CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

bimekizumab (Bimzelx)

(UCB Canada Inc.)

Indication: The treatment of adult patients with active ankylosing spondylitis who have responded inadequately or are intolerant to conventional therapy.

May 3, 2024

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0809
Name of the drug and Indication(s)	Bimekizumab (Bimzelx) for the treatment of adult patients with active ankylosing spondylitis who have responded inadequately or are intolerant to conventional therapy
Organization Providing Feedback	FWG

1. Recommendation revisions Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.		
Request for Reconsideration	**Major revisions:** A change in recommendation **category** or patient **population** is requested	☐
	Minor revisions: A change in reimbursement **conditions** is requested	☐
No Request for Reconsideration	**Editorial revisions:** Clarifications in recommendation **text** are requested	X
	No requested revisions	☐

2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested
Please identify the specific text from the recommendation and provide a rationale for requesting a change in recommendation.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
Please provide details regarding the information that requires clarification.
b) Reimbursement conditions and related reasons
Please provide details regarding the information that requires clarification.
c) Implementation guidance
Define 'conventional therapies' in the case of ankylosing spondylitis as part of initiation implementation guidance.

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0809
Brand name (generic)	BIMZELX (bimekizumab)
Indication(s)	For the treatment of adult patients with active ankylosing spondylitis who have responded inadequately or are intolerant to conventional therapy.
Organization	UCB Canada Inc.
Contact information[a]	[redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐

UCB Canada Inc. agrees with the recommendation to reimburse BIMZELX (bimekizumab) for the treatment of adult patients with active ankylosing spondylitis (AS) who have responded inadequately or are intolerant to conventional therapy. While UCB Canada Inc. agrees with the recommendation to reimburse BIMZELX (bimekizumab) for AS, we would ask the CDEC to kindly consider the following editorial revisions:

1. There is a high probability that bimekizumab has some advantages over existing treatment options for active AS, further supporting the potential improved benefit of bimekizumab.
On page 5 of the draft recommendation, under Discussion Points, it is stated by CDEC that there is "insufficient evidence to suggest that the clinical efficacy or safety benefit of bimekizumab was superior or inferior to the comparative treatments that were assessed in the ITC."

UCB Canada Inc. respectfully disagrees with CDEC's statements concluding uncertainty of bimekizumab's advantages over currently available treatment options for active AS. As direct comparisons between bimekizumab and relevant comparators cannot be made using data from BE MOBILE 2, evidence for the efficacy of bimekizumab is supported by the indirect treatment comparisons (ITCs) which demonstrate that across both patient populations (bio-naïve and TNFi-inadequate responders [TNFi-IR]), bimekizumab was statistically superior in treatment effects across various disease domains.

Based on NMAs (12-16 weeks) and MAICs (52 weeks), bimekizumab was associated with **similar efficacy vs. TNFis and JAKis and statistically significantly improved efficacy vs. IL-17is** in some of the endpoints: in the NMA, outcomes in the purely naïve and predominantly naïve networks were similar, however, some exceptions were noted in the predominantly naïve network, which indicated that **bimekizumab was significantly better than secukinumab (with loading dosage) in improving ASAS-PR and SF-36 PCS**, as well as **significantly better than adalimumab in improving SF-36 PCS**. Additionally, the MAICs demonstrated significantly **higher long-term relative efficacy at week 52 in bimekizumab compared with secukinumab 150 mg and ixekizumab 80 mg**, and similar efficacy to secukinumab 300 mg at the same timepoint. Based on these results, **bimekizumab may be considered a preferred treatment option to IL-17is, for active AS patients**.

As such, UCB Canada Inc. is requesting that CADTH **acknowledge bimekizumab's potential advantages and more stringent endpoints** over currently available treatment options for active AS by including the following statement:

"*Although the results of the NMA and MAIC are subject to some uncertainty, evidence based on the NMA shows that bimekizumab demonstrated similar efficacy to the TNFi and JAKi classes and ixekizumab, and similar or higher efficacy to secukinumab. In addition, based on the MAIC analysis at week 52, patients treated with bimekizumab achieved higher response rates against secukinumab 150 mg and ixekizumab 80 mg on ASAS40 and further endpoints in patients with AS. This further strengthens the need for new treatment options, such as bimekizumab, which can achieve rapid and sustained improvement in patients' pain, stiffness, fatigue, and physical function."*

2. Bimekizumab provides an additional treatment option that produces rapid, consistent, and sustained improvements in clinical response across a broad range of axial and non-axial AS symptoms, function/disability, and HRQoL.

On page 5 of the draft recommendation, under Discussion Points, it is stated by CDEC that "The sponsor submitted another study (BE AGILE 2 trial, N=255) to address this gap. However, CDEC discussed that there was insufficient evidence to conclude any long-term comparative efficacy and safety advantages of bimekizumab over other treatments for AS."

