) at Week 16 were 75.6% and 5.8%, in the bimekizumab and placebo groups, respectively.

In BE VIVID, DLQI 0/1 response rates at Week 16 were 67.3%, 42.3% and 12.0%, in the bimekizumab, ustekinumab and placebo groups, respectively. DLQI 0/1 response rates continued to increase beyond week 16 and then were maintained through week 52 (74.8% in patients treated with bimekizumab 320 mg every 4 weeks).

In BE SURE, DLQI 0/1 response rates at Week 16 were 63.0% and 46.5%, in the bimekizumab and adalimumab groups, respectively. At week 56, 78.9% and 74.1% of patients had a DLQI 0/1 with bimekizumab 320 mg every 8 weeks and bimekizumab 320 mg every 4 weeks, respectively.

Phase 3 Open Label Extension study

Patients who completed one of the pivotal phase 3 studies (‘feeder studies’) could enter a 144-week open-label extension study (PS0014) to assess the long-term safety and efficacy of bimekizumab.

344 patients who were treated with bimekizumab 320 mg every 8 weeks (BKZ 320 mg Q8W) or every 4 weeks (BKZ 320 mg Q4W) during the feeder study, and who achieved PASI 90 at the end of the feeder study, received bimekizumab 320 mg Q8W throughout PS0014. Of these, 293 (85.2%) patients

completed 144 weeks of treatment with bimekizumab 320 mg Q8W. 48 patients (14.0%) discontinued the study during the treatment period, of which 21 (6.1%) discontinued due to an adverse event and 4 (1.2%) discontinued due to lack of efficacy.

Among the patients remaining in the study, improvements achieved with bimekizumab for the efficacy endpoints PASI 90 and IGA 0/1 in the feeder studies were maintained through an additional 144 weeks of open-label treatment.

Phase 3b Open Label Extension period

The efficacy and safety of bimekizumab were also evaluated in a 48-week double-blind study compared with secukinumab, an IL-17A inhibitor, (BE RADIANT - PS0015).

At week 48, patients were allowed to enter a 96-week open label extension period (OLE) and started or continued with bimekizumab 320 mg Q4W or 320 mg Q8W depending on their PASI 90 responder status at week 48. Study participants who had initially received bimekizumab 320 mg Q4W as part of the OLE were switched to bimekizumab 320 mg Q8W at week 72 or later.

231 patients who were treated with bimekizumab 320 mg Q8W or bimekizumab 320 mg Q4W and achieved PASI 90 at week 48 received bimekizumab 320 mg Q8W throughout the OLE. Of these patients, 31 (13.4%) discontinued the study during the OLE, of which 10 (4.3%) discontinued due to an adverse event and 1 (0.4%) discontinued due to lack of efficacy.

116 patients who were treated with secukinumab and achieved PASI 90 at week 48 received bimekizumab 320 mg Q8W throughout the OLE. Of these patients, 16 (13.8%) discontinued the study during the OLE, of which 6 (5.2%) discontinued due to an adverse event and 1 (0.9%) discontinued due to lack of efficacy.

Among the patients remaining in the study, improvements achieved with bimekizumab or secukinumab for the efficacy endpoints PASI 100, PASI 90, PASI 75 and PASI ≤2 responder at week 48 were maintained on treatment with bimekizumab 320 mg Q8W through an additional 96 weeks of open label treatment.

The safety profile of bimekizumab up to week 144 was consistent with the safety profile observed up to 48 weeks.

Psoriatic arthritis (PsA)

The safety and efficacy of bimekizumab were evaluated in 1112 adult patients (at least 18 years of age) with active psoriatic arthritis (PsA) in two multicentre, randomized, double-blind, placebo-controlled studies (PA0010 - BE OPTIMAL and PA0011- BE COMPLETE). The BE OPTIMAL study included an active reference treatment arm (adalimumab) (N=140).

For both studies, patients had a diagnosis of active psoriatic arthritis for at least 6 months based on the Classification Criteria for Psoriatic Arthritis (CASPAR) and had active disease with tender joint count (TJC) ≥3 and swollen joint count (SJC) ≥3. Patients had a diagnosis of PsA for a median of 3.6 years in BE OPTIMAL and 6.8 years in BE COMPLETE. Patients with each subtype of PsA were enrolled in these studies, including polyarticular symmetric arthritis, oligoarticular asymmetric arthritis, distal interphalangeal joint predominant, spondylitis predominant and arthritis mutilans. At baseline, 55.9% of patients had ≥ 3% Body Surface Area (BSA) with active plaque psoriasis. 10.4% of patients had moderate to severe plaque psoriasis and 31.9% and 12.3% had enthesitis and dactylitis at baseline, respectively. The primary efficacy endpoint in both studies was the American College of Rheumatology (ACR) 50 response at Week 16.
The key secondary point at week 16 in both studies were as follows: Change from baseline in the Health Assessment Questionnaire - Disability Index (cfB HAQ-DI), reduction of 90% from baseline in the Psoriasis Area and Severity Index (PASI90), change from baseline in the Short Form 36-item Health Survey (SF-36) Physical Component Summary (PCS) score, Minimal Disease Activity (MDA) response, and enthesitis- and dactylitis-free status, which are based on pooled data from both studies. In the BE OPTIMAL study, the change from baseline in the Van der Heijde modified Total Sharp Score (vdHmTSS) was also an important secondary endpoint.

The BE OPTIMAL study evaluated 852 patients not previously exposed to any biologic disease-modifying anti-rheumatic drug (bDMARD) for the treatment of psoriatic arthritis or psoriasis. Patients were randomized (3:2:1) to receive bimekizumab 160 mg every 4 weeks through Week 52 or placebo up to Week 16 followed by bimekizumab 160 mg every 4 weeks through Week 52 or an active reference treatment arm (adalimumab 40mg every 2 weeks) up to Week 52. In this study, 78.3% of patients had received prior treatment with ≥ 1 cDMARDs and 21.7 % of patients had no prior treatment with cDMARDs. At baseline, 58.2% of patients were receiving concomitant methotrexate (MTX), 11.3% were receiving concomitant cDMARDs other than MTX, and 30.5% were receiving no cDMARDs.

