BIMZELX®
(bimekizumab)

Formulary application support

Purpose of this document

This document is to support healthcare professionals within the NHS in the completion of a formulary application for bimekizumab for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy. (UCB Pharma Limited BIMZELX SmPC)

Further information is available from the UCB Medical Information department

Email: UCBCares.UK@ucb.com
Tel: 01753 777100

UK: Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.
Ireland: Adverse events should be reported to the HPRA Pharmacovigilance either by phone +353 1 6764971 or via the website at www.hpra.ie Adverse events should also be reported to UCB Pharma Ltd.

Prescribing Information and adverse event reporting can be found at the end of this document.

This formulary application support document has been produced by UCB Pharma Ltd
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### Abbreviations

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<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>BAD</td>
<td>British Association of Dermatology</td>
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<td>BADBIR</td>
<td>British Association of Dermatology Biologics and Immunomodulators Register</td>
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<tr>
<td>BSA</td>
<td>Body surface area</td>
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<td>CI</td>
<td>Confidence interval</td>
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<td>CYP</td>
<td>Cytochrome</td>
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<td>DLQI</td>
<td>Dermatology life quality index</td>
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<td>GIRFT</td>
<td>Getting It Right First Time</td>
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<td>GMMMG</td>
<td>Greater Manchester Medicines Management Group</td>
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<td>IGA</td>
<td>Investigator’s global assessment</td>
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<td>IL</td>
<td>Interleukin</td>
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<tr>
<td>NHS</td>
<td>National Health Service</td>
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<td>NICE</td>
<td>National Institute for Health and Care Excellence</td>
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<tr>
<td>PASI</td>
<td>Psoriasis area and severity index</td>
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<td>PUVA</td>
<td>Psoralen and ultraviolet A</td>
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<tr>
<td>SAEs</td>
<td>Serious adverse events</td>
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<td>TEAEs</td>
<td>Treatment emergent adverse events</td>
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<tr>
<td>TNF</td>
<td>Tumor necrosis factor</td>
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<td>US</td>
<td>United States of America</td>
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**How to use this document**

This document is intended to provide a starting point for healthcare professionals wishing to submit a local formulary application for bimekizumab in the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy. (UCB Pharma Limited BIMZELX SmPC)

Local formulary applications can vary in their structure and wording, but generally they will require the following medicine information: (NICE, 2015)

- Details of the health professionals making the application, including a declaration of interests (not covered in this document)
- General medicine details (indication, dose, administration, mechanism of action etc.)
- Evidence submission with relevant supporting literature, including efficacy, safety and cost effectiveness
- Comparison with existing treatments
- Likely place in therapy, including recommendations for displacement of current formulary medicines if applicable
- Resource impact, including the likely local patient population

This document provides information and guidance to help support your application. Some sections provide general information which can be used directly in the local formulary pack if applicable, but other sections will require customisation according on the demographics and priorities of your local area.

*You must check that all information included in the formulary pack is up to date, relevant, and consistent with the expected format of the local formulary application (e.g., use of generic drug names, abbreviations, referencing style etc.)*

*It is your responsibility to declare conflicts of interest appropriately where required.*

<table>
<thead>
<tr>
<th>Key:</th>
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<tbody>
<tr>
<td>Grey text</td>
<td>Suitable for direct inclusion in a local formulary application, provided the information is up to date and relevant. May require formatting for consistency</td>
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<tr>
<td><strong>Mid blue text</strong></td>
<td>Requires customisation prior to inclusion</td>
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<tr>
<td><strong>Dark violet text</strong></td>
<td>Provides guidance on what the application form is asking for and how to approach filling the section in</td>
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</tbody>
</table>
**Reason for the formulary application request**

Despite existing treatment options available, significant unmet medical need remains for effective and long-lasting therapies for moderate to severe psoriasis patients who are candidates for systemic therapy. (Feldman et al, 2016b, Kragballe et al, 2014)

Additional biologic treatments for psoriasis can contribute to flexibility for patients for whom existing treatment options may not be suitable. (Kerdel et al, 2015)

**Need for complete skin clearance**

*The ultimate treatment goal for patients with psoriasis is to achieve and maintain completely clear skin* (Kouwenhoven et al, 2020)

PASI 75 has traditionally been considered a marker of adequate response and is still considered so by NICE. (Abrouk et al, 2017, NICE, 2017) Other groups suggest that more optimistic treatment goals such as PASI 90 or PASI 100 should now be considered. (Strober et al, 2016) BADDIR suggest a treat to target approach, using PASI ≤2 (equivalent to PASI 90) as the target. (Mahil et al, 2020)

Despite the availability of numerous therapies that can be highly effective and well tolerated, psoriasis is often undertreated such that patients do not achieve substantial skin clearance. (Kerdel et al, 2015)

- PASI 100 response was achieved by only 23% and 26% of patients at 6 and 12 months, while only 36% and 42% achieved PASI 90 at the same timepoints respectively in a recent multinational real-world study (PSO-BIO-REAL, n=846). (Seneschal et al, 2020)

PASI 100 represents a clinically meaningful, possible end point and outcome for patients, reflected in experiences of no psoriasis symptoms and no impairment on health-related quality of life. (Strober et al, 2016)

- 95% of patients rated completely clear skin as their most important treatment goal in a patient needs questionnaire of 3,066 patients. (Blome et al, 2016)

- 55% of 8,338 patients did not believe completely clear skin is possible in the Clear About Psoriasis survey. (Warren R et al, 2018)

**Need for a long-lasting treatment**

*Loss of response over time (secondary failure) can occur in people with psoriasis treated with biologics, which may be related to the formation of anti-drug antibodies* (Kerdel et al, 2015, British Association of Dermatologists, 2017)

- Some patients experience an inadequate response within just one year of starting their first biologic treatment. According to a retrospective analysis in the US (n=13,995) 73% of included patients experienced an inadequate response (n=10,213). (Sheahan A et al, 2018) In a large real-world cohort of patients with severe psoriasis (n=9,652), around half of discontinuations in the first year were due to ineffectiveness for adalimumab (54%), secukinumab (54%), and ustekinumab (47%). (Yu et al, 2020)

- Loss of response varies in frequency between types of biologics, and between drugs within groups, and it is a major reason for discontinuation of their first biologic. (British Association of Dermatologists, 2017)

- Loss of response can lead to unforeseen costs due to treatment strategies for mitigating lost response. These can include dose escalation, increased administration frequency, additional treatments, or switching to an alternative biologic. (Haidari et al, 2020, British Association of Dermatologists, 2017)
The durability of a treatment is an important aspect for patients:

- 94% of patients value durable response, citing it as one of the most important attributes a treatment can offer in a cross sectional US survey (n=500) (Gorelick et al, 2019)
- Patients whose psoriasis impacts more heavily on their quality of life have more preference and need for durable treatments compared with patients with less severe impact on quality of life (Gan et al, 2020)