Through a robust clinical trial program, **bimekizumab demonstrated rapid, sustained, and consistent results on stringent outcomes** (e.g., ASAS40) for a mixed population of biologic-naïve and TNFi-experienced patients with AS. In addition, bimekizumab addressed a broad range of axial and non-axial symptoms and improved quality of life (QoL). Results from long-term extension (LTE) studies demonstrated that **bimekizumab can be safely and effectively used long-term**, with data available up to approximately 5 years, which combined 48 weeks of treatment in BE AGILE and an additional 204 weeks of treatment in BE AGILE 2, with a safety follow-up at week 272. These results demonstrate the efficacy level achieved in BE AGILE at week 48 being sustained to week 256. In BE AGILE 2, ASAS assessments were conducted every 12 weeks from entry into BE AGILE 2 to week 208 (week 256 from the start of BE AGILE). According to the clinical experts consulted by CADTH, ASAS20 at week 12 has been considered an acceptable clinical response for the bDMARDs trials in AS. **Therefore, ASAS40 at week 16 is considered a major clinical improvement**.[1]

As such, UCB Canada Inc. is requesting that CADTH **acknowledge bimekizumab's potential long-term efficacy and safety advantages** for active AS by including the following statement:

"*Despite limitations identified by CDEC, prolonged bimekizumab treatment for up to 204 weeks in BE AGILE 2 was associated with sustained efficacy across all key endpoints, including long-term clinically meaningful improvements in measures of clinical response (ASAS40, ASAS20, ASAS-PR), disease activity (patient-reported BASDAI, ASDAS-MI), patient-reported physical functioning (BASFI, SF-36 PCS), and patient-reported HRQoL (ASQoL). These findings demonstrate that patients experienced rapid, consistent, and sustained improvements in their axial and non-axial manifestations of AS, as well as improvements in their HRQoL.*"

3. Bimekizumab is the 1st and only available humanised monoclonal antibody that binds to both IL-17F and IL-17A, demonstrating consistent and sustained efficacy on stringent endpoints for patients with AS all while addressing important outcomes valued by patients.

UCB Canada Inc. would like to highlight key benefits of bimekizumab that were absent from the draft recommendation. Bimekizumab is the **first and only humanized monoclonal antibody with dual specificity that selectively inhibits the biological activity of both IL-17A and IL-17F**, a pivotal driver of inflammation. Studies have demonstrated that dual neutralization of both IL-17A and IL-17F

suppresses inflammation processes to a greater extent than inhibition of IL-17A alone. Bimekizumab achieved a consistent improvement in ASAS40 response rates for patients with AS, which was **rapidly detected**, **significantly superior** to placebo at week 16, and **sustained** to week 52. The primary endpoint of ASAS40 at week 16 is a stringent treatment target and is considered a meaningful and worthy treatment goal from the patient perspective. In addition, achievement of ASAS40 has been found to provide a **greater improvement in physical function and HRQoL** than achieved with ASAS20. In addition, bimekizumab also provides **consistent** and **sustained low disease activity** (ASDAS<2.1), consistent for patients with AS, with **higher rates of remission** (ASDAS<1.3) compared with placebo. ASDAS<2.1 as a measure of low disease activity, including inactive disease, has become an important treatment target in AS as it is highly discriminatory and sensitive to change, better reflects the inflammatory disease processes compared with BASDAI, and more reliably determines the disease activity status of patients. Bimekizumab has demonstrated **significant efficacy compared with placebo for rates of low disease activity/inactive disease** (ASDAS<2.1). **Bimekizumab fills the gap for a need for new treatments that help patients to reach stringent outcomes with AS.**

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐

UCB Canada Inc. agrees that the committee has considered the stakeholder input provided to CADTH and would like to highlight key attributes of the clinician and patient group input that further strengthens the need for new innovative therapies in AS, such as bimekizumab.

CDEC acknowledged clinician- and patient-identified unmet needs such as **effective and safe treatment** that work well for all patients, a **limited availability of targeted therapies**, waning effectiveness of current therapies over time, and a **continuing need for effective treatment options for AS patients** who do not respond adequately to currently available treatments. Based on the results from the BE MOBILE 2 trial, **bimekizumab may address some of these unmet needs**. Input from the CADTH clinical expert stated: "They would not reserve bimekizumab for patients with refractory disease or patients who are intolerant to other therapies **as there are no other drugs targeting both IL17A and F cytokines**." It was also noted "that given **bimekizumab's efficacy in both musculoskeletal and skin disease**, it may be the **drug of choice** following treatment with NSAIDs in **patients with severe skin psoriasis**." The clinical expert lastly stressed that "**the treatment options for patients with active AS are limited and thus bimekizumab provides an additional treatment option for such patients.**"

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

UCB Canada Inc. agrees that the reasons for the recommendation are clearly stated.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐

UCB Canada Inc. agrees that the implementation issues have been clearly articulated and adequately addressed in the recommendation.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

UCB Canada Inc. agrees that the reimbursement conditions are clearly stated and the rationale for the conditions are provided in the recommendation.

[a] CADTH may contact this person if comments require clarification.

References:

1. CADTH. Clinical Review Report: Ixekizumab (TALTZ). 2020.