CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

bimekizumab (Bimzelx)

(UCB Canada Inc.)

Indication: The treatment of adult patients with active psoriatic arthritis. Bimzelx can be used alone or in combination with a conventional non-biologic disease-modifying antirheumatic drug (cDMARD) (e.g., methotrexate).

October 17, 2023

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CADTH in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings.

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Patient Group Input

C/O: Canadian Agency for Drugs and Technologies in Health (CADTH)

Re: Patient Input for Bimzelx

Date of submission: October 17, 2023

Section 1 — General Information

Name of the drug: bimekizumab (Bimzelx®)

Indication of interest: treatment of adult patients with active psoriatic arthritis

Name of patient group: Arthritis Consumer Experts

Name of the primary contact for this submission:
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Name of author (if different):
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Permission is granted to post this submission: Yes

Section 1 – About your Patient Group

Canada's largest, longest running national arthritis patient organization headquartered in Vancouver, BC, Arthritis Consumer Experts (ACE) provides free, science-based information and education programs in both official languages to people with arthritis. ACE and its team members acknowledge that they gather and work on the traditional, ancestral and unceded territory of the Coast Salish peoples - xʷməθkʷəy̓əm (Musqueam), Sḵwx̱wú7mesh (Squamish), and Səl̓ílwətaʔ/Selilwitulh (Tsleil-Waututh) Nations.

ACE serves people living with all forms of arthritis by helping them take control of their disease and improve their quality of life through education and (em)powerment. Founded and led by people with arthritis, ACE also advocates on arthritis health policy and provides research-based education through ACE's JointHealth™ family of programs and the Arthritis Broadcast Network, directly to consumers/patients, media, and government. ACE operates as a non-profit in a fully transparent manner and is guided by a strict set of guiding principles, set out by an advisory board comprised of leading scientists, medical professionals, and informed arthritis consumers. Ultimately, we are guided by the needs of our members, who are people living with arthritis, and their caregivers.

Link to website: www.jointhealth.org

Section 2 – Information Gathering

The information was gathered from patients who submitted their response via email on October 16, 2023 (Patients A and B) and patients who completed ACE's patient input survey through SurveyMonkey from December 18, 2020 to January 26, 2021 (Patient C to G).

Section 3 — Disease Experience

3.1 How does the disease impact the patients' day-to-day life and quality of life?

- **Patient A** was diagnosed with rheumatoid arthritis 22 years ago; however, a few years later, it was changed to psoriatic arthritis. They have difficulty walking up and down stairs, showering, and doing household chores.
- **Patient B:** "I am in pain most of the time - day and night. It is not severe and not always constant, but staying too long in one position or certain moves trigger it. The pain is in my hands, mostly the wrists, one hip at the sacroiliac and sometimes the lower back. Due to the pain, I cannot enjoy long walks or many other activities which I used to do. It also affects my mood."
- **Patient C:** Living with PsA for 47 years and also has fibromyalgia and is living with obesity. "My psoriatic arthritis is under control because of the medication I take and my quality of life is very good as a result."
- **Patient D:** Living with PsA for 22 years. They have "restricted ability to walk distances, difficulty opening door knobs and lids on jars, and using cutlery for meals". This patient experiences joint pain on a daily basis.
- **Patient E:** Living with PsA for 11 years. With medication therapies, they are able to control their PsA and maintain an active and busy life.
- **Patient F:** Living with PsA for 6 months. As a result of their PsA, they experience pain and reduced mobility function.
- **Patient G** was "diagnosed with PsA in 2015, but started to show symptoms in mid-eighties." They experience pain in many joints and require 45 minutes warm-up exercises every morning before their day starts. They also experience big toes problems and have "psoriasis in scalp and on face" that requires lotions.

3.2 How does the disease impact the caregivers' day-to-day life and quality of life?

- **Patient A** needs help "showering, cutting vegetables, and fruits."
- **Patient B:** "My mood affects my family. Also, I will soon have a granddaughter and want to be able to take care of her and hold her without fear that my wrists will give out."
- **Patient C:** "Since I am not a caregiver, I cannot say what these may be."
- **Patient D, E, F:** N/A
- **Patient G**: "None in my case."

3.3 Are there any aspects of the illness that are more important to control than others?

- **Patient A, D, E, F:** N/A
- **Patient B:** "My mood affects my family. Also, I will soon have a granddaughter and want to be able to take care of her and hold her without fear that my wrists will give out."
- **Patient C:** "Since I am not a caregiver, I cannot say what these may be."
- **Patient G**: "None in my case."

Section 4 – Experiences with Currently Available Treatments

How well are patients managing their disease/condition with currently available treatments?

- **Patient A:** "I am on Amgevita, prednisone, leflunomide, and Tylenol."
- **Patient B:** "I have just started Methotrexate. It has only been a month. I notice no positive effects yet, but have some side effects which so far are not too bad. Though it seems to me the pain has increased since I started taking it. The side effects are headache, some bouts of nausea and I find I am not able to sleep as well. Folic tablets help with the nausea. I would have liked to have been put on biosimilars as apparently, they can lead to permanent remission in many cases if they are used early enough. Due to cost, I was put on Methotrexate, at least for the beginning. No problem in taking the pills. My lifestyle is not impacted."
- **Patient C** is currently taking Humira and methotrexate. "This is very effective in controlling my psoriatic arthritis. I have so far been lucky in that I haven't experienced any adverse effects." This patient has no hardships accessing Humira and methotrexate.
- **Patient D** is currently taking Erelzi, methotrexate, Plaquenil, Tylenol and ibuprofen and is not aware of any adverse effects. "All have moderate success." This patient has no hardships accessing current therapies.
- **Patient E** is taking a combination of a Remicade infusion every 7 weeks and a weekly dose of methotrexate. They experience feeling of nausea for a couple days after methotrexate and higher level of fatigue all the time. When asked if there are any needs that are not met by current therapy, this patient stated: "Not for me to say – but many friends and relatives have asked about my treatments and their inability to access them or their acceptance of arthritis/pain as part of getting old." This patient has no hardships in accessing current therapies; they added: "But I have private coverage for Remicade, which is roughly $3K every 7 weeks – roughly $21-25,000."
- **Patient F** is controlling their psoriatic arthritis with medication and exercise; they state that both are not very useful and have no adverse effects. This patient would like warm water therapy to be available but this has stopped due to the pandemic.
- **Patient G:** "Exercise. Scalp lotion. Soak toes in yellow Listerine daily. Ointment on big toes twice a day. Skin cream on face once a day. Tylenol before heavy exercise. No therapy adverse effects." When asked if there are any needs that are not met by current therapy, this patient stated: "Access to gyms and recreation centres. COVID-19 has closed gyms – tough for exercise issue." This patient has trouble finding the time to exercise.