**Need to improve quality of life**

The impact of psoriasis on a patient’s health-related quality of life has been shown in various studies. Impact is more severe in people with more severe or extensive disease, but even small lesions can lead to a substantial reduction in quality of life. (Lacour et al, 2020, Feldman et al, 2016b, Feldman et al, 2016a)

Long-lasting PASI 100 improves a patient’s quality of life to a significantly greater degree than partial clearance, even if only small residual plaques remain (PASI 90-99): (Lacour et al, 2020)

- The PASI scoring system may disregard the effect of treatment on the specific symptoms that are the most troublesome to patients, such as itch, burning, pain, stinging, and psychologic impact of psoriasis (Sampogna et al, 2019, Strober et al, 2019, Svoboda et al, 2020)
- Achieving PASI 100, and maintaining it over time is more effective in improving quality of life than achieving PASI 90-99: (Lacour et al, 2020)
  - 84% patients who experience PASI 100 also experience DLQI 0/1 (No impact on health-related quality of life, compared with 70% in patients who achieve PASI 90-99 in the PSO-BIO-REAL prospective observational study (n=846) (Lacour et al, 2020)
    - Of those, 69% experience DLQI 0, compared with 46% in patients who achieve PASI 90-99 (Lacour et al, 2020)
**Bimekizumab: medicine details**

**Approved name**
Bimekizumab (UCB Pharma Limited BIMZELX SmPC)

**Brand name**
BIMZELX (UCB Pharma Limited BIMZELX SmPC)

**Form**
- Pre-filled syringe: Solution for injection containing 160 mg bimekizumab in 1 mL (UCB Pharma Limited BIMZELX SmPC)
- Pre-filled pen: Solution for injection containing 160 mg bimekizumab in 1 mL (UCB Pharma Limited BIMZELX SmPC)

**Excipients:**
- Glycine
- Sodium acetate trihydrate
- Glacial acetic acid
- Polysorbate 80
- Water for injections

The formulation is citrate-free. (UCB Pharma Limited BIMZELX SmPC)

**Licensed indication**
The treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy. (UCB Pharma Limited BIMZELX SmPC)

**Proposed indication**
The treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy. (UCB Pharma Limited BIMZELX SmPC)

**Intended dose and route**

Bimekizumab is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of plaque psoriasis. (UCB Pharma Limited BIMZELX SmPC)

The recommended dose for adult patients with plaque psoriasis is 320 mg (given as 2 subcutaneous injections of 160 mg each) at Week 0, 4, 8, 12, 16 and every 8 weeks thereafter. (UCB Pharma Limited BIMZELX SmPC)

Bimekizumab is administered by subcutaneous injection. (UCB Pharma Limited BIMZELX SmPC)

- 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. (UCB Pharma Limited BIMZELX SmPC)
- The pre-filled syringe or pen must not be shaken. (UCB Pharma Limited BIMZELX SmPC)
- After proper training in subcutaneous injection technique, patients may self-inject with the pre-filled syringe or pen if their physician determines that it is appropriate, and with medical follow-up as necessary. (UCB Pharma Limited BIMZELX SmPC)
- Patients should be instructed to inject the full amount of bimekizumab according to the instructions for use provided in the package leaflet. (UCB Pharma Limited BIMZELX SmPC)
**Expected duration of treatment**
Consideration should be given to discontinuing treatment in patients who have shown no improvement by 16 weeks of treatment. *(UCB Pharma Limited BIMZELX SmPC)*

**Manufacturer**
UCB Pharma Limited

**License status**
Licensed product

**Mechanism of action**

*Bimekizumab’s selective dual IL-17A & F inhibition results in normalisation of skin inflammation and as a consequence improvement in clinical symptoms associated with psoriasis* *(UCB Pharma Limited BIMZELX SmPC)*

Bimekizumab is a humanised 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. *(UCB Pharma Limited BIMZELX SmPC)*

Elevated concentrations of IL-17A and IL-17F have been implicated in the pathogenesis of several immune-mediated inflammatory diseases including plaque psoriasis. *(UCB Pharma Limited BIMZELX SmPC)*

From *in vitro* models, bimekizumab was shown to inhibit psoriasis-related gene expression and cytokine production to a greater extent than inhibition of IL-17A alone. *(UCB Pharma Limited BIMZELX SmPC)*

**Contraindications**

Hypersensitivity to the active substance or to any of the excipients. *(UCB Pharma Limited BIMZELX SmPC)*

Clinically important active infections (e.g. active tuberculosis). *(UCB Pharma Limited BIMZELX SmPC)*

**Special populations**

**Overweight patients**
For some patients with 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. *(UCB Pharma Limited BIMZELX SmPC)*

**Elderly**
No dose adjustment is required. *(UCB Pharma Limited BIMZELX SmPC)*

**Renal or hepatic impairment**
Bimekizumab has not been studied in these patient populations. Dose adjustments are not considered necessary based on pharmacokinetics. *(UCB Pharma Limited BIMZELX SmPC)*

**Drug interactions**

No interaction studies have been performed. *(UCB Pharma Limited BIMZELX SmPC)*

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 bimekizumab, may result in normalisation of CYP450 levels with
accompanying lower exposure of CYP450-metabolised medicinal products. 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 bimekizumab therapy in patients being treated with these types of medicinal products, therapeutic monitoring should be considered. (UCB Pharma Limited BIMZELX SmPC)

Live vaccines should not be given concurrently with bimekizumab. (UCB Pharma Limited BIMZELX SmPC)

For special warnings and precautions for use, please see page 18.
**Proposed place in therapy**

**Patients:**

Adult patients with moderate to severe plaque psoriasis who are candidates for systemic therapy, including those who have failed to gain adequate treatment response with an anti-TNF biologic treatment.

**Prescribers and clinical responsibility:**

Bimekizumab is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of plaque psoriasis.

**Suggested Red-Amber-Green rating: Red (Hospital only)**

Check what ratings are used in your local area, and ensure you use similar wording. Check what rating your local area has applied to similar treatments.

**Example wording (GMMMG):** Drugs considered to be specialist medicines and prescribing responsibility for these medicines should normally remain with the consultant or specialist clinician. These drugs should not be initiated or prescribed in primary care. It is recommended that the supply of these specialist medicines should be organised via the hospital pharmacy, this may include arranging for supply via a home care company. (GMMMG, 2021)

Shared care/transfer of care is not anticipated.