The BE COMPLETE study evaluated 400 patients with an inadequate response (lack of efficacy) or intolerance to treatment with 1 or 2 tumour necrosis factor alpha inhibitors (anti-TNFα – IR) for either psoriatic arthritis or psoriasis. Patients were randomized (2:1) to receive bimekizumab 160 mg every 4 weeks or placebo up to Week 16. At baseline, 42.5% of patients were receiving concomitant MTX, 8.0% were receiving concomitant cDMARDs other than MTX, and 49.5% were receiving no cDMARDs. In this study, 76.5% of participants had an inadequate response to 1 TNFα inhibitor, 11.3% had an inadequate response to 2 TNFα inhibitors and 12.3% were intolerant to TNFα inhibitors.

Signs and symptoms

In bDMARDs-naïve patients (BE OPTIMAL) and anti-TNFα IR patients (BE COMPLETE) treatment with bimekizumab resulted in significant improvement in signs and symptoms and measures of disease activity compared to placebo at Week 16, with similar response rates seen in both patient populations (see Table 5). Clinical responses were sustained up to Week 52 in BE OPTIMAL as assessed by ACR 50, MDA, PASI 90.

Table 5: Clinical response in study BE OPTIMAL and BE COMPLETE

	BE OPTIMAL (bDMARD-naïve)				**BE COMPLETE (anti TNFα-IR)**		
	Placebo (N=281) n (%)	**BKZ 160mg Q4W (N=431)** n (%)	**Difference from placebo (95% CI)[(d)]**	**Reference Arm(e) (Adalimumab) (N=140)** n (%)	**Placebo (N=133)** n (%)	**BKZ 160 mg Q4W (N=267)** n (%)	**Difference from placebo (95% CI)[(d)]**
ACR 50							
Week 16	28 (10.0)	189 (43.9)*	33.9 (27.4, 40.4)	64 (45.7)	9 (6.8)	116 (43.4)*	36.7 (27.7, 45.7)
Week 24	-	196 (45.5)		66 (47.1)			
Week 52		235 (54.5)		70 (50.0)			
MDA[(a)]							
Week 16	37 (13.2)	194 (45.0)*	31.8 (25.2, 38.5)	63 (45.0)	8 (6.0)	118 (44.2)*	38.2 (29.2, 47.2)
Week 24	-	209 (48.5)		67 (47.9)			
Week 52		237 (55.0)		74 (52.9)			
Patients with ≥3% BSA	**(N=140)**	**(N=217)**		**(N=68)**	**(N=88)**	**(N=176)**	
PASI 90							
Week 16	4 (2.9)	133 (61.3)*	58.4 (49.9, 66.9)	28 (41.2)	6 (6.8)	121 (68.8)*	61.9 (51.5, 72.4)
Week 24	-	158 (72.8)		32 (47.1)			
Week 52		155 (71.4)		41 (60.3)			
Patients with LDI>0 [(b)]	**(N=47)**	**(N=90)**					
Dactylitis free state [(b)]							
Week 16	24 (51.1)	68 (75.6)***	24.5 (8.4, 40.6)				
Patients with LEI>0 [(c)]	**(N=106)**	**(N=249)**					
Enthesitis free state [(c)]							
Week 16	37 (34.9)	124 (49.8)**	14.9 (3.7, 26.1)				

BKZ 160 mg Q4W= bimekizumab 160 mg every 4 weeks. CI= confidence interval. NC=Not calculable

[a] A patient was classified as achieving Minimal Disease Activity (MDA) when meeting 5 of the 7 following criteria: tender joint count ⩽1; swollen joint count ⩽1; Psoriasis Activity and Severity Index ⩽1 or body surface area ⩽3; patient pain visual analogue scale (VAS) ⩽15; patient global disease activity VAS ⩽20; Health Assessment Questionnaire Disability Index ⩽0.5; tender entheseal points ⩽1

[b] Based on pooled data from BE OPTIMAL and BE COMPLETE studies for patients with baseline Leeds Dactylitis Index (LDI) >0. Dactylitis free state is LDI=0

[c] Based on pooled data from BE OPTIMAL and BE COMPLETE studies for patients with baseline Leeds Enthesitis Index (LEI) >0. Enthesitis free state is LEI =0[d] Unadjusted differences are shown

[e] No statistical comparison to bimekizumab or placebo performed

* p<0.001 versus placebo adjusted for multiplicity. ** p=0.008 versus placebo adjusted for multiplicity. *** p=0.002 versus placebo adjusted for multiplicity. NRI is used. Other endpoints at Week 16 and all endpoints at Week 24 and Week 52 were not part of the sequential testing hierarchy and any comparisons are nominal.

In BE OPTIMAL, the results for patients pretreated with cDMARD were similar (ACR50 week 16: bimekizumab 160mg Q4W: 43.5%, placebo: 9.5%).

Improvements from baseline were shown in all individual ACR components with bimekizumab at Week 16 and were sustained up to Week 52 in BE OPTIMAL.

Treatment responses on bimekizumab were significantly greater than those on placebo as early as Week 4 for ACR 50 (BE OPTIMAL, 17.6% versus 3.2 %, nominal p<0.001) and BE COMPLETE, 16.1% versus 1.5%, nominal p<0.001).

For the bimekizumab-treated patients who achieved an ACR 50 response at Week 16 in BE OPTIMAL, 87.2% maintained this response at Week 52.

The efficacy and safety of bimekizumab were demonstrated regardless of age, gender, race, baseline body weight, baseline psoriasis involvement, baseline CRP, disease duration and prior cDMARDs use. In both studies, similar responses were observed with bimekizumab regardless of whether patients were on concomitant cDMARDs, including MTX, or not.

Radiographic response

In BE OPTIMAL, inhibition of progression of structural damage was assessed radiographically and expressed as the change from baseline in the Van der Heijde modified total Sharp Score (vdHmTSS) and its components, the Erosion Score (ES) and the Joint Space Narrowing score (JSN) at Week 16 (see Table 6).