Section 5 – Improved Outcomes

- **Patient A** hopes that the new medication will have cause her to have less stiffness and allow her greater mobility. They also hope that there will no longer be a need for daily prednisone.
- **Patient B:** "I would like the pain to disappear permanently if possible. When on anti- inflammatory for 2 weeks at one point, I felt like a different person. My mood improved tremendously. I was happy. This is not the case when I have pain every day. Of course, my mood affects my family. Also, I will soon have a granddaughter and want to be able to take care of her and hold her without fear that my wrists will give out.

  All arthritis medications seem to have serious adverse effects. Depending on how much they help with the disease, we are all willing to make trade offs. So far with the Methotrexate, I do not see any improvement so I am less willing to accept more side effects. If it improves the pain, then of course that would make me more willing to tolerate the downsides."

- **Patient C:** "Potential side effects. In my case, how small an amount of these powerful drugs can be taken while still being effective (in order to minimize side effects)."
- **Patient D:** Cost
- **Patient E:** Side effects.
- **Patient F:** Investment of time when not really working.
- **Patient G:** Avoid drugs.

Section 6 – Experience with Drug Under Review

- None of the patients have had experience with the drug under review.

Section 7 – Companion Diagnostic Test

Not applicable to this submission.

Section 8 – Anything Else?

Arthritis Consumer Experts is providing this patient input submission based on patients who submitted their response via email on October 16, 2023 (Patients A and B) and patients living with psoriatic arthritis who completed ACE's patient input survey on SurveyMonkey between December 18, 2020 and January 26, 2021 (Patients C to G).

ACE made minor grammatical corrections to input where needed but in no way altered the meaning or intent of the input.

Appendix: Conflict of Interest Declaration

1) Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

This submission was summarized and written solely by the staff of Arthritis Consumer Experts, free from consultation, advice, influence, or financial support from any outside individual, group, or company.

2) Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

No.

3) List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

We have no direct or indirect financial support from the manufacturer of the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
UCB			X	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Cheryl Koehn

Position: President

Patient Group: Arthritis Consumer Experts

Date: October 17, 2023

Name of Drug: bimekizumab
Indication: psoriatic arthritis

Name of Patient Group: The Canadian Psoriasis Network (CPN), Arthritis Society Canada (ASC), the Canadian Arthritis Patient Alliance (CAPA), the Canadian Association of Psoriasis Patients (CAPP), the Canadian Spondyloarthritis Association (CSA), and CreakyJoints (CJ) collaborated on this joint submission.

Author of Submission: Antonella Scali, CPN, Brenda Delodder, CSA, Laurie Proulx, CAPA, Adam Kegley, CreakyJoints, Margretha Gonzalvez, ASC, Helen Crawford, CAPP

1. About Your Patient Group

The Canadian Psoriasis Network (CPN) is a national not-for-profit organization with a mission to enhance the quality of life of people with psoriasis and psoriatic arthritis. We do this in part by providing current information on research and treatment options and by working with others to build awareness and advocacy about the complexity of these conditions. www.canadianpsoriasisnetwork.com

Canadian Spondyloarthritis Association is the only patient-led organization in Canada solely dedicated to supporting people living with spondyloarthritis (SpA). CSA is the voice for Canadians living with SpA, which includes Axial Spondyloarthritis and Peripheral Spondyloarthritis, Ankylosing Spondylitis (AS), Psoriatic Arthritis (PsA), Enteropathic Arthritis and related conditions. CSA develops and delivers innovative programs to educate, support, advocate and raise awareness for patients, caregivers, and healthcare professionals. www.sparthritis.ca

The Canadian Arthritis Patient Alliance (CAPA) is a grassroots, patient-driven and managed, independent, national education and advocacy organization with members and supporters across Canada. CAPA creates links between Canadians with arthritis, assists them to become more effective advocates and seeks to improve the quality of life of all people living with the disease. CAPA believes the first expert on arthritis is the individual who has the disease, as theirs is a unique perspective. We assist members to become advocates not only for themselves but all people with arthritis. CAPA welcomes all Canadians with arthritis and those who support CAPA's goals to become members. Our website is updated regularly and can be viewed at: www.arthritispatient.ca.

For more than two decades, CreakyJoints has served as a digital community for millions of arthritis patients and caregivers worldwide who seek education, support, advocacy, and patient-centred research. All of our programming and services are always provided free of charge. CreakyJoints is part of the non-profit Global Health Living Foundation, whose mission is to improve the quality of life for people living with chronic illnesses. In keeping with our work at CreakyJoints USA, CreakyJoints Canada, available in English and French, inspires, empowers, and supports arthritis patients – and patients living with other chronic conditions – and their caregivers to put themselves at the centre of their care by providing evidence-based education and tools that help people make informed decisions about the daily and long-term management of arthritis and other chronic conditions. At the heart of CreakyJoints Canada is collaboration. We will continue and strengthen our work with Canadian arthritis organizations and patient advocates that you know, love and respect. We are all stronger together. For more information, please visit www.creakyjoints.ca.

Arthritis Society Canada is dedicated to extinguishing arthritis. We represent the six million Canadians living with arthritis today, and the millions more who are impacted or at risk. Fueled by the trust and support of our donors and volunteers, Arthritis Society Canada is fighting the fire of arthritis with research, advocacy, innovation, information and support. We are Canada's largest charitable funder of cutting-edge arthritis research. We will not give up our efforts until everyone is free of the scorching pain of arthritis. Arthritis Society Canada is accredited under Imagine Canada's Standards Program. For more detailed information, please visit www.arthritis.ca.

The Canadian Association of Psoriasis Patients (CAPP) is a national not-for-profit organization that was formed to better serve the needs of people living with psoriasis and psoriatic arthritis in Canada. We raise awareness about the burden of psoriatic disease, provide education, support research into psoriatic disease and advocate on behalf of our community. www.canadianpsoriasis.ca

2. Information Gathering

1.1. Data gathering

Information for this submission was obtained primarily through a survey hosted on Survey Monkey and made available through all the collaborating organizations' communication channels (including websites, social media platforms, and e- newsletters) from September 27-October 11, 2023, in English and French.