**Place in psoriasis treatment pathway:**

**Bimekizumab provides an additional treatment option for patients with moderate to severe psoriasis who are candidates for systemic therapy**

NICE and BAD guidance recommend considering a biologic in patients with severe psoriasis requiring systemic therapy, if phototherapy, methotrexate and ciclosporin have failed, are not tolerated, or are contraindicated. (Smith et al, 2020, NICE, 2021b)

More specifically, the BAD guidance recommends that biologic therapy should be offered if the patient has DLQI score >10 and PASI score ≥10, body surface area >10%, or if localised psoriasis is severe and associated with significant functional impairment or high levels of distress. (Smith et al, 2020)

Existing NICE guidance for subcutaneous biologics for severe psoriasis is consistent across treatments. They are recommended for patients in whom: (NICE, 2021b, NICE, 2021a)

- The disease is severe, as defined by a total PASI of ≥10 and a DLQI of >10
- The psoriasis has not responded to standard systemic therapies including ciclosporin, methotrexate and PUVA; or the person is intolerant of, or has a contraindication to, these treatments

The NICE recommendation for bimekizumab is consistent with that for other biologics. (NICE, 2021a)

NHS trusts are encouraged to use the best value biologic as the first-line option in psoriasis given the emergence of biosimilars. (NHS, 2017)

Treatment decisions should not be based solely on price, but should take into account the likelihood of meaningful treatment success. (Puig et al, 2020)
Discontinuation criteria
Stop bimekizumab treatment at 16 weeks if the psoriasis has not responded adequately. An adequate response is defined as:

- PASI 75 from when treatment started, or
- PASI 50 and a 5-point reduction in DLQI from baseline from when treatment started

Evidence base
*Bimekizumab has been reviewed by NICE in a Fast Track technology appraisal, with a positive recommendation.*

Bimekizumab is recommended by NICE as an option for treating plaque psoriasis in adults, only if:

- The disease is severe, as defined by a total PASI of 10 or more and a DLQI of more than 10, and
- The disease has not responded to other systemic treatments, including ciclosporin, methotrexate and phototherapy, or these options are contraindicated or not tolerated, and
- The company provides the drug according to the commercial arrangement

Evidence of effectiveness
*Only trials featuring an active comparator are covered in this document. If your local formulary application requires information on the phase 3 BE READY placebo-controlled trial, please contact your Health & Access Partner.*

For more information on trial designs, please see the appendix.


Three trials provided direct, head-to-head evidence for the efficacy and safety profile of bimekizumab compared with active comparators across three different mechanisms of action (secukinumab, ustekinumab and adalimumab).

- **BE SURE** – a pivotal, phase 3, randomised 56-week switch trial in which bimekizumab was compared with adalimumab (Warren et al, 2021)
- **BE VIVID** – a pivotal, phase 3, randomised, 52-week controlled trial in which bimekizumab was compared with placebo and ustekinumab (Reich et al, 2021a)
- **BE RADIANT** – a phase 3b, randomised, 48-week controlled trial in which bimekizumab was compared with secukinumab (Reich et al, 2021b)

All trials met their primary endpoints (Reich et al, 2021a, 2021b, Warren et al, 2021)

- **BE SURE**: PASI 90 in all patients receiving bimekizumab was 86.2% versus 47.2% with adalimumab ($P<0.001$) and Investigator’s Global Assessment 0/1 with at least a 2-category improvement relative to baseline was 85.3% and 57.2%, respectively at Week 16 ($P<0.001$, N=478) (Warren et al, 2021)
- **BE VIVID**: Bimekizumab showed improvements versus ustekinumab in both co-primary endpoints of PASI 90 (85% vs. 50%, $P<0.001$) and Investigator’s Global Assessment 0/1 response with at least a 2-category improvement relative to baseline, both at Week 16 (84% vs. 53%, $P<0.001$, N=567) (Reich et al, 2021a)
• BE RADIANT: Bimekizumab showed significant improvement compared with secukinumab in the primary endpoint of PASI 100 at Week 16 (61.7% vs. 48.9%, adjusted risk difference 12.7 [95% CI: 5.8 to 19.6], \(P<0.001\), N=743) (Reich et al, 2021b)
Efficacy in comparison with other treatments - head to head trials

Skin clearance

Bimekizumab produced significantly higher rates of PASI 100 response vs., adalimumab, ustekinumab, and secukinumab (P<0.001 for all comparisons)(Reich et al, 2021b, Reich et al, 2021a, Warren et al, 2021)

59% to 61.7% of bimekizumab-treated patients achieved PASI 100 vs. <50% with comparators at Week 16(Reich et al, 2021b, Reich et al, 2021a, Warren et al, 2021)

- BE SURE: 60.8% of patients treated with bimekizumab experienced PASI 100, compared with 23.9% with adalimumab at Week 16 (adjusted risk difference 37.0%, 95% CI: 28.6 to 45.3, P<0.001. Bimekizumab n=319, adalimumab n=159, secondary endpoint)(Warren et al, 2021)
- BE VIVID: 59% of patients treated with bimekizumab experienced PASI 100, compared with 21% of patients treated with ustekinumab at Week 16 (odds ratio 5.7, 95% CI: 3.6 to 8.9, P<0.0001. Bimekizumab n=321, ustekinumab n=163, secondary endpoint)(Reich et al, 2021a)
- BE RADIANT: 61.7% of patients treated with bimekizumab experienced PASI 100, compared with 48.9% of patients who received secukinumab at Week 16 (adjusted risk difference 12.7%, 95% CI: 5.8 to 19.6, P<0.001. Bimekizumab n=373, secukinumab n=370, primary endpoint)(Reich et al, 2021b)

Durability of response

NOTE: This section contains data pertaining to bimekizumab every 8 weeks maintenance dosing only. Results from the BE VIVID trial, in which patients receive bimekizumab every 4 weeks maintenance dosing, is therefore excluded.

Bimekizumab provided long-lasting treatment responses in trials lasting up to 1 year(Warren et al, 2021, Reich et al, 2021b)

66.0% to 70.2% of patients maintain PASI 100 through one year with bimekizumab.(Reich et al, 2021b, Warren et al, 2021)

- BE SURE: PASI 100 response rates continued to increase from 60.8% at Week 16 to 70.2% at Week 56 with bimekizumab(Warren et al, 2021)

Bimekizumab was administered as 320 mg every 4 weeks to Week 16, then every 8 weeks thereafter (n=161). Secondary endpoint at Week 16, exploratory endpoint at Week 56(Warren et al, 2021)

- BE RADIANT: PASI 100 response rates continued to increase from 61.7% at Week 16 to 66.0% at Week 48 with bimekizumab, compared with from 48.9% at Week 16 to 48.3% at Week 48 in patients treated with secukinumab (adjusted risk difference 17.3%, 95% CI: 9.3 to 25.3%) (Reich et al, 2021b)

Bimekizumab was administered as 320 mg every 4 weeks to Week 16, then every 8 weeks thereafter (n=215). Secukinumab was administered as 300 mg weekly to Week 4 then every 4 weeks (n=354). Primary endpoint at Week 16, prespecified exploratory endpoint for other time points. (Reich et al, 2021b)
Effects on quality of life

*Bimekizumab resulted in improved quality of life (exploratory endpoint): two-thirds of bimekizumab-treated patients reported psoriasis has no effect at all on health-related quality of life after 24 weeks of treatment, which was maintained to 56 weeks* (Warren et al., 2021)