Table 6: Change in vdHmTSS in BE OPTIMAL at Week 16

	Placebo	BKZ 160mg Q4W	Difference from placebo (95% CI)[a)]
Population with elevated hs-CRP and/or at least 1 bone erosion at baseline	**(N=227)**	**(N=361)**	

	Placebo	BKZ 160mg Q4W	Difference from placebo (95% CI)[a)]
Mean change from baseline (SE)	0.36 (0.10)	0.04 (0.05)*	-0.32 (-0.35, -0.30)
Overall population	**(N=269)**	**(N=420)**	
Mean change from baseline (SE)	0.32 (0.09)	0.04 (0.04)*	-0.26 (-0.29, -0.23)

*p =0.001 versus placebo. p-values are based on reference-based imputation using difference in LS Mean using an ANCOVA model with treatment, bone erosion at Baseline and region as fixed effects and Baseline score as a covariate. Week 16 summary data is based on the first set of reads for the primary analysis.
[a)]Unadjusted differences are shown

Bimekizumab significantly inhibited the progression of joint damage at Week 16 in both the population with elevated hs-CRP and/or at least 1 bone erosion at baseline and the overall population compared to placebo. While reference-based imputation was specified as the missing data handling method in the statistical testing procedure comparing bimekizumab versus placebo, changes from baseline were also calculated using standard multiple imputation in both the population with elevated hs-CRP and/or at least 1 bone erosion at baseline and the overall population at Week 16 in the bimekizumab arm (mean change from baseline 0.01 and 0.01 respectively) and the adalimumab arm (mean change from baseline -0.05 and -0.03 respectively). Inhibition of the progression of joint damage was sustained in both the population with elevated hs-CRP and/or at least 1 bone erosion at baseline and the overall population to Week 52 in both the bimekizumab arm (mean change from baseline 0.10 and 0.10 respectively) and the adalimumab arm (mean change from baseline -0.17 and -0.12 respectively).
The observed percentage of patients with no radiographic joint damage progression (defined as a change from baseline in mTSS of ≤0.5) from randomization to Week 52 was 87.9% (N=276/314) for bimekizumab and 84.8% (N=168/198) for placebo study participants switching to bimekizumab and 94.1% (N=96/102) for adalimumab in the population with elevated hs-CRP and/or at least 1 bone erosion. Similar rates were observed in the overall population (89.3% (N=326/365) for bimekizumab and 87.3% (N=207/237) for placebo study participants switching to bimekizumab and 94.1% (N=111/118) for adalimumab).

Physical function and other health-related outcomes
Both bDMARD-naïve (BE OPTIMAL) and anti-TNFα-IR (BE COMPLETE) patients receiving bimekizumab showed significant improvement from baseline in physical function compared to placebo patients at Week 16 (p<0.001) as assessed by the HAQ-DI (LS Mean change from baseline: - 0.3 versus - 0.1 in BE OPTIMAL and - 0.3 versus 0 in BE COMPLETE, respectively). In both studies, a greater proportion of patients achieved a clinically meaningful reduction of at least 0.35 in HAQ-DI score from baseline in the bimekizumab group compared with placebo at Week 16.

Bimekizumab-treated patients reported significant improvement from baseline in the Short Form-36 item Health Survey Physical Component Summary (SF-36 PCS) score at Week 16 compared to

placebo (LS Mean change from baseline: 6.3 versus 1.9, p<0.001 in BE OPTIMAL and 6.2 versus 0.1, p<0.001 in BE COMPLETE).

In both studies, bimekizumab-treated patients reported meaningful reduction from baseline in fatigue as measured by the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score at Week 16 compared to placebo. Meaningful improvement from baseline was also observed in the Psoriatic Arthritis Impact of Disease-12 (PsAID-12) score in the bimekizumab-treated group compared to the placebo group at Week 16.
Patients with axial involvement at baseline, approximately 74% of patients, (defined as a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score ≥4) showed greater improvement from baseline in BASDAI compared with placebo at Week 16.
Improvements achieved at Week 16 in all measures of physical function and other health-related outcomes mentioned above (HAQ-DI, SF-36 PCS, FACIT-Fatigue, PsAID-12 scores and BASDAI) were sustained up to Week 52 in BE OPTIMAL.

In BE OPTIMAL, at Week 52, 65.5% of patients treated with bimekizumab achieved complete nail clearance (mNAPSI resolution in patients with mNAPSI higher than 0 at Baseline).

Axial spondyloarthritis (nr-axSpA and AS)
The efficacy and safety of bimekizumab was evaluated in 586 adult patients (at least 18 years of age) with active axial spondyloarthritis (axSpA) in two multicenter, randomized, double-blind, placebo-controlled studies, one in non-radiographic axial spondyloarthritis (nr-axSpA) and one in ankylosing spondylitis (AS), also known as radiographic axSpA. The primary endpoint in both studies was the percentage of patients achieving an Assessment of SpondyloArthritis International Society (ASAS) 40 response at Week 16. Consistent results were seen across both patient populations.

The BE MOBILE 1 study (AS0010) evaluated 254 patients with active nr-axSpA. Patients had axSpA (age of symptoms onset < 45 years) meeting the ASAS classification criteria and had active disease as defined by a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4 and spinal pain ≥4 on a 0 to 10 numeric rating scale (NRS) (from BASDAI Item 2) and no evidence of radiographic changes in the sacroiliac joints that would meet the modified New York criteria for AS. Patients also had objective signs of inflammation as indicated by elevated C-reactive protein (CRP) level and/or evidence of sacroiliitis on Magnetic Resonance Imaging (MRI) as well as a history of inadequate response to 2 different non-steroidal anti-inflammatory drugs (NSAIDs) or intolerance or contraindication to NSAIDs. Patients were randomized (1:1) to receive bimekizumab 160 mg every 4 weeks up to Week 52 or placebo up to Week 16 followed by bimekizumab 160 mg every 4 weeks up to Week 52. At baseline, patients had symptoms of nr-axSpA for a mean of 9 years (median of 5.5 years). 10.6% of patients were previously treated with an anti-TNFα agent.

The BE MOBILE 2 study (AS0011) evaluated 332 patients with active AS determined by documented radiologic evidence (x-ray) fulfilling the Modified New York criteria for AS. Patients had active disease as defined by a BASDAI ≥4 and spinal pain ≥4 on a 0 to 10 numeric rating scale (NRS) (from BASDAI Item 2). Patients had to have a history of inadequate response to 2 different NSAIDs or intolerance or contraindication to NSAIDs. Patients were randomized (2:1) to receive bimekizumab 160 mg every 4 weeks up to Week 52 or placebo up to Week 16 followed by bimekizumab 160 mg every 4 weeks up to Week 52. At baseline, patients had symptoms of AS for a mean of 13.5 years (median of 11 years). 16.3% of patients were previously treated with an anti-TNFα agent.

Clinical response

Treatment with bimekizumab resulted in significant improvement in signs and symptoms and measures of disease activity compared to placebo at Week 16 in both nr-axSpA and AS patient populations (see Table 7). Clinical responses were sustained up to Week 52 in both patient populations as assessed by all the endpoints presented in Table 7.

Table 7: Clinical responses in BE MOBILE 1 and BE MOBILE 2

	BE MOBILE 1 (nr-axSpA)			**BE MOBILE 2 (AS)**		
	Placebo (N=126) n (%)	**BKZ 160 mg Q4W (N=128) n (%)**	**Difference from placebo (95% CI) [a)]**	**Placebo (N=111) n (%)**	**BKZ 160 mg Q4W (N=221) n (%)**	**Difference from placebo (95% CI) [a)]**
ASAS 40						
Week 16	27 (21.4)	61 (47.7)*	26.2 (14.9, 37.5)	25 (22.5)	99 (44.8)*	22.3 (11.5, 33.0)
Week 52		78 (60.9)			129 (58.4)	
ASAS 40 in anti-TNFα naives	(N=109)	(N= 118)		(N=94)	(N=184)	
Week 16	25 (22.9)	55 (46.6)	24.8 (12.4, 37.1)	22 (23.4)	84 (45.7)*	22.3 (10.5, 34.0)
Week 52		73 (61.9)			108 (58.7)	
ASAS 20						
Week 16	48 (38.1)	88 (68.8)*	30.7 (19.0, 42.3)	48 (43.2)	146 (66.1)*	22.8 (11.8, 33.8)
Week 52		94 (73.4)			158 (71.5)	
ASDAS-major improvement						
Week 16	9 (7.1)	35 (27.3)*	20.2 (11.2, 29.3)	6 (5.4)	57 (25.8)*	20.4 (11.7, 29.1)
Week 52		47 (36.7)			71 (32.1)	
BASDAI-50						
Week 16	27(21.4)	60 (46.9)	25.3 (14.0, 36.6)	29 (26.1)	103 (46.6)	20.5 (9.6, 31.4)
Week 52		69 (53.9)			119 (53.8)	

BKZ 160 mg Q4W = bimekizumab 160 mg every 4 weeks. ASDAS = Ankylosing Spondylitis Disease Activity Score.

NRI is used.

a) Unadjusted differences are shown.

*p<0.001 versus placebo, adjusted for multiplicity.

The proportion of patients in BE MOBILE 1 reaching ASDAS <2.1 (combining ASDAS-inactive disease (ID) and ASDAS-low disease (LD)) at Week 16 was 46.1% in the bimekizumab group versus 21.1% in the placebo group (multiple imputation). At Week 52, 61.6% of patients in the bimekizumab group achieved an ASDAS <2.1, including 25.2% in inactive disease state (ASDAS <1.3).

The proportion of patients in BE MOBILE 2 reaching ASDAS <2.1 (combining ASDAS-ID and ASDAS-LD) at Week 16 was 44.8% in the bimekizumab group versus 17.4% in placebo group (multiple imputation). At Week 52, 57.1% of patients in the bimekizumab group achieved an ASDAS <2.1, including 23.4 % in inactive disease state (ASDAS <1.3).

All four ASAS 40 components (total spinal pain, morning stiffness, Bath Ankylosing Spondylitis Functional Index [BASFI] and Patient's Global Assessment of Disease Activity [PGADA]) were improved with bimekizumab treatment and contributed to the overall ASAS 40 response at week 16, and these improvements were sustained up to Week 52 in both patient populations.
Improvements in other measures of efficacy are shown in Table 8.

Table 8: Other measures of efficacy in BE MOBILE 1 and BE MOBILE 2

	BE MOBILE 1 (nr-axSpA)		**BE MOBILE 2 (AS)**	
	Placebo (N= 126)	**BKZ 160 mg Q4W (N= 128)**	**Placebo (N= 111)**	**BKZ 160 mg Q4W (N=221)**
Nocturnal spinal pain				
Baseline	6.7	6.9	6.8	6.6
Mean change from baseline at Week 16	-1.7	-3.6*	-1.9	-3.3*
Mean change from baseline at Week 52		-4.3		-4.1
BASDAI				
Baseline	6.7	6.9	6.5	6.5
Mean change from baseline at Week 16	-1.5	-3.1*	-1.9	-2.9*
Mean change from baseline at Week 52		-3.9		-3.6

	BE MOBILE 1 (nr-axSpA)		BE MOBILE 2 (AS)	
	Placebo (N= 126)	**BKZ 160 mg Q4W (N= 128)**	**Placebo (N= 111)**	**BKZ 160 mg Q4W (N=221)**
BASMI				
Baseline	3.0	2.9	3.8	3.9
Mean change from baseline at Week 16	-0.1	-0.4	-0.2	-0.5**
Mean change from baseline at Week 52		-0.6		-0.7
hs-CRP (mg/L)				
Baseline (Geometric Mean)	5.0	4.6	6.7	6.5
Ratio to baseline at Week 16	0.8	0.4	0.9	0.4
Ratio to baseline at Week 52		0.4		0.3