The organizations also sent the survey to clinics in Canada that conducted bimekizumab trials for PsA, requesting that that they share it with clinical trial patients and that they invite any patients who are interested to have an interview with our organizations to help inform the HTA submission.

The survey captured the experiences of people with psoriatic arthritis (PsA) and with ankylosing spondylitis (AS) as well as people who identified as caregivers of people with PsA or AS.

We received a total of 214 survey responses.

This submission reflects the perspectives of the 100 survey participants (47%) who identified as living with PsA. No survey participants identified as a caregiver of someone with PsA.

2.2 Regional data

Survey responses from people with PsA came from all provinces and territories except Northwest Territories, Nunavut, Nova Scotia, and Prince Edward Island. The majority (49.0%, n=49) of respondents were from Ontario, followed by Quebec (14%, n=14), and British Columbia (13%, n=13). The remaining responses came from: Alberta (9%), Manitoba (5%), New Brunswick (4%), Saskatchewan (3%), Newfoundland and Labrador (2%), and Yukon (1%).

2.3. Survey demographics

Of the 79 survey participants with PsA who indicated their age, 39% (n=31) are 55-64, just over a third (33%, n=26) are 65+, 22% (n=17) are 45-54, and 6% (n=5) are 35-44. Eighty per cent (n=63) identified as female and 20% (n=16) as male. The same ratio identified their gender as woman (80%) and man (20%).

Most survey participants who answered this question rate the severity of their PsA right now as "moderate" (52%, n=41), with 19% (n=15) stating that it is "severe". Several survey participants with PsA (n=77) reported living with additional conditions, including psoriasis (66%, n=51), another type of arthritis (42%, n=32), another inflammatory condition (31%, n=24), anxiety (30%, n=23), other (20%, n=15) which included asthma and "severe degenerative disc disease", diabetes (16%, n=12), and uveitis (10%, n=8). Fewer than 10% of respondents to this question also identified having liver disease, heart disease or stroke, another type of skin disorder, lung disease, kidney disease, and cancer respectively.

When asked about social demographics, of the 78 people who answered this question, 62 (79%) said that they are "white", and one respondent each stated that they are "Indigenous", "East Asian", "Latino" and "Middle Eastern" respectively. Approximately 40% (n=31) of respondents identified as a person with a disability. Two people (3%) identified as LGBTQ2S+.

Most survey participants (24%, n=18) who answered this question stated that their household income is $50,000-

$69,900; fourteen respondents (19%) stated $150,000 or more; six people (8%) stated $0-$29,999; five people (7%) said $30,000-49,999; with the rest falling in between.

Three of the 100 survey participants with PsA indicated that they have taken bimekizumab for PsA, however only one answered the questions related to their use of this drug.

3. Disease Experience

3.1 Disease experience

Survey participants were asked to identify the symptoms of PsA that they experience. Their responses are captured in Table 1.

Table 1: Symptoms of PsA identified by survey respondents (total of 92 respondents)

Symptom	Total (%)	Total (n)
Joint stiffness	94.57%	87
Fatigue	86.96%	80
Hip pain	64.13%	59
Back pain	64.13%	59
Changes in fingernails or toes	60.87%	56
Difficulties concentrating	57.61%	53
Sore heels	50.00%	46
Stress	43.48%	40
Anxiety	39.13%	36
Other (please specify)	38.04%	35
Redness and pain in the eyes	34.78%	32

Respondents who chose “Other”, identified the following symptoms (captured here as written in open-ended responses):

- Pinched nerve in neck / back and tension headaches
- Stiff feet, sore shoulder, muscle spasms
- Seized digits
- Knee, hands, wrists, feet, shoulders and tendon detachment
- Douleurs poignets, genoux, chevilles, orteils, etc
- I am just starting to feel achiness and pain in my left elbow down to the outside of my left hand.
- Pain in most of my fingers. Pain in my shoulders
- Extreme Feverish feeling, extreme pain in multiple joints
- Skin problems
- Hair loss
- Infection in fingers and toes do *[sic]* to meds lower immune system
- Unable to bend or stand and stomach pain
- Swollen toes
- Neuropathy
- pain in toes, feet, ankles, knees and hips, fingers and sometimes shoulder
- Orteils et dessous des pieds enfles et douloureux, doigts enfles, difficultes a ecrire et lire, douleur aux cervicales, aux épaules, aux bras…
- Pustular palmoplantar psoriasis
- Douleurs mains, genoux, pieds, hanches

- Easily bruise

Many who selected “other” also responded with pain in various areas including, ‘hands, elbows, knees, and feet’.

3.2 Impact on day-to-day life and quality of life

Survey participants were asked about the impacts of PsA on various areas of their lives. Their responses are captured in Table 2.

Table 2: Impacts of PsA on Survey Respondents Lives (total of 92 respondents)

Area of Life that is Impacted	**Total (%)**	**Total (n)**
Difficulties exercising/being active	80.43%	74
Challenges with sleep	75.00%	69
Ability to work	58.70%	54
Family life	51.09%	47
Social connections	50.00%	46
Mental health	50.00%	46
Intimacy	47.83%	44
Self-esteem	47.83%	44
Friendships	40.22%	37
Strain on finances	34.78%	32
Parenting	13.04%	12
Other (please specify)	6.52%	6
Participation in school	0.00%	0

Given that survey participants were over the age of 35, it is possible that we did not reach any participants actively in school and would suspect that impacts on school are present for people as well.

Respondents who answered “Other” shared the following (captured here as written in open-ended responses):

- Home maintenance, food preparation, hobbies snow removal etc.
- Psoriatic Disease has made me slow down so much!!! I can barely Walk anymore. I'm 54& I feel 80!
- During flares the above is true.
- None of the above
- Arrêt de travail, retraite anticipée.
- Stress

Table 3 captures how many days of work survey participants miss per month on average.