DLQI is the most widely used patient-reported outcomes measure. It addresses the effect of a dermatologic condition on work, leisure activities personal relationships, feelings of embarrassment, and other aspects of life. (Mease, 2011)

A DLQI 0/1 response indicates that the dermatologic condition has no impact on the patient’s life. (British Association of Dermatologists)

78.6% and 67.1% of patients treated with bimekizumab achieved DLQI 0/1 at Week 16, which increased or was maintained through to the end of the trials. (Warren et al., 2021, UCB Data on File, 2021, Reich et al., 2021b)

**Quality of life in the BE VIVID, BE READY, and BE SURE studies** (UCB Pharma Limited BIMZELX SmPC)

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<th>BE VIVID</th>
<th>BE READY</th>
<th>BE SURE</th>
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<tr>
<td></td>
<td>Placebo (n=83)</td>
<td>Bimekizumab 320 mg Q4W (n=321)</td>
<td>Ustekinumab (n=163)</td>
</tr>
<tr>
<td>Baseline DLQI 0/1 n(%)</td>
<td>3 (3.6)</td>
<td>16 (5.0)</td>
<td>5 (3.1)</td>
</tr>
<tr>
<td>Week 16 DLQI 0/1 n(%)</td>
<td>10 (12.0)</td>
<td>216 (67.3)</td>
<td>69 (42.3)</td>
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- **BE SURE:** More patients treated with bimekizumab achieved DLQI 0/1 than those treated with adalimumab (67.1% vs. 47.8%, nominal $P<0.001$) at Week 24 (Warren et al., 2021, UCB Data on File, 2021)

  Bimekizumab was administered as 320 mg every 4 weeks to Week 16, then every 8 weeks thereafter (n=161). Adalimumab was administered as 80 mg at baseline then 40 mg 1 week later then every 2 weeks thereafter (n=159). Exploratory endpoint.

- **BE RADIANT:** 78.6% of patients treated with bimekizumab achieved DLQI 0/1 at Week 16, which was maintained at 77.7% through 48 weeks (UCB Data on File, 2021, Reich et al., 2021b)

  Compared with 73.8% of patients treated with secukinumab at Week 16 (nominal $P=0.123$), and 70.3% at Week 48 (nominal $P=0.020$) (UCB Data on File, 2021, Reich et al., 2021b)

  Bimekizumab was administered as 320 mg every 4 weeks to Week 16, then every 8 weeks thereafter (n=215). Secukinumab was administered as 300 mg weekly to Week 4 then every 4 weeks (n=354). Exploratory endpoint. (Reich et al., 2021b)
**Efficacy in comparison with other treatments – Network meta-analysis**

Please note that the network meta-analysis includes trials which have already been discussed in the ‘efficacy in comparison with other treatments - head to head trials’ section of this document. If you are using information from both sections in the application form, you will need to ensure it is clear that the same trials are included in both sections.

More patients were likely to achieve PASI 100 with bimekizumab compared with currently available biologics/biosimilars in a network meta-analysis\(^{(\text{Slim M et al, 2021})}\)

- Bimekizumab was associated with a higher probability of reaching PASI 100 compared with the majority of comparators at Weeks 10-16 (0.578 vs. 0.445 to 0.003)\(^{(\text{Slim M et al, 2021})}\)
- Bimekizumab was associated with a higher probability of reaching PASI 90 compared with the majority of comparators at Weeks 10-16 (0.840 vs. 0.732 to 0.018)\(^{(\text{Slim M et al, 2021})}\)

A systematic literature review and network meta-analysis (sponsored by the manufacturer of bimekizumab, UCB) aimed to provide an indirect comparison of the efficacy of bimekizumab with active biologic or non-biologic treatments available for moderate to severe psoriasis.\(^{(\text{Slim M et al, 2021})}\)

**Study design information**

- The systematic literature review was carried out in July of 2020 to identify randomised controlled trials of biologics (anti-IL-17, anti-IL-23, anti-IL-12/23, anti-TNFs), small molecules and conventional systemic agents\(^{(\text{Slim M et al, 2021})}\)
- 86 studies were included in total. Data from five bimekizumab trials (1 x Phase IIb, 3x Phase III, and 1x Phase IIIb) were included\(^{(\text{Slim M et al, 2021})}\)
  - These included the BE READY, BE SURE, BE VIVID, and BE RADIANT trials\(^{(\text{Slim M et al, 2021})}\)
- The key efficacy measures were PASI 90 and PASI 100 responses at 10–16 weeks in the included studies and clinically relevant timepoints to assess whether treatments produced complete or nearly complete resolutions of psoriasis in the involved areas\(^{(\text{Slim M et al, 2021})}\)
- To compare the efficacy of treatments across the psoriasis landscape, a Bayesian, multinomial, probit, baseline, risk-adjusted, random effects model was used, leveraging data from the PASI 50, 75, 90, and 100 response rates. The baseline risk was adjusted via the placebo rate, which has become a common approach with psoriasis as the relative effects of drugs in autoimmune diseases are often dependent on it\(^{(\text{Slim M et al, 2021})}\)
- The multinomial assumption of the standard model was relaxed by allowing for a given treatment to have different efficacies (and, thus, different rankings) for different levels of PASI. This novel, enhanced model was referred to as the “REZ” model because it added a random effects component to the parameter z, which reflected the difficulty of going from one PASI cut-off to the next\(^{(\text{Slim M et al, 2021})}\)
- The baseline-risk-adjusted random effects REZ model had the smallest mean residual deviance, but the unadjusted fixed effect REZ model had the best fit (with the lowest deviance information criterion) since the adjusted model involved extra parameters and penalties. Given the relatively small difference in deviance information criterion compared to the number of data points that contributed to the multinomial analysis, the level of significance for the estimate of the slope, and recommendations from clinical
experts about the importance of the baseline risk adjustment, we maintained our a priori choice of a baseline-risk adjusted random effects REZ as the base case (Slim M et al, 2021)

Results

Over 10-16 weeks:

- Bimekizumab was the highest ranked treatment for PASI 75, PASI 90 and PASI 100 compared with all non-biologic and biologic treatments included (adalimumab, brodalumab, certolizumab pegol, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, ustekinumab, apremilast, methotrexate, ciclosporin, dimethyl fumarate, and acitretin) (Slim M et al, 2021)

- The probability of achieving PASI 100 in the initial treatment period was 0.578 with bimekizumab, compared with a range of 0.445 to 0.013 for the comparators (adalimumab, brodalumab, certolizumab pegol, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, ustekinumab, apremilast, methotrexate, ciclosporin, dimethyl fumarate, and acitretin) (Slim M et al, 2021)

- The number needed to treat to achieve PASI 100 for bimekizumab was 1.74, compared with a range of 2.26 to 100.59 for comparators (adalimumab, brodalumab, certolizumab pegol, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, ustekinumab, apremilast, methotrexate, ciclosporin, dimethyl fumarate, and acitretin) (Slim M et al, 2021)

- The probability of achieving PASI 90 in the initial treatment period with bimekizumab was 0.840, compared with a range of 0.732 to 0.077 for the comparators (adalimumab, brodalumab, certolizumab pegol, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, ustekinumab, apremilast, methotrexate, ciclosporin, dimethyl fumarate, and acitretin) (Slim M et al, 2021)

- The number needed to treat to achieve PASI 90 for bimekizumab was 1.22, compared with a range of 1.40 to 16.77 for comparators (adalimumab, brodalumab, certolizumab pegol, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, ustekinumab, apremilast, methotrexate, ciclosporin, dimethyl fumarate, and acitretin) (Slim M et al, 2021)
Safety profile and tolerability

Adverse reactions

The most frequently reported adverse reactions were upper respiratory tract infections (14.5%, most frequently nasopharyngitis) and oral candidiasis (7.3%).

Table 1: List of adverse reactions in clinical studies

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 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000), not known (cannot be estimated from the available data).

<table>
<thead>
<tr>
<th>System organ class</th>
<th>Frequency</th>
<th>Adverse reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections and infestations</td>
<td>Very common</td>
<td>Upper respiratory tract infections</td>
</tr>
<tr>
<td>Common</td>
<td>Oral candidiasis</td>
<td></td>
</tr>
<tr>
<td>Tinea infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ear infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Herpes simplex infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oropharyngeal candidiasis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Folliculitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uncommon</td>
<td>Mucosal and cutaneous candidiasis (including oesophageal candidiasis)</td>
<td></td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Uncommon</td>
<td>Neutropenia</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Common</td>
<td>Headache</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Uncommon</td>
<td>Inflammatory bowel disease</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Common</td>
<td>Dermatitis and eczema</td>
</tr>
<tr>
<td>Acne</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Common</td>
<td>Infection site reactions (includes injection site erythema, reaction, oedema, pain, swelling)</td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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. Serious infections occurred in 0.3% of patients treated with bimekizumab and 0% treated with placebo.

The majority of infections consisted of non-serious mild to moderate upper respiratory tract infections such as nasopharyngitis. 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). More than 98% of cases were non-serious, mild or moderate in severity, and did not require treatment discontinuation. A slightly higher incidence of oral candidiasis was reported in patients <70 kg (8.5% versus 7.0% in patients ≥70 kg).
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). (UCB Pharma Limited BIMZELX SmPC)

**Neutropenia**

Neutropenia was observed with bimekizumab in phase III clinical studies in plaque psoriasis. Over the entire treatment period of Phase III studies, neutropenia grade 3/4 were observed in 1% of patients treated with bimekizumab. Most cases were transient and did not require treatment discontinuation. No serious infections were associated with neutropenia. (UCB Pharma Limited BIMZELX SmPC)

**Hypersensitivity**

Serious hypersensitivity reactions including anaphylactic reactions have been observed with IL-17 inhibitors. (UCB Pharma Limited BIMZELX SmPC)

**Immunogenicity**

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 neutralising. No evidence of altered clinical response, or significantly altered safety profile was associated with anti-bimekizumab antibodies development. (UCB Pharma Limited BIMZELX SmPC)

**Elderly patients (≥65 years)**

Elderly patients may be more likely to experience certain adverse reactions such as oral candidiasis, dermatitis and eczema when using bimekizumab. In the placebo-controlled period of Phase III clinical studies in plaque psoriasis, oral candidiasis was observed in 18.2% of patients ≥65 years versus 6.3% in <65 years, dermatitis, and eczema in 7.3% of patients ≥65 years versus 2.8% in <65 years. (UCB Pharma Limited BIMZELX SmPC)

**Special warnings and precautions for use**

**Traceability**

The name and the batch number of the administered product should be clearly recorded. (UCB Pharma Limited BIMZELX SmPC)

**Infections**

Bimekizumab may increase the risk of infections such as upper respiratory tract infections and oral candidiasis. (UCB Pharma Limited BIMZELX SmPC)

- Caution should be exercised when considering use in patients with a chronic infection or a history of recurrent infection. Treatment must not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated. (UCB Pharma Limited BIMZELX SmPC)

- Patients treated with bimekizumab should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a clinically important infection or is not responding to standard therapy, the patient should be monitored carefully and bimekizumab should not be administered until the infection resolves. (UCB Pharma Limited BIMZELX SmPC)
Pre-treatment evaluation for tuberculosis
Prior to initiating treatment, patients should be evaluated for tuberculosis infection:

- Bimekizumab should not be given in patients with active tuberculosis.
- Patients should be monitored for signs and symptoms of active tuberculosis.
- Anti-tuberculosis therapy should be considered prior to initiation in patients with a history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed.

Inflammatory bowel disease
Cases of new or exacerbations of inflammatory bowel disease have been reported with bimekizumab. Bimekizumab 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, bimekizumab should be discontinued and appropriate medical management should be initiated.

Hypersensitivity
Serious hypersensitivity reactions including anaphylactic reactions have been observed with IL-17 inhibitors.

If a serious hypersensitivity reaction occurs, administration should be discontinued immediately, and appropriate therapy initiated.

Vaccinations
Prior to initiation, consider completion of all age appropriate immunisations according to current immunisation guidelines:

- Live vaccines should not be given in patients treated with bimekizumab.
- Patients treated with bimekizumab may receive inactivated or non-live vaccinations.
- Healthy individuals who received a single 320 mg dose of bimekizumab two weeks prior to vaccination with an inactivated seasonal influenza vaccine had similar antibody responses compared to individuals who did not receive bimekizumab prior to vaccination.

Fertility, pregnancy, and lactation

- Women of childbearing potential should use an effective method of contraception during treatment and for at least 17 weeks after treatment.
- There is a limited amount of data on the use of bimekizumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition, or postnatal development. As a precautionary measure, it is preferable to avoid the use of bimekizumab during pregnancy.
- It is unknown whether bimekizumab is excreted in human milk. A risk to the new born/infant cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from bimekizumab therapy taking into account...
the benefit of breast-feeding for the child and the benefit of therapy for the woman\textsuperscript{(UCB Pharma Limited BIMZELX SmPC)}

- The effect of bimekizumab on human fertility has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to fertility\textsuperscript{(UCB Pharma Limited BIMZELX SmPC)}
Local health economy resource impact

Customise this section with information on number of potential patients in your local area.

Table 2: Number of plaque psoriasis patients eligible to be treated with bimekizumab (NICE, 2021c)

<table>
<thead>
<tr>
<th>Per 100,000 general population</th>
<th>Percentage (%)</th>
<th>No. of people</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total adult population</td>
<td>N/A</td>
<td>78,651</td>
</tr>
<tr>
<td>Prevalence of people with psoriasis</td>
<td>1.75</td>
<td>1,376</td>
</tr>
<tr>
<td>Prevalence of people with chronic plaque psoriasis</td>
<td>90</td>
<td>1,239</td>
</tr>
<tr>
<td>People eligible for biologic treatment</td>
<td>2.55</td>
<td>32</td>
</tr>
<tr>
<td>Estimated number of people eligible for bimekizumab treatment</td>
<td>Complete with local data</td>
<td>Complete with local data</td>
</tr>
</tbody>
</table>

*Percentages (%) are applied to the numbers in the row above.

Each pack of two 160 mg bimekizumab pre-filled pens or syringes costs £2,443. (UCB Pharma Limited BIMZELX PI, Sept 2021)

The annual maintenance cost per patient per year is £14,658.00. Multiply this by the estimated number of people eligible for bimekizumab treatment in your area to complete this section

The company has a commercial arrangement. This makes bimekizumab available to the NHS with a discount. The size of the discount is commercial in confidence. (NICE, 2021a) Details of the patient access price can be found within the NHS Commercial Access and Pricing (CAP) portal, which can be accessed by the relevant NHS Pharmacists including your Chief Pharmacist at your local Trust.

Funding Stream

National Tariff excluded CCG funded

Service implications

The high likelihood of achieving complete skin clearance with bimekizumab may mean patients require fewer outpatient follow up and review appointments compared to patients with incomplete response. (Reich et al, 2021a, Reich et al, 2021b, Warren et al, 2021, NHS England, 2019)

The high likelihood of achieving complete skin clearance with bimekizumab may mean patients can access an effective, appropriate treatment rapidly following anti-TNF treatment failure, reducing the potential for treatment delays. (Reich et al, 2021a, Reich et al, 2021b, Warren et al, 2021)
Bimekizumab and NHS drivers

Long term plan

The high likelihood of achieving complete skin clearance with bimekizumab may mean patients require fewer outpatient follow up and review appointments compared to patients with incomplete response\footnote{Reich et al, 2021a, Reich et al, 2021b, Warren et al, 2021, NHS England, 2019}

The NHS Long Term Plan specifically highlights outpatient appointments as a priority for reform, with a commitment to reduce appointments by one-third across the NHS, saving patients 30 million visits to hospital and saving the NHS over £1 billion.\footnote{NHS England, 2019}

Dermatology has been identified as a service that should be at the forefront of service transformation, with technology highlighted as a key enabler of more streamlined pathways. The dermatology pathway aims to support the use of apps and teledermatology to improve services and reduce waiting times for treatment and diagnosis of skin lesions.\footnote{NHSX, 2021}

Integrated care systems

The high likelihood of achieving complete skin clearance with bimekizumab may mean patients can access an effective, appropriate treatment rapidly following anti-TNF treatment failure, reducing the potential for treatment delays\footnote{Reich et al, 2021a, Reich et al, 2021b, Warren et al, 2021}

Delays to referral and disjointed care between primary care centres and secondary care can lead to disease progression and reduced quality of life. Once referred, patients may experience a lengthy wait to find an appropriate treatment, resulting in cumulative impacts on quality of life, or further delays in their treatment journey.\footnote{Berendsen et al, 2009, Feldman et al, 2016b}

Dermatology services are particularly well suited to a whole pathway approach given the nature of conditions like psoriasis, and there is untapped potential in the use of treatments to support patients to stay well.

Getting It Right First Time

Appropriate use of bimekizumab may be able to assist with the dermatology GIRFT programme recommendations when they are published

Possible areas may include addressing variations in patient follow up, increasing the use of telephone consultations and implementing NICE guidance to address variation in the uptake and use of biologic treatments. Treating appropriately at the point of presentation to secondary care could reduce delays in primary care, and save on treatments that are unlikely to be sufficient to control disease in the short and long-term\footnote{Levell, 2020}

This section will require updating once the dermatology GIRFT recommendations are published.
Appendix: Trial designs

BE SURE (NCT03412747)


Aims and objectives:
A Phase III pivotal trial to compare the efficacy and safety of bimekizumab with adalimumab in patients with plaque psoriasis, and to assess the maintenance of efficacy with bimekizumab when administered every 8 weeks or every 4 weeks. (Warren et al, 2021)

NOTE: The recommended dose of bimekizumab for adult patients with plaque psoriasis is 320 mg (given as 2 subcutaneous injections of 160 mg each) at Week 0, 4, 8, 12, 16 and every 8 weeks thereafter. For some patients with 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. (UCB Pharma Limited BIMZELX SmPC)

This document contains data pertaining to bimekizumab every 8 weeks maintenance dosing only

Design:
Double-blind, active-controlled, multicentre 56-week trial consisting of four periods. (Warren et al, 2021)

• Screening period (2 to 5 weeks)
• Double-blind, active comparator initial treatment period (16 weeks)
• Dose-blind maintenance treatment period (40 weeks)
• Safety follow-up period (20 weeks after the last dose of treatment)

Population:
The study population consisted of adult patients (≥18 years of age) with a diagnosis of moderate to severe plaque psoriasis (baseline PASI≥12 and BSA affected by psoriasis ≥10% and IGA score ≥3 [on a 5-point scale]) who were candidates for adalimumab or for systemic psoriasis therapy, and/or phototherapy, and/or photochemotherapy. (Warren et al, 2021)

A total of 478 patients were enrolled. (Warren et al, 2021)

Patient baseline characteristics were well-balanced between treatment groups and reflective of a population with moderate to severe plaque psoriasis who are candidates for treatment with a biologic. The mean age across groups was approximately 45 years and most patients were male (approximately 69% across groups). Approximately 32% of patients had received prior biologic therapy. (Warren et al, 2021)

Intervention and comparator:
During the double-blind period, eligible patients were randomised 1:1:1 to receive one of the following blinded regimens subcutaneously: (Warren et al, 2021)

• Bimekizumab 320 mg every 4 weeks administered throughout the study
• Bimekizumab 320 mg every 4 weeks administered until week 16, followed by every 8 weeks from Week 16 through Week 56
• Adalimumab 80 mg administered as an initial dose, followed by 40 mg one week later then every 2 weeks thereafter until Week 23, and then bimekizumab 320 mg every 4 weeks from Week 24 until Week 56
Outcomes:
The co-primary efficacy endpoints were: (Warren et al, 2021)

- PASI 90 response at Week 16
- IGA 0/1 response with at least a 2-category improvement relative to baseline at Week 16

Secondary efficacy endpoints included: (Warren et al, 2021)

- PASI 90 response at Week 24
- IGA 0/1 response with at least 2-category improvement relative to baseline at Week 24
- PASI 75 response at Week 4
- PASI 100 response at Week 16 and 24
- PASI 90 response at Week 56

Safety endpoints included: (Warren et al, 2021)

- TEAEs adjusted by duration of exposure to treatment
- SAEs adjusted by duration of exposure to treatment
- TEAEs leading to withdrawal adjusted by duration of exposure to treatment
**BE VIVID (NCT03370133)**

*Citation: Reich K. et al. Bimekizumab versus ustekinumab for the treatment of moderate to severe plaque psoriasis (BE VIVID): efficacy and safety from a 52-week, multicentre, double-blind, active comparator and placebo-controlled phase 3 trial. The Lancet. 2021;397(10273):487-498*

**Aims and objectives:**
A Phase III pivotal trial to evaluate the efficacy and safety of bimekizumab in moderate to severe plaque psoriasis over 1 year compared with both placebo (first 16 weeks only) and the active comparator ustekinumab. (Reich et al, 2021a)

**NOTE:** The recommended dose of bimekizumab for adult patients with plaque psoriasis is 320 mg (given as 2 subcutaneous injections of 160 mg each) at Week 0, 4, 8, 12, 16 and every 8 weeks thereafter. For some patients with 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. (UCB Pharma Limited BIMZELX SmPC)

**This document contains data pertaining to bimekizumab every 8 weeks maintenance dosing only**

**Design:**
Double-blind, placebo and active-controlled, multicentre 52-week trial consisting of four periods; (Reich et al, 2021a)

- Screening period (2 to 5 weeks)
- Double-blind, active comparator initial treatment period (16 weeks)
- Dose-blind, active-comparator-controlled maintenance treatment period (36 weeks)
- Safety follow-up period (20 weeks after the last dose of treatment)

**Population:**
The study population consisted of adult patients (≥18 years of age) with a diagnosis of moderate-to-severe plaque psoriasis (PASI ≥12 and BSA affected by psoriasis ≥10% and IGA score ≥3 [on a 5-point scale] for at least 6 months before screening) who were a candidate for ustekinumab, or for systemic psoriasis therapy, and/or phototherapy. (Reich et al, 2021a)

A total of 567 patients were randomised. (Reich et al, 2021a)

Patient baseline characteristics were well-balanced between treatment groups and reflective of a population with moderate-to-severe plaque psoriasis who are candidates for treatment with a biologic. The mean age across groups ranged from 46.0 years to 49.7 years and most patients were male (approximately 72% across groups). Nearly 40% of patients had received prior biologic therapy. (Reich et al, 2021a)

**Intervention and comparator:**
Eligible patients were randomised 4:2:1 to receive the following blinded regimens; (Reich et al, 2021a)

- Bimekizumab 320 mg administered subcutaneously every 4 weeks
- Ustekinumab (45 mg or 90 mg, depending on patient weight) administered subcutaneously at baseline and 4 weeks later, followed by ustekinumab subcutaneously every 12 weeks
• Placebo administered subcutaneously every 4 weeks for 16 weeks during the initial treatment period, followed by bimekizumab 320 mg administered subcutaneously every 4 weeks during the maintenance treatment period

**Outcomes:**
The co-primary efficacy endpoints were: (Reich et al. 2021a)
- PASI 90 response at Week 16
- IGA 0/1 response with at least a 2-category improvement relative to baseline at Week 16

Secondary efficacy endpoints included: (Reich et al. 2021a)
- PASI 100 response at Week 16
- IGA response of 0 with at least a 2-category improvement relative to baseline at Week 16
- PASI 75 response at Week 4
- P-SIM responses for pain, itch, and scaling at Week 16
- Scalp 0/1 IGA response at Week 16 for study participants with scalp psoriasis at baseline
- PASI 90 response at Week 12 and Week 52
- IGA 0/1 response with at least a 2-category improvement relative to baseline at Week 12 and Week 52

Safety endpoints included: (Reich et al. 2021a)
- TEAEs adjusted by duration of exposure to treatment
- SAEs adjusted by duration of exposure to treatment
- TEAEs leading to withdrawal adjusted by duration of exposure to treatment
**BE RADIANT (NCT03536884)**

*Citation: Reich K. et al. Bimekizumab versus secukinumab in plaque psoriasis. New England Journal of Medicine. 2021*

**Aims and objectives:**
Phase IIIb trial to evaluate the efficacy of bimekizumab compared with secukinumab in moderate to severe plaque psoriasis through 48 weeks. (Reich et al, 2021b)

NOTE: The recommended dose of bimekizumab for adult patients with plaque psoriasis is 320 mg (given as 2 subcutaneous injections of 160 mg each) at Week 0, 4, 8, 12, 16 and every 8 weeks thereafter. For some patients with 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. (UCB Pharma Limited BIMZELX SmPC)

*This document contains data pertaining to bimekizumab every 8 weeks maintenance dosing only*

**Design:**
Double-blind, active-controlled, multicentre 48-week trial consisting of four periods. (Reich et al, 2021b)
- Screening period (2 to 5 weeks)
- Double-blind treatment period (48 weeks with a final dose at 44 weeks)
- Optional open-label extension period (96 weeks with a final dose at week 136 for patients receiving bimekizumab 320 mg every 8 weeks and at week 140 for patients receiving bimekizumab 320 mg every 4 weeks)
- Safety follow-up period (20 weeks after the final dose)

**Population:**
The study population consists of adult patients (≥18 years of age) with a diagnosis of moderate-to-severe plaque psoriasis (PASI score ≥12 and BSA affected by psoriasis ≥10% and IGA score ≥3 [on a 5-point scale]) who are candidates for secukinumab, or for systemic psoriasis therapy and/or phototherapy. (Reich et al, 2021b)

A total of 743 patients were enrolled. (Reich et al, 2021b)

Patient baseline characteristics were well-balanced between treatment groups and reflective of a population with moderate to severe plaque psoriasis who are candidates for treatment with a biologic. The mean age was about 45 years and most patients were male (approximately 65% across groups). Approximately 33% of patients had received prior biologic therapy. (Reich et al, 2021b)

**Intervention and comparator:**
During the treatment period, eligible patients were randomised 1:1 to receive one of the following blinded regimens: (Reich et al, 2021b)
- Bimekizumab 320 mg subcutaneously every 4 weeks (and placebo subcutaneously during weeks 1, 2, and 3)
  - At Week 16 patients in this arm were re-randomised to receive either bimekizumab 320 mg subcutaneously every 4 weeks, or bimekizumab 320 mg every 8 weeks (respectively)
- Secukinumab 300 mg subcutaneously at baseline and weeks 1, 2, 3, and 4 followed by every 4 weeks
Outcomes:
The primary efficacy endpoint is PASI 100 response at Week 16.\textsuperscript{(Reich et al, 2021b)}

Secondary efficacy endpoints include:\textsuperscript{(Reich et al, 2021b)}
- PASI 75 response at Week 4
- PASI 90 response at Week 16
- PASI 100 response at Week 48
- IGA 0/1 response at Week 16

Secondary safety endpoints include:\textsuperscript{(Reich et al, 2021b)}
- TEAEs adjusted by duration of exposure to treatment
- SAEs adjusted by duration of exposure to treatment
- TEAEs leading to withdrawal adjusted by duration of exposure to treatment
References


Feldman, SR. et al. Differences in psoriasis signs and symptom severity between patients with clear and almost clear skin in clinical practice. J Dermatolog Treat 2016a;27(3):224-227


Mease, PJ Measures of psoriatic arthritis: Tender and Swollen Joint Assessment, Psoriasis Area and Severity Index (PASI), Nail Psoriasis Severity Index (NAPSI), Modified Nail Psoriasis Severity Index (mNAPSI), Mander/Newcastle Enthesitis Index (MEI), Leeds Enthesitis Index (LEI), Spondyloarthritits Research Consortium of Canada (SPARCC), Maastricht Ankylosing Spondylitis Enthesis Score (MASES), Leeds Dactylitis Index (LDI), Patient Global for Psoriatic Arthritis, Dermatology Life Quality Index (DLQI), Psoriatic Arthritis Quality of Life (PsAQOL), Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F), Psoriatic Arthritis Response Criteria (PsARC), Psoriatic
Arthritis Joint Activity Index (PsAJAI), Disease Activity in Psoriatic Arthritis (DAPSA), and Composite Psoriatic Disease Activity Index (CPDAI). *Arthritis Care & Research* 2011;63(S11):S64-S85


Sain, N. et al. The importance of understanding patient and physician preferences for psoriasis treatment characteristics: a systematic review of discrete-choice experiments. *Current Medical Research and Opinion* 2020;36(8):1257-1275

Sampogna, F. et al. Use of the SF-12 questionnaire to assess physical and mental health status in patients with psoriasis. *J Dermatol* 2019;46(12):1153-1159


Strober, BE. *et al.* Clinical goals and barriers to effective psoriasis care. *Dermatology and Therapy* 2019;9(1):5-18


UCB Data on File. 2021. FINAL BKZ PSO GVD launch version 1.1_10Feb2021

UCB Pharma Limited BIMZELX PI, Sept 2021. BIMZELX (bimekizumab) Prescribing Information. Slough, United Kingdom.

UCB Pharma Limited BIMZELX SmPC. BIMZELX (bimekizumab) Summary of Product Characteristics. Slough, United Kingdom.


Prescribing information

(Please consult the Summary of Product Characteristics (SmPC) before prescribing)

Bimzelx® ▼ (Bimekizumab)

Active Ingredient: Bimekizumab – solution for injection in pre-filled syringe or pre-filled pen: 160 mg of bimekizumab in 1 mL of solution (160 mg/mL).

Indications: Moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

Dosage and Administration: Should be initiated and supervised by a physician experienced in the diagnosis and treatment of plaque psoriasis. Recommended dose: 320 mg (given as two subcutaneous injections of 160 mg each) at week 0, 4, 8, 12, 16 and every 8 weeks thereafter. For some patients with 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. Consider discontinuing if no improvement by 16 weeks of treatment. Renal or hepatic impairment: No dose adjustment needed. Elderly: No dose adjustment needed. Administer by subcutaneous injection to thigh, abdomen or upper arm. Rotate injection sites and do not inject into psoriatic plaques or skin that is tender, bruised, erythematous or indurated. Do not shake pre-filled syringe or pre-filled pen. Patients may be trained to self-inject.

Contraindications: Hypersensitivity to bimekizumab or any excipient; Clinically important active infections (e.g. active tuberculosis).

Warnings and Precautions: Record name and batch number of administered product.

Infection: Bimekizumab may increase the risk of infections e.g. upper respiratory tract infections, oral candidiasis. Caution when considering use in patients with a chronic infection or a history of recurrent infection. Must not be initiated if any clinically important active infection until infection resolves or is adequately treated. Advise patients to seek medical advice if signs or symptoms suggestive of an infection occur. If a clinically important infection develops or is not responding to standard therapy, carefully monitor and do not administer bimekizumab until infection resolves. TB: Evaluate for TB infection prior to initiating bimekizumab – do not give if active TB. While on bimekizumab, monitor for signs and symptoms of active TB. Consider anti-TB therapy prior to bimekizumab initiation if past history of latent or active TB in whom adequate treatment course cannot be confirmed. Inflammatory bowel disease: Bimekizumab is not recommended in patients with inflammatory bowel disease. Cases of new or exacerbations of inflammatory bowel disease have been reported. If inflammatory bowel disease signs/symptoms develop or patient experiences exacerbation of pre-existing inflammatory bowel disease, discontinue bimekizumab and initiate medical management. Hypersensitivity: Serious hypersensitivity reactions including anaphylactic reactions have been observed with IL-17 inhibitors. If a serious hypersensitivity reaction occurs, discontinue immediately and treat. Vaccinations: Complete all age appropriate immunisations prior to bimekizumab initiation. Do not give live vaccines to bimekizumab patients. Patients may receive inactivated or non-live vaccinations.

Interactions: 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. Therapeutic monitoring should be considered.

Fertility, pregnancy and lactation: Women of childbearing potential should use an effective method of contraception during treatment and for at least 17 weeks after treatment. Avoid use of bimekizumab during pregnancy and breastfeeding. Discontinue breastfeeding or discontinue bimekizumab during breastfeeding. It is unknown whether bimekizumab is excreted in human milk, hence a risk to the newborn/infant cannot be excluded. No data available on human fertility.

Driving and use of machines: No or negligible influence on ability to drive and use machines.

Adverse Effects: Refer to SmPC for full information. Very Common (≥ 1/10): upper respiratory tract infection; Common (≥ 1/100 to < 1/10): oral candidiasis, lice infections, ear infections, herpes simplex infections, oropharyngeal candidiasis, folliculitis; headache, dermatitis and eczema, acne, injection site reactions, fatigue; Uncommon (≥ 1/1000 to < 1/100): mucosal and cutaneous candidiasis (including oesophageal candidiasis), conjunctivitis, neutropenia, inflammatory bowel disease.

Storage precautions: Store in a refrigerator (2ºC – 8ºC), do not freeze. Keep in outer carton to protect from light. Bimzelx can be kept at up to 25ºC for a single period of maximum 25 days with protection from light. Product should be discarded after this period or by the expiry date, whichever occurs first.

Legal Category: POM

Marketing Authorisation Numbers: Northern Ireland: EU/1/21/1575/002 (2 x 1 Pre-filled Syringes), EU/1/21/1575/006 (2 x 1 Pre-filled Pens) Great Britain: PLGB 00039/0802 (Pre-filled Syringe), PLGB 00039/0803 (Pre-filled Pen).

UK NHS Costs: £2,443 per pack of 2 pre-filled syringes or pens of 160 mg each.

Marketing Authorisation Holder: UCB Pharma S.A., Allée de la Recherche 60, B-1070 Brussels, Belgium (Northern Ireland): UCB Pharma Ltd, 208 Bath Road, Slough, Berkshire, SL1 3WE, United Kingdom (Great Britain).

Further information is available from: UCB Pharma Ltd, 208 Bath Road, Slough, Berkshire, SL1 3WE. Tel: +44 (0)1753 777100 Email: ucbcares.uk@ucb.com

Date of Revision: September 2021 IE-P.

Bimzelx is a registered trademark.

UK: Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.

Adverse events should also be reported to UCB Pharma Ltd.