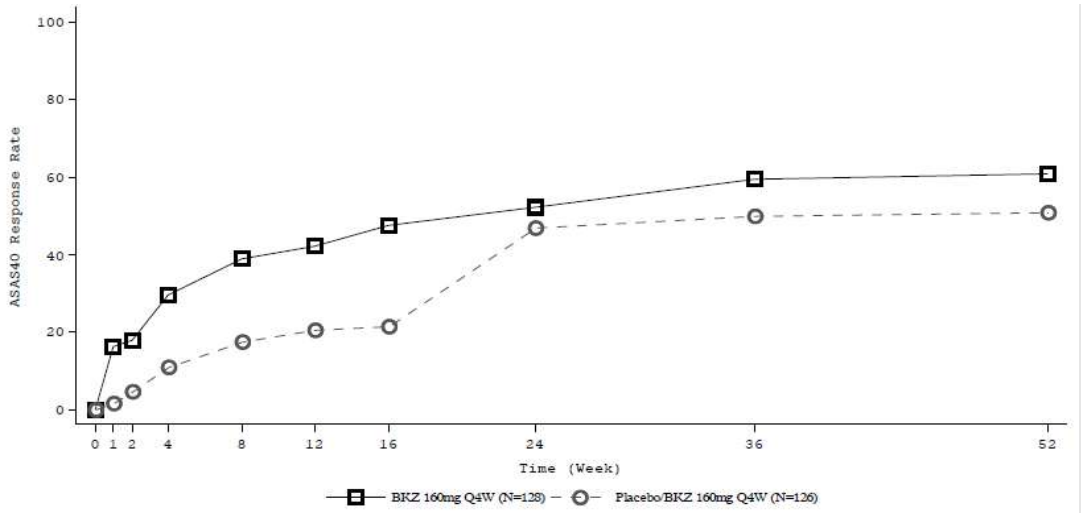
BASMI = Bath Ankylosing Spondylitis Metrology Index. Hs-CRP = high sensitivity C-reactive protein

MI is used.

*p<0.001 reference-based imputation, versus placebo, adjusted for multiplicity. **p<0.01 reference-based imputation, versus placebo, adjusted for multiplicity.

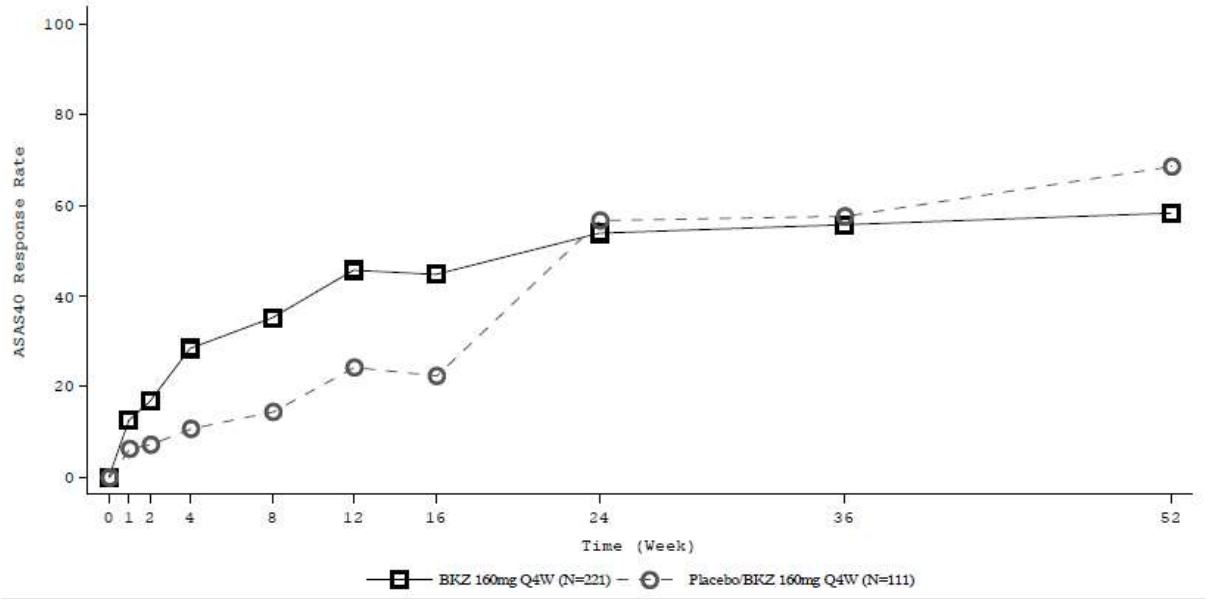
Bimekizumab was associated with a rapid onset of efficacy in both nr-axSpA and AS patient population.

Figure 4: ASAS 40 response over time up to Week 52 in BE MOBILE 1 (NRI)



Patients on placebo switched to bimekizumab 160 mg Q4W at Week 16

Figure 5: ASAS 40 response over time up to Week 52 in BE MOBILE 2 (NRI)



Patients on placebo switched to Bimekizumab 160 mg Q4W at Week 16

In an integrated analysis of BE MOBILE 1 and BE MOBILE 2, of bimekizumab-treated patients who achieved an ASAS 40 response at Week 16, 82.1% maintained this response at Week 52.

The efficacy of bimekizumab was demonstrated regardless of age, gender, race, disease duration, baseline inflammation status, baseline ASDAS and concomitant cDMARDs.

At Week 16, among patients with enthesitis at baseline, the proportion of patients (NRI) with enthesitis resolution as assessed by the Maastricht Ankylosing Spondylitis Enthesitis (MASES) index was greater with bimekizumab compared to placebo (BE MOBILE 1: 51.1% versus 23.9% and BE MOBILE 2: 51.5% versus 32.8%). The resolution of enthesitis with bimekizumab was sustained up to Week 52 in both studies (BE MOBILE 1: 54.3% and BE MOBILE 2: 50.8%).

Reduction of inflammation

Bimekizumab reduced inflammation as measured by hs-CRP (see Table 9) and as assessed by MRI in an imaging sub-study. Signs of inflammation were assessed by MRI at baseline and Week 16 and expressed as change from baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) score for sacroiliac joints and Ankylosing Spondylitis spine Magnetic Resonance Imagine-activity (ASspiMRI-a score in the Berlin modification) for the spine. Reduction of inflammatory signs in both sacroiliac joints and the spine was observed in patients treated with bimekizumab as compared with placebo (see Table 9). Reduction of inflammation as measured by hs-CRP and as assessed by MRI was sustained to Week 52.

Table 9: Reduction of inflammation as assessed by MRI in BE MOBILE 1 and BE MOBILE 2

	BE MOBILE 1 (nr-axSpA)	**BE MOBILE 2 (AS)**

	Placebo	**BKZ 160 mg Q4W**	**Placebo**	**BKZ 160 mg Q4W**
SPARCC score				
Mean change from baseline [a)] at week 16	-1.56 (N=62)	-6.15 (N=78)	0.59 (N=46)	-4.51 (N=81)
Mean change from baseline [a)] at week 52		-7.57 (N=67)		-4.67 (N=78)
ASspiMRI-a (Berlin modifications) score Mean change from baseline [a)] at week 16	0.03 (N=60)	-0.36 (N=74)	-0.34 (N=46)	-2.23 (N=81)
Mean change from baseline [a)] at week 52		-0.70 (N=65)		-2.38 (N=77)

Change from baseline values are based on observed cases as assessed by central read of Week 52 dataset.

Physical function and other health-related outcomes

Patients treated with bimekizumab showed significant improvement from baseline in physical function as assessed by the BASFI compared to placebo (LS Mean change from baseline at Week 16 in BE MOBILE 1: -2.4 versus -0.9, p<0.001 and in BE MOBILE 2: -2.0 versus -1.0, p<0.001). Patients treated with bimekizumab reported significant improvement from baseline compared to placebo-treated patients in SF-36 PCS score (LS Mean change from baseline at Week 16 in BE MOBILE 1: 9.3 versus 5.4, p<0.001 and in BE MOBILE 2: 8.5 versus 5.2, p<0.001).

Patients treated with bimekizumab reported significant improvement from baseline in health-related quality of life as measured by the AS Quality of Life Questionnaire (ASQoL) compared to placebo (LS Mean change from baseline at Week 16 in BE MOBILE 1: -4.9 versus -2.3, p<0.001 and in BE MOBILE 2: -4.6 versus -3.0, p<0.001) as well as meaningful reduction in fatigue as assessed by the FACIT-Fatigue score (Mean change from baseline at Week 16 in BE MOBILE 1: 8.5 for bimekizumab versus 3.9 for placebo and in BE MOBILE 2: 8.4 for bimekizumab versus 5.0 for placebo).

Improvements achieved at Week 16 in all measures of physical function and other health-related outcomes mentioned above (BASFI, SF-36 PCS, ASQoL and FACIT-Fatigue scores) were sustained up to Week 52 in both studies.

Extra-articular manifestation

In pooled data from BE MOBILE 1 (nr-axSpA) and BE MOBILE 2 (AS), at Week 16, the proportion of patients developing a uveitis event was lower with bimekizumab (0.6%) compared to placebo (4.6%). The incidence of uveitis remained low with long-term treatment with bimekizumab (1.2/100 patient-years in the pooled phase 2/3 studies).

Hidradenitis suppurativa

The safety and efficacy of bimekizumab was evaluated in 1014 adult patients (at least 18 years of age) with moderate to severe Hidradenitis Suppurativa (HS) in two Phase 3 multicenter, randomized, double-blind, placebo-controlled studies (HS0003 – BE HEARD I and HS0004 – BE HEARD II). Patients had a diagnosis of HS for at least 6 months with Hurley Stage II or Hurley Stage III disease, and with ≥5 inflammatory lesions (i.e. number of abscesses plus number of inflammatory nodules) and had a history of inadequate response to a course of systemic antibiotics for the treatment of HS.

In both studies patients were randomized (2:2:2:1) to receive bimekizumab 320 mg every 2 weeks for 48 weeks (320 mg Q2W/Q2W) or bimekizumab 320 mg every 4 weeks for 48 weeks (320 mg Q4W/Q4W) or bimekizumab 320 mg every 2 weeks to Week 16 followed by 320 mg every 4 weeks up to Week 48 (320 mg Q2W/Q4W) or placebo to Week 16 followed by bimekizumab 320 mg every 2 weeks up to Week 48. Concomitant oral antibiotic use was allowed if the patient was on a stable dose regimen of doxycycline, minocycline, or an equivalent systemic tetracycline for 28 days prior to baseline.

The primary efficacy endpoint in both studies was the Hidradenitis Suppurativa Clinical Response 50 (HiSCR50) at Week 16, i.e. at least a 50% reduction in the total abscess and inflammatory nodule count with no increase in abscess or draining tunnel count relative to baseline. Secondary endpoints included the proportion of subjects who achieved HiSCR75.

Baseline characteristics were comparable across both studies and reflective of a population with moderate to severe HS. Patients had a median disease duration of 5.3 years (mean 8.0 years). The proportions of Hurley Stage II and Stage III patients were 55.7% (50.3% in HS0003 and 61.1% in HS0004) and 44.3% (49.7% in HS0003 and 38.9% in HS0004) respectively, and 8.5% were receiving concomitant antibiotic therapy for HS. The mean baseline Dermatology Life Quality (DLQI) total score was 11.4.

56.8% of patients were female and the mean age of all patients was 36.6 years. 79.7% of patients were White, and 10.8% were Black or African American. 45.6% of patients were current smokers.

Clinical response

Treatment with bimekizumab resulted in clinically relevant improvement in disease activity compared to placebo at Week 16. Key efficacy results are shown in Table 10.The results in Table 10 reflect the predefined primary analysis in which any systemic antibiotic use prior to Week 16 resulted in imputation of nonresponse.

Table 10: Response in BE HEARD I and BE HEARD II at Week 16 - primary analysis[a]

	BE HEARD I		BE HEARD II	
	Placebo (N=72)	**BKZ 320 mg Q2W (N=289)**	**Placebo (N=74)**	**BKZ 320 mg Q2W (N=291)**
$HiSCR_{50}$, % (95% CI)	28.7 (18.1, 39.3)	47.8* (41.8, 53.7)	32.2 (21.4, 42.9)	52.0* (46.1, 57.8)
$HiSCR_{75}$, % (95% CI)	18.4 (9.3, 27.5)	33.4* (27.8, 39.1)	15.6 (7.2, 24.0)	35.7* (30.1, 41.3)

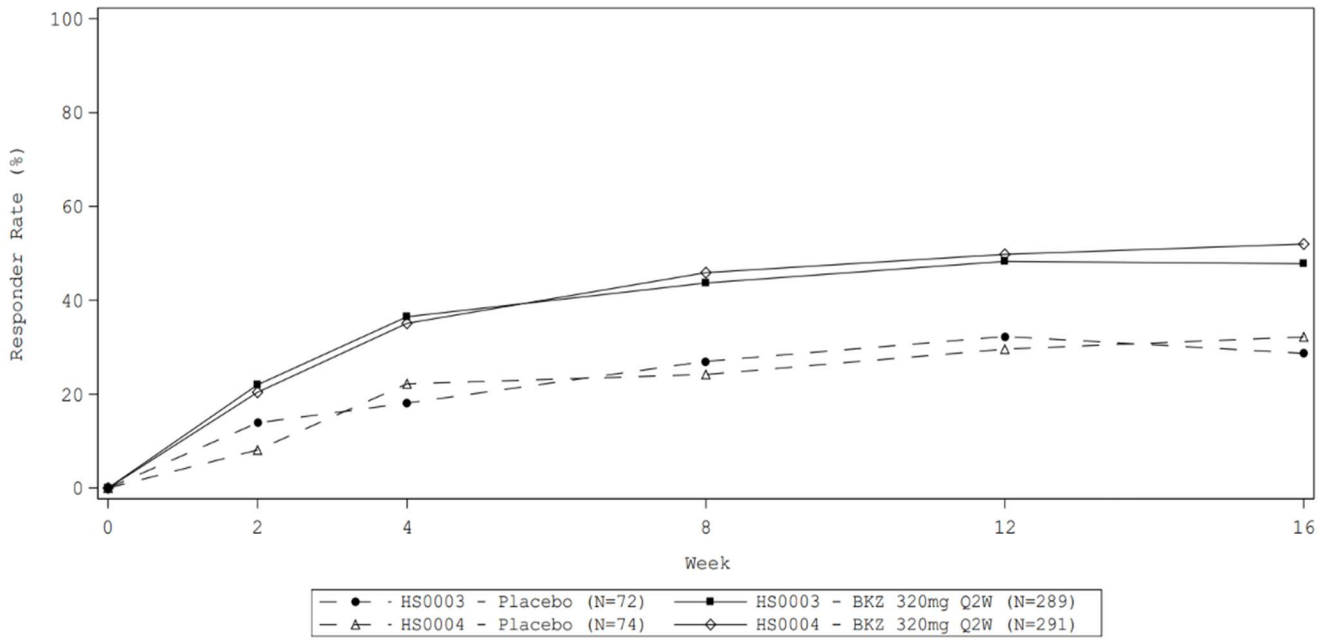
[a)] Patients who initiated systemic antibiotics (new antibiotic or change in the dose/type of current antibiotic) for any reason through Week 16 or who discontinued due to adverse event or lack of efficacy were treated as non-responders at all subsequent visits. Other missing data were imputed via multiple imputation.
.*p<0.025 versus placebo, adjusted for multiplicity by hierarchical testing.

Across both studies, patients treated with bimekizumab experienced numerically greater reduction in worst skin pain (lesion pain) as measured on a 0 to 10 NRS compared to placebo at Week 16.

In both studies, the effect of bimekizumab started as early as Week 2, and efficacy increased until Week 16.

Figure 1 presents the proportion of patients achieving HiSCR50 response by Week 16 in BE HEARD I and BE HEARD II.

Figure 1: Proportion of patients achieving HiSCR50 Response by Week 16 in BE HEARD I and BE HEARD II



BKZ=bimekizumab; HiSCR=Hidradenitis Suppurativa Clinical Response; HS=hidradenitis suppurativa; Q2W=every two weeks
Patients who initiated systemic antibiotics (new antibiotic or change in the dose/type of current antibiotic) for any reason through Week 16 or who discontinued due to adverse event or lack of efficacy were treated as non-responders at all subsequent visits. Other missing data were imputed via multiple imputation.

The efficacy of bimekizumab was demonstrated regardless of age, gender, race, disease duration, weight, prior biologics therapy, systemic antibiotic use, Hurley stage and smoking status at Week 16.

Clinical responses (HiSCR50 response) were sustained in patients on the 320 mg Q2W/Q4W dosing scheme through Week 48 in both studies with a response of 61.4% in BE HEARD I and 63.8% in BE HEARD II.

Health-related quality of life

Across both studies, patients treated with bimekizumab experienced numerically greater improvement in their health-related quality of life as measured by DLQI compared to placebo at Week 16.

Pharmacokinetics

The pharmacokinetic (PK) properties of bimekizumab were similar in patients with plaque psoriasis, psoriatic arthritis and axial spondyloarthritis (nr-axSpA and AS).
Based on population PK analyses and using a reference bodyweight of 90 kg, the bimekizumab apparent clearance and volume of distribution, respectively, in patients with hidradenitis suppurativa were estimated to be approximately 31 and 18 % higher than for the aforementioned indications, with an estimated half-life in HS of 20 days. Consequently, the median steady state trough concentration

at a dose of 320 mg every 4 weeks was approximately 40 % lower in HS compared to other indications.

Absorption

Based on population pharmacokinetic analysis, following a single subcutaneous dose of 320 mg in plaque psoriasis patients, bimekizumab reached a median (2.5^{th} and 97.5^{th} percentile) peak plasma concentration of 25 (12-50) µg/ml, between 3 and 4 days post dose.
Population pharmacokinetic analysis showed that bimekizumab was absorbed with an average absolute bioavailability of 70.1% in healthy volunteers.

Distribution

Based on population pharmacokinetic analyses, the median (coefficient of variation %) volume of distribution (V/F) at steady state was 11.2 (30.5%) L in plaque psoriasis patients.

Metabolism

Bimekizumab is a monoclonal antibody and is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous immunoglobulins.

Elimination

Based on population pharmacokinetic analyses, the median (coefficient of variation %) apparent clearance (CL/F) of bimekizumab was 0.337 L/day (32.7%) and the mean terminal elimination half-life of bimekizumab was 23 days in clinical studies in patients with plaque psoriasis.

Based on simulated data, the median (2.5^{th} and 97.5^{th} percentile) peak and trough concentration at steady-state following subcutaneous administration of 320 mg every 4 weeks are 43 (20-91) µg/ml and 20 (7-50) µg/ml respectively and steady-state is reached after approximately 16 weeks with every 4 weeks dosing regimen. Compared with exposure after a single dose, the population pharmacokinetic analysis showed that patients exhibited a 1.74-fold increase in peak plasma concentrations and area under the curve (AUC) following repeated four weekly dosing.
After switching from the 320 mg every 4 weeks dosing regimen to 320 mg every 8 weeks dosing regimen at Week 16, steady-state is achieved approximately 16 weeks after the switch. Median (2.5^{th} and 97.5^{th} percentile) peak and trough plasma concentrations are 30 (14-60) µg/ml and 5 (1-16) µg/ml respectively.

Linearity/non-linearity

Bimekizumab exhibited dose-proportional pharmacokinetics in patients with plaque psoriasis over a dose range from 64 mg to 480 mg following multiple subcutaneous administrations, with apparent clearance being independent of dose.

Pharmacokinetic (PK) / Pharmacodynamic (PD) relationship

A population pharmacokinetic/pharmacodynamic model was developed using all available data in moderate to severe plaque psoriasis patients. The analysis showed that higher bimekizumab concentrations are related to better Psoriasis Area and Severity Index (PASI) and Investigators Global Assessment (IGA) response and a dose of 320 mg at Week 0, 4, 8, 12, 16 and every 8 weeks thereafter provides maximum benefit to the majority of moderate to severe plaque psoriasis patients (see Kinetics in specific patient groups and *Body Weight*).

Kinetics in specific patient groups

Hepatic and renal impairment

No specific studies have been conducted to determine the effect of renal or hepatic impairment on the pharmacokinetics of bimekizumab. The renal elimination of intact bimekizumab, an IgG monoclonal antibody, is expected to be low and of minor importance. Similarly, IgGs are mainly eliminated via intracellular catabolism and hepatic impairment is not expected to influence clearance of bimekizumab. Based on population pharmacokinetic analyses, hepatic function markers (ALT/ bilirubin) did not have any impact on bimekizumab clearance in patients with plaque psoriasis.

Elderly patients

Based on population pharmacokinetic analysis with a limited number of elderly patients (n = 355 for age ≥ 65 years and n = 47 for age ≥ 75 years), apparent clearance (CL/F) in elderly patients and patients less than 65 years of age was similar. No dose adjustment is required.

Body weight

Population pharmacokinetic modelling indicated that exposure decreased as body weight increased. The average plasma concentration in adult patients weighing ≥120 kg following a 320 mg subcutaneous injection was predicted to be at least 30% lower than in adult patients weighing 90 kg. Dose adjustment may be appropriate in some patients (see “*Dosage/Administration*”).

Race / Gender

No clinically meaningful differences in bimekizumab exposure were observed in Japanese or Chinese subjects compared to Caucasian subjects in a clinical pharmacokinetic study. No dose adjustment is required. A population pharmacokinetic analysis indicated females may have 10% faster apparent clearance (CL/F) compared to males and it is not clinically meaningful. No dose adjustment is required.

Preclinical data

Non-clinical data revealed no special hazards for humans based on tissue cross-reactivity testing, repeat-dose toxicity studies (including safety pharmacology endpoints and assessment of fertility-related endpoints) and evaluation of pre- and postnatal development.

Genotoxicity / Carcinogenicity

No mutagenicity or carcinogenicity studies were conducted with bimekizumab. However monoclonal antibodies are not expected to damage DNA or chromosomes. In a 26-week chronic toxicology study in cynomolgus monkeys there were no pre-neoplastic or neoplastic lesions observed at a dose resulting in 109 times the human exposure at 320 mg every 4 weeks.

Reproductive toxicity

In an enhanced peri- and postnatal development study in the cynomolgus monkey, bimekizumab showed no effects on gestation, parturition, infant survival, fetal and postnatal development when administered throughout organogenesis until parturition at a dose resulting in 27 times the human exposure at 320 mg every 4 weeks based on AUC. At birth, serum bimekizumab concentrations in infant monkeys were comparable to those of mothers.

Other information

Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

Shelf life

Do not use this medicine after the expiry date ("EXP") stated on the pack.

Special precautions for storage

Store in the refrigerator (2-8°C).

Do not freeze.
Keep the pre-filled pen in the outer carton in order to protect from light.
Keep the pre-filled syringe in the outer carton in order to protect from light.
The Bimzelx pre-filled pen and pre-filled syringe may be stored at room temperature (up to 25°C) for a single period of maximum 25 days with protection from light. Once removed from the refrigerator and stored at room temperature, discard after 25 days or by the expiry date printed on the container, whichever occurs first. A field for the date is provided on the carton to record the date removed from the refrigerator.
Keep out of the reach of children.

Authorisation number

68548, 68612 (Swissmedic)

Packs

Bimzelx 160 mg solution for injection in pre-filled pen.

1 pre-filled pen (B).

2 pre-filled pens (B).

Bimzelx 320 mg solution for injection in pre-filled pen.

1 pre-filled pen (B).

Bimzelx 160 mg solution for injection in pre-filled syringe.

1 pre-filled syringe (B).

2 pre-filled syringes (B).

Bimzelx 320 mg solution for injection in pre-filled syringe.

1 pre-filled syringe (B).

Marketing authorisation holder

UCB-Pharma AG, Bulle

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December 2025