Table 3: Number of days of work missed each month on average by PsA survey participants due to symptoms or side effects (total of 90 respondents)

Number of days of work missed each month on average	Total (%)	Total (n)
I do not work or attend school for other reasons	32.22%	29
I do not typically miss school or work because of symptoms or side effects of PsA	27.78%	25
I cannot work or attend school due to PsA	22.22%	20
1-5 days	10.00%	9
6-10 days	5.56%	5
11-15 days	1.11%	1
>20 days	1.11%	1
16-20 days	0.00%	0

3.3 Experiences with barriers to accessing care and treatment

When asked if the cost of medication, travel to and from appointments, or time involved to receive medication limited one's use of treatments, or one's doctor's ability to prescribe a particular treatment option, some of the 78 respondents to this question said "no"; however, several others responded with the following (captured here as written in open-ended responses; italicized, bracketed words are by the author):

- It's difficult to get all my doctors to work together given my diagnosis. Ever *[sic]* Dr just treats the individual problem and does not work together. I am also seeking a second opinion for a Rheumatologist and it has been very difficult to get to see someone.
- Travel to appointments to a rheumatologist is a 6 hour drive return, yet I still prefer to consult with her in person at least once a year.
- Trop cher
- Two hours away hard to travel sometimes
- Yes *[systemic oral drug]* was prescribed to me and is not covered by my insurance. The out of pocket cost is extremely expensive
- Could not afford medication. So did not start until I was a senior
- Non car ils étaient payés par la cie
- When my doctor(s) have prescribed medication, it's been available and I've had help from different agencies with the cost; ie. Pharmacare, *[pharmaceutical manufacturer]*.
- The cost meant I did not get on a biosimilar for over a year. the other drugs did not help so it delayed my response to the disease once on the proper treatment for me

- If the government or my insurance provider did not cover my medication. I would not be able to afford it at. I think it's around 1400 a treatment, something like that or 1300 I'm not sure and I take it every 3 weeks so 2,600 every 3 weeks is not doable. So far it is been the only biologic that has worked for me and the add-on of mexotrexate *[sic]* and such is not great even though it is supposed to help
- too many specialists over a year with no pain relief
- My family doctor had no clue. Nearest decent rheumatologist is almost 2 hrs away. I failed most treatments- it's all discouraging
- Non. J'ai une bonne assurance au travail. Mais je ne pourrais pas me permettre de payer le *[systemic drug]*
- entirerement de ma poche.
- I wanted to get on *[biologic drug]* but was unable to. They could only offer me methotrexate.
- I have to travel over 2 hours to my doctor. And 2 hours home. This cause a huge amount of stress as well as expense.
- Just a lot of waiting and patience.
- Provincial coverage rules have. I need my biologic every 10 days since having Covid and province won't cover it
- I couldn't afford the medication if it wasn't covered by my benefits. Driving to my rheumatologist takes at least 2 hours out of my day which can be challenging but I only see them every 3 months so I guess that isn't too bad
- Yes, my drug coverage will not cover biologics
- No but if I didn't have an extended medical coverage through my employer (I'm on LTD) it would.
- The cost of traveling for in person rheumatologist appointments and dermatologist treatments causes strain on my finances.. i am only able to work part time and have difficulty securing employment due to my meed to attend medical appointments and recover from surgeries or flare ups. I no longer have a family doctor which means my follow up care and disease monitoring has become minimal or non existent. Side effects of medication are causing issues with my internal organs , daily life. My only option now is to attend urgent care or hospital emergency departments.
- À mon avis je trouvais que ça ne faisait aucun sens que je continue de travailler juste parce que j'avais une
- assurance médicament. J'ai donc appris a vivre sans....
- No as I have benefit coverage through my husband's employer
- Due to the Coverage my husband has being a Firefighter, That's the only way I can afford Medication!!!!

When asked specifically about how people pay for their treatments, most people (37%, n=30) indicated that they have private insurance through their employer, union or professional association; 32% (n=26) said that they are covered through a public (provincial/territorial/federal) program; 28% (n=23) indicated that they have coverage through their partner/spouse; 15% (n=12) say they receive coverage through a Patient Support Program or compassionate access; and 11% (n=9) say they pay for their medications out of pocket. We also heard (captured here as written in open-ended responses):

- I pay for the deductible in some of my meds
- Even though my employer benefits cover part of my prescriptions, with all of the medications, it can still be too much to afford.
- Doesn't cover completely and won't cover new drugs. My first specialist said I couldn't afford the drugs I needed, so would have to accept what I could…What an intro to the world of chronic conditions
- We pay for our own insurance through Canada Life. Doesn't mean they will cover it. But I'd love to participate in a trial!
- Not all meds are covered by the limited plan
- Retired and lost my plan
- If I am not working, I pay for private insurance. This puts a strain on my finances, as I am no longer able to work full time and I have limitations as to the type of work I can now do

We also heard from 33% (n=27) of survey participants who answered this question, that they have had trouble paying for medications, but they managed; 11% (n=9) said that they have stopped taking their medication when they could not afford it; and 5% (n=4) said that they have not filled their prescription or took less medication than prescribed when they have had trouble paying for medications.

3.4 Impact on Caregivers

When asked about caregiving support that people receive from family and/or friends, 71 survey participants responded to this question. Many indicated “N/A”, “No”, and “I did it all on my own”. Many others provided insights into the various ways that families/caregivers support them including the following (captured here as written in open-ended responses):

- Husband helps a bit but doesn’t fully understand my disease.
- Mon chum fait les emplettes, prépare quelques repas, fait la vaisselle il est très aidant
- Mon conjoint m'aide avec toutes ces choses.
- My wife has been very helpful with certain tasks.
- Daughter - does laundry, cooking, shopping, cleaning etc
- Il fait TOUT. Épicerie, ranger, laver, nettoyer, ménage, repas, tout
- I receive no support from my family; rather, I provide support for my elderly mother. My family still - after 25 years - don't understand how I can be well one day and not well the next.
- My husband helps with housework and errands. The fact that we both have a good income means I can afford the portion of medication costs I must pay each month.
- At times my family have helped me extensively with household chores, drives to appts etc. my husband is a very busy president of a large company, so I now have a cleaning lady / helper weekly bi always had her to do the cleaning biweekly and now to help me weekly. Have hired drivers for appts as my kids live across country. I went from being a very successful pharmaceutical rep & national trainer to retired too early financially & needing help. Can barely ever do my own minimal gardening or grocery shopping.

Many other responses indicated caregiver/family help with driving to appointments and when one cannot drive, providing emotional support, and offering financial support because “disability doesn’t pay me enough”.

4. Experiences With Currently Available Treatments

We asked survey participants to rate the effectiveness of the treatments that they have used. Their responses (n=85) are outlined in Table 4 below.

Table 4: Rating of effectiveness of treatment used by survey participants

Type of treatment	Very effective	Effective	Ineffective	Very ineffective	N/A
Non-steroidal anti-inflammatory drugs (NSAIDs) (e.g., ibuprofen, naproxen)	0.00%	**31.71%**	**37.80%**	17.07%	13.41%
Disease-modifying antirheumatic drugs (DMARDs) (e.g., methotrexate, azathioprine, cyclosporine, sulphasalazine)	7.32%	**39.02%**	**30.49%**	9.76%	13.41%
Leflunomide	3.28%	11.48%	14.75%	11.48%	59.02%
Apremilast (Otezla)	0.00%	8.20%	4.92%	3.28%	83.61%
Tofacitinib (Xeljanz)	0.00%	3.39%	1.69%	0.00%	94.92%
Upadacitinib (Rinvoq)	1.61%	4.84%	3.23%	3.23%	87.10%
Hydroxychloroquine	0.00%	12.31%	20.00%	9.23%	58.46%

Biologics (e.g., adalimumab-Humira, infliximab-Remicade, etc.)	**24.29%**	**40.00%**	10.00%	4.29%	21.43%
Steroid injections	7.35%	44.12%	7.35%	4.41%	36.76%
Oral steroids	6.45%	20.97%	3.23%	3.23%	66.13%
Medical cannabis	3.17%	14.29%	9.52%	4.76%	68.25%

Not surprisingly, given the heterogeneity of psoriatic arthritis and responses to treatments, the responses vary. NSAIDs are found to be “effective” by 32% (n=26) of respondents and “ineffective” by 38% (n=31) of respondents. DMARDs have a similar split with 39% (n=32) of respondents indicating that they are “effective” and 31% (n=25) stating that they are “ineffective”. Biologics have the highest proportion of "very effective" (24%, n=17) or "effective" (40%, n=28) ratings.

When asked about their experiences with current treatments, 22% (n=18) strongly agreed and 63% (n=52) agree that the dosing schedule is convenient; 27% (n=22) strongly agree and 52% (n=43) agree that their prescriber can prescribe the preferred/appropriate treatment for their circumstances; 14% (n=11) strongly agree and 41% agree that treatment allows them to resume daily activities, like work, parenting, household tasks; and 11% (n=9) strongly agree and 39% (n=32) agree that any side effects caused by treatment are tolerable.

When asked if their current treatment is affordable, 24% (n=20) strongly disagree and 13% (n=11) disagree. Moreover, over 18% disagree or strongly disagree that their current treatment allows them to resume daily activities. Overall, almost 30% disagreed or strongly disagreed with the statement “my needs are met with the treatment I receive”.

In the general comments about experiences with treatments, we heard the following (captured here as written in open- ended responses):

- I have a really good double drug plan. I would have difficulty affording my drugs otherwise.
- My insurance will not approve otezla on methotrexate and it’s not effective
- Treatment is expensive but i can afford the portion my insurance does not pay. my rheumatologist has to constantly justify my continuing this expensive treatment
- Biologic does not last until next dose, leaving me with new symptoms and pain all over again
- Wish drugs (biological)weren’t so expensive and that my dr would try a newer drug as I believe my body not responding to Enbrel as it first did many years ago when I started it.
- Insurance covers my prescription currently but I won’t be able to afford them when I retire
- No improvement to deformation but no progression either.
- Could not get in person instruction for injections for some time. Cannot take oral medication without real awful side effects
- I can afford my prescriptions, only because Alberta non-group health care is willing to cover my biologic, and the drug company is supplementing my premiums for AB non-group coverage. My benefit plan through work would not cover my biologic. Without the assistance from AB Blue Cross Non Group, I would not be able to afford my treatment.
- Le méthotrexate me donnait l'envie de vomir après 2 ans.

In terms of side effects that they found intolerable or difficult to manage, survey participants reported the following experiences with their current medications (captured here as written in open-ended responses):

- Yes my feet became numb and irritated in the leflunomide. Methotrexate hurt my liver.
- Methotrexate spikes my liver numbers so a reduced dose is ineffective for me
- Certains médicaments me causent beaucoup de nausées/vomissements
- Allergies to Methotrexate were the reason for turning to biologics
- initially redness/itching at injection site with biologic; resolved initailly GI upset with methotrexate resolved

- Difficult to manage body temperature. Extreme fatigue after treatment.
- Arrêt dû aux effets secondaires: infections, champignons, à répétition
- I have stomach and intestinal problems with all the medications I've been taking.
- I had headaches from methotrexate and still have them occasionally as I am taking it in combination with simponi. I have tinnitus which is not going away and has gotten more severe with the medication. I am tired.
- Methotrexate side effects were extremely difficult to manage and needed to be discontinued after many years of taking it.
- Hair loss
- Migraines
- Headaches

5. Improved Outcomes

Regarding what they would like to see in a new treatment, respondents expressed the following (captured here as written in open-ended responses):

- Reduce further damage to joints
- Pills are easy to swallow, but having autoimmune issues leaves you on many medications and adding another pill is not what I would hope for. If it is daily okay, but if it is weekly or semi-monthly, I would prefer injection.
- It should last until the next scheduled dose
- I would like the new med that helps with hair loss (not approved yet in Canada) but rheumatologist says I'm doing too well on my current meds to warrant a change
- Assists with fatigue
- Less risk of damage your organs or increased risk of cancer.
- I would love a medication that doesn't make me immunocompromised.
- Helps with fatigue and pain
- If it works better than my current tx

When asked about what survey participants would like to see as the biggest improvement in PsA treatment, we heard several insights from the 79 respondents to this question. Several indicated, less fatigue, less pain, less stiffness. Many stated that they wanted to see the progression of disease diminished. Moreover, several said “a cure”. We also heard the following (captured here as written in open-ended responses):

- A med that treats all my symptoms and Physicians that treat people and collaborate together for their patients
- *[sic]* best health
- Get my energy back. Decrease in muscle fatigue and joint stiffness. Improved mood.
- Less joint pain, fatigue and fewer flares with so much rolling aches along the limbs.
- Something that will actually work
- More recognized
- Elimination of pain and swelling
- Improved strength and pain reduction in my hands back and shoulders.
- Better access to physiotherapists, massage therapists, nutritionists etc
- Diminution effets secondaires
- Stabiliser la maladie sur plus de 9 mois consécutifs. Être en mesure d’avoir une vie normale
- Less pain - back, hips, feet, better sleep, better concentration, memory

- Would like medication that works but has no side effects. Also one that is cost effective enough so that patients don't have to wait over a year and go through other medications and side effects for months on end in order to get put on it.
- Just more help being able to get the biologic medicine easier than having to jump through so many hoops to get it covered.
- Better and quicker treatment options when first diagnosed. it took several years and change in doctor (which I had to fight for) to get where I am today.
- Reduced side effects and require less bloodwork
- Affordable biologic treatment. Less frequent doses
- Easier coverage from provinces as most group plans no longer cover biologics

6. Experience With Drug Under Review

We made several attempts to contact clinical trial participants that had taken bimekizumab for PsA but were unable to speak with anyone directly. The survey responses provided insights into the expectations of people with PsA with regards to new therapies which are expressed below as a percentage of total respondents:

- Improves symptoms (77%, n=62)
- Better quality of life, e.g., return to work, able to socialize more, mental wellbeing, fewer doctor visits (72%, n=58)
- Affordable to purchase (67%, n=53)
- Reduced side effects (59%, n=48)
- Treatments are easier to take, e.g., dosing schedules are simpler, pill easier to swallow (36%, n=29)

As highlighted in sections above, symptoms reported by people with PsA (expressed as a percentage of total respondents) include joint stiffness (95%), fatigue (87%), back pain (64%), hip pain (64%), changes in fingernails or toes (61%), sore heels (50%), stress (43%), difficulties concentrating (58%), anxiety (39%), and redness and pain in the eyes (35%). Quality of life most impacted by PsA (expressed as a percentage of total respondents) includes difficulties exercising / being active (81%), challenges with sleep (75%), ability to work (58%), family life (51%), mental health (50%), social connections (50%), self-esteem (48%), intimacy (48%), friendships (40%), strain on finances (35%), and parenting (13%).

We also heard from one survey participant who answered questions from the perspective of having used bimekizumab for PsA. They agreed with the following statements about bimekizumab:

- Bimekizumab is easier to use than other therapies
- Bimekizumab’s instructions are easier to follow than other therapies
- Bimekizumab improved quality of life
- Bimekizumab helped me to return to daily activities

This survey participant also indicated that they experienced an intolerable side effect and that, “…sans cet effet secondaire, je l’aurais pris durant longtemps… ma qualité de vie avait augmenté mais ces champignons récalcitrants

+l’assurance qui ne le couvrait pas …”

7. Companion Diagnostic Test

N/A

8. Anything Else?

PsA is complicated, frustrating and can be debilitating without access to appropriate treatments. Patients are very different in how they react to changes in lifestyle, topical treatments, oral treatments, and biologics. What works for one patient may not work for the other, even if their symptoms are very similar.

For many, PsA is a disease that often “falls through the cracks.” Some patients are seen by a dermatologist while others are seen by rheumatologists. Joint pain is not always discussed with a dermatologist and plaques on the skin are not always discussed with rheumatologists. These challenges often lead to delays in diagnosis of PsA and consequently potential damage to the joints. PsA is also linked with other associated conditions, including an increased risk of cardiovascular disease, specifically atherosclerotic disease (low grade inflammation in blood vessels). People with PsA may have to navigate multiple health care professionals, treatments, and other supports (like physiotherapy or occupational therapy) to manage their disease.

All patients are looking for a treatment that will control all their symptoms but, ultimately, they would like a cure to this debilitating disease. Earlier treatment of PsA can result in better outcomes and reduce the risk of permanent and debilitating joint damage.

9. Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

N/A

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

N/A

2. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
AbbVie Canada			X	X
Amgen Canada			X	
Bausch Health			X	
Bristol Myers Squibb			X	
Boehringer Ingelheim International		X		
Boehringer Ingelheim Canada			X	
Janssen Canada			X	
LEO Pharma Canada			X	
Novartis Canada			X	
Pfizer			X	
UCB Canada			X	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Antonella Scali

Position: Executive Director

Patient Group: Canadian Psoriasis Network

Date: October 18, 2023

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
AbbVie Canada			X	X
Amgen Canada			X	
Bausch Health			X	
Bristol Myers Squibb			X	
Boehringer Ingelheim International		X		
Boehringer Ingelheim Canada			X	
Janssen Canada			X	
LEO Pharma Canada			X	
Novartis Canada			X	
Pfizer			X	
UCB Canada			X	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Brenda Delodder

Position: Executive Director

Patient Group: Canadian Spondyloarthritis Association

Date: October 18, 2023

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
AbbVie			X	
Amgen		X		
Boehringer Ingelheim		X		
BMS		X		
Eli Lilly	X			
Fresenius Kabi	X			
Innovative Medicines Canada	X			
J+J Shared Services			X	
JAMP Pharma		X		
Janssen Canada			X	
Nordic Pharma				X
Novartis	X			
Organon			X	
Pfizer				X
UCB Canada		X		
Valeo		X		

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Joanne Di Nardo/Kelly Gorman

Position: Senior Director, Public Policy and Government Affairs (job share)

Patient Group: Arthritis Society Canada

Date: October 18, 2023

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Abbvie Corporation			X	
Brooks Group Inc.	X			
CADTH	X			
Canadian Association of Occupational Therapists	X			
Sparkplug Coffee	X			
FingerPost Consulting Ltd.	X			
GlaxoSmithKline	X			
Government of Canada (Canada Summer Jobs)	X			
Government of Canada (Canadian Heritage)	X			
Innomar Strategies Inc.	X			
Innovative Medicines Canada			X	
Janssen Inc.		X		
McMaster University		X		
Pfizer Inc.			X	
Queens University	X			
Save You Skin Foundation	X			
The Arthritis Society			X	
The Brooks Group	X			
Toronto General Hospital Research Institute (UHN)	X			
UCB Canada Inc.			X	
UCB Inc.	X			
University of British Columbia		X		
University of Calgary	X			
University of Manitoba	X			
University of Toronto	X			
University of Waterloo	X			
University of Western Ontario & Queens University	X			

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Laurie Proulx

Position: Managing

Director Patient

Group: CAPA

Date: October 18, 2023

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
AbbVie Corporation			X	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Adam Kegley

Position: Manager, Global Partnerships

Patient Group: CreakyJoints Canada

Date: October 18, 2023

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Arcutis Canada			X	
Janssen Canada			x	
BMS	x			
Novartis Canada			x	
Novartis Global	x			
Pfizer Canada			x	
Sun Pharma			x	
Boerhringer Ingelheim			x	
Boerhringer Ingelheim Global	x			

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Helen Crawford

Position: Programs Manager

Patient Group: Canadian Association of Psoriasis Patients

Date: October 18, 2023

Clinician Group Input

CADTH Project Number: **SR0803-00**

Generic Drug Name (Brand Name): **Bimekizumab (Bimzelx)**

Indication: **The treatment of adult patients with active psoriatic arthritis. Bimzelx can be used alone or in combination with a conventional non-biologic disease-modifying antirheumatic drug (cDMARD) (e.g., methotrexate).**

Name of Clinician Group: **Canadian Rheumatology Association**

Author of Submission: **Therapeutics committee**

1. About Your Clinician Group

The Canadian Rheumatology Association (CRA) is the national professional association for Canadian rheumatologists.
The **mission** of the Canadian Rheumatology Association is to represent Canadian rheumatologists and promote the pursuit of excellence in arthritis and rheumatic disease care, education, and research. http://rheum.ca/about-us/
The CRA Therapeutics Committee Identify and address all therapeutic issues that are relevant to the CRA membership as well as develop position statements and respond to drug shortages/withdrawals as required.

2. Information Gathering

We searched within the collection of our guidelines and position papers and previous submissions to CADTH; we added a complementary search on TRIPDatabase for further guidelines and relevant synthesis and primary evidence.

3. Current Treatments and Treatment Goals

Psoriatic arthritis (PsA) is an autoimmune disease that can cause inflammation, pain, and stiffness. It is reported in less than 1% of the general population. It is present in 20 to 30% patients with psoriasis. It usually presents at 30-50 years old, but it can occur at any age. The clinical presentation is variable and might change over time. Most patients (95%) have peripheral arthritis: this observation may be biased though as they might have other types of musculoskeletal involvement that can be mislabelled (such as having axial spondyloarthritis if the only manifestation is axial disease) or underdiagnosed (mechanical enthesopathies). For patients with arthritis, the number of inflamed joints may vary. Some patients present with oligoarthritis (less than 5 joints affected), whereas others present with polyarticular disease. In addition, the patterns may change over time (such as a patient presenting with <5 inflamed joints initially, then having >5 inflamed joints at follow-up). Mostly due to the change in patterns over time, the frequency of oligoarthritis varies between 25% to 65% (Gladman DD. Ann Rheum Dis 2005;64Suppl 2: ii14–7, Dhir V. Clinic Rev Allerg Immunol 2013;33:141–8). The severity of skin and arthritis symptoms are usually independent. Axial disease is reported in 24-78% of PsA, depending on the definition of axial disease. However, only 2% of psoriatic arthritis patients have axial disease in isolation (Hanly JG. Ann Rheum Dis.1988;47:386-93, Battistone MJ. Skeletal Radiol 1999; 28:196-201, Jadon DR Ann Rheum Dis. 2017;76:701-7). Most patients have psoriasis before the onset of psoriatic arthritis, but 15 to 20% of patients develop both simultaneously (T Kwok. Ann Rheum Dis 2022;81(12):1678-1684).

The predominant goal of therapy is to maximize health-related quality of life through control of symptoms, improvement of function, prevention of structural damage. This is usually achieved by controlling the inflammation. One of the challenges of the management of psoriatic arthritis is that treatments for the skin and the joint rarely work at the same time. Additionally, many patients might have also enthesitis, inflammatory bowel disease or other comorbidities like diabetes, hypertension, cardiovascular disease and depression.

In the Canadian context, non-pharmacologic therapies such as graded exercise program, occupational therapy, diet, weight loss, and smoking cessation are recommended for all patients although it is unlikely that they could be adequately controlled in this manner alone. In addition, access to non-pharmacological therapies is inconsistent across the country.

For the treatment of the skin disease, the treatments are the same as the patients with psoriasis, and they might include topical emollients, corticosteroids, vitamin D analogs, tazarotene, dithranol (anthralin), and coal tar; phototherapy with psoralen plus ultraviolet A (PUVA) or narrowband ultraviolet B (UVB); traditional nonbiologic disease-modifying antirheumatic drugs (csDMARDs) (methotrexate [MTX], cyclosporine A [CSA], acitretin, fumaric acid esters); phosphodiesterase (PDE)4 inhibitor (apremilast) or biologic therapy (tumor necrosis factor [TNF] inhibitors, interleukin [IL] inhibitors [IL-12/23i, IL-17i]).

For the management of the peripheral arthritis, a csDMARD such as methotrexate, sulfasalazine, or leflunomide may be considered. In some jurisdictions they recommend TNF-inhibitors as a first line of treatment (ACR guidelines, L Gossec. Ann Rheum Dis. 2020;79(6):700-712), but in most parts of the world the recommendation is to limit biologic therapy to those who have an inadequate response to csDMARDs. In the Canadian context, SPARCC considered trying two different csDMARD before considering a first biologic therapy.

Enthesitis is typically managed with a trial of NSAIDs, physiotherapy, and local corticosteroid injection (with caution due to the risk of rupture and only if appropriate) (Tsechelidis OB. Clin Ther. 2023 Sep;45(9):852-859). A csDMARD may be trialled for persistent enthesitis. Finally, a targeted synthetic DMARD (such as a JAK inhibitor) may be initiated if patients with peripheral inflammatory arthritis or enthesitis are unresponsive to these measures.

Extra-articular manifestations are typically managed by their corresponding specialist (dermatologist for psoriasis, ophthalmologist for uveitis, and gastroenterologist for inflammatory bowel disease).

The use of glucocorticoids can be considered as adjunctive therapy, preferable as local injections. Systemic treatment might be used at the lowest dose.

All approved treatments have been demonstrated to improve symptoms, function, and health related quality of life in patients. These treatments are summarized in the EULAR and ACR treatment recommendations (J Singh. Arthritis Care Res (Hoboken). 2019;71(1): 2–29; L Gossec. Ann Rheum Dis. 2020;79(6):700-712.)

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

There is still unmet need in the management of psoriatic arthritis. Limitations to current therapies include:

1. Patients showing improvement in arthritis measure but not in skin and vice versa. Similarly, one musculoskeletal domain (such as peripheral arthritis) may respond to a therapy, but may be unresponsive for axial disease (more with IL 12/23 inhibitor therapies) or other domains (such as enthesitis or dactylitis).
2. Not all patients respond to treatment. csDMARDS can achieve response in about half of patients with arthritis, and clear or almost clear skin on 2/3 of patients.
3. Secondary loss of effect with biologics results in either dose creep, trial of untested combination therapies and/or the need to switch medications.
4. Persistence of active extra-articular manifestations such as inflammatory bowel disease despite improvement in MSK symptoms despite treatment with current biologics
5. Side effect profiles with current biologics such as drug induced lupus, psoriasis, multiple sclerosis (with TNFi), increased risk of infections and inflammatory bowel disease (IL-17i) or increase cardiovascular risk (JAKi) limit the use of the approved biologics

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

Bimekizumab is a monoclonal antibody that uniquely targets both IL-17A and IL-17F, two closely related cytokines that contribute to inflammation in PsA. This dual inhibition provides a more comprehensive approach to suppressing the inflammatory pathways responsible for the disease(Glatt S. Ann Rheum Dis. 2018;77: 523-532, Adams R. Front Immunol. 2020; 11: 1894). In psoriatic arthritis, skin lesion and inflamed synovia have similar patterns of expression and upregulation with IL17-A and IL17-F, suggesting it could influence both manifestations.

Bimekizumab was approved in the European Union in 2021 for the treatment of moderate to severe plaque psoriasis, active psoriatic arthritis, non-radiographic axial spondylarthritis, and active ankylosing spondylitis. In Canada bimekizumab is approved for severe plaque psoriasis.

Results from the dose-response phase of the BE-ACTIVE study have shown that the dual inhibition results in clinically meaningful improvements in both skin and musculoskeletal outcomes compared to placebo.

BE OPTIMAL compared bimekizumab against placebo and adalimumab in biologic naïve patients with psoriatic arthritis. It showed substantial benefit against placebo, but similar results on the benefits and harms to adalimumab. There are no other head-to-head trials to test superiority of Bimekizumab. Therefore, it is not expected that Bimekizumab will cause a shift in treatment algorithm for muscusloskeletal domains of Psoriatic Arthritis. However, in psoriasis clinical trials, Bimekizumab was shown to be noninferior and superior to Secukinumab for PASI100 response. (K Reich. N Engl J Med 2021; 385:142-15). The superiority of IL17 A-F blockage over IL17 A may impact the within class therapy decisions for patients with severe skin involvement.

The BE COMPLETE study compared use of bimekizumab against placebo in psoriatic arthritis patients with incomplete response to TNF inhibitors. It showed a rapid and clinically important response in all outcomes measured, both in skin and musculoskeletal symptoms.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

There is no data that supports which subset of Psoriatic Arthritis patients are most likely to respond to bimekizumab.

Patients most in need of intervention would be those who have failed treatment with csDMARDs and continue to have high measures of disease activity. As psoriatic arthritis involves different domains, choice of treatment is usually determined for which of them are responding to treatment or not. The following treatment flow developed by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) captures how to incorporate the different options of treatment depending on which domains of disease are not responding.

Fig 2 from L Coates. Nature Reviews Rheumatology 2022;18,465–479 (Coates LC, Soriano ER, Corp N, et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021. *Nat Rev Rheumatol.* 2022;18(8):465-479.)

Bimekizumab was originally approved for plaque psoriasis, and later showed efficacy as well for axial disease, enthesitis and dactylitis, in addition to peripheral arthritis. From this perspective, it is a useful addition when any of these domains are involved.

The clinical trials involve patients with certain levels of disease activity for arthritis and skin psoriasis as the inclusion criteria and subsets of patients have enthesitis and dactylitis- which are secondary outcomes. All of these domains in clinical trials are diagnosed and severity assessed with physical examination, which is the current standard to judge disease activity in daily practice. The radiographic features can be helpful for diagnosis if positive, and for prediction of disease course; however, the radiographs do not usually play a role in deciding the best treatment, since the aim of the treatment is to prevent any radiographic damage from happening.

The assessment of axial disease in psoriatic arthritis is mostly borrowed from axial spondyloarthritis trials. Two Bimekizumab trials in axial spondyloarthritis included patients with nr-axSpA (active sacroiliitis on MRI fulfilling the ASAS criteria (MRI+) (RGW Lambert. Ann Rheum Dis 2016;75:1958–63) and/or elevated C-reactive protein (CRP+) ≥6.0 mg/L) and r-axSpA (fulfilling modified New York (mNY) criteria by having radiographic evidence of sacroiliitis: grade ≥2 bilateral or grade ≥3 unilateral). Therefore, the decision of treatment for axial disease is likely to benefit from imaging of the sacroiliac joints and/or CRP.

Enthesitis is an early manifestation and debilitating symptom in Psoriatic arthritis patients, even in the absence of (severe) arthritis. It might be an area that leads to underdiagnosis. Since the physical examination lacks specificity to differentiate mechanical

enthesopathies from inflammatory enthesitis, it is becoming an increasing practice to perform musculoskeletal ultrasound or other imaging techniques such as MRI to diagnose inflammatory enthesitis, if the domain will impact therapy decisions. Incorporating a musculoskeletal ultrasound assessment to diagnose enthesitis would lower the false positivity and allow the identification of patients who are likely to benefit from bimekizumab or other advanced therapies for enthesitis domain. However, musculoskeletal ultrasound or MRI is not yet available in every center. Therefore, an imaging mandate for enthesitis may impact the equity in accessing the treatment. Currently, psoriatic arthritis patients with isolated enthesitis generally are not able to access similar therapies across Canada, which is an unmet need / undertreated domain.

In the absence of head-to-head trials, bimekizumab is not tested to be superior or inferior to the alternative therapies, such as anti-TNs, other IL-17i's, IL23i's or JAKi's to treat peripheral arthritis, enthesitis or dactylitis. Biologic therapy is a not a first line of treatment in the GRAPPA treatment recommendations. Which medication will be chosen after failure of initial treatment within the effective options for that domain is usually based on patient-related factors (for example not using IL-17i's if the patient has IBD; or not using the JAKi's if there are multiple cardiovascular risk factors...) as well as the patient's preference.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Clinical evolution is usually determined by the different disease domains. Representing the heterogeneity of the disease, clinical trials have multiple outcome measures, some focusing on the response in the joints, whereas some others focus on enthesitis, dactylitis, axial disease and skin response. Most composite indices that are commonly used in clinical trials include a combination of some or all these domains, such as Composite Psoriatic Disease Activity Index (CPDAI), disease activity in psoriatic arthritis (DAPSA), and Psoriatic Arthritis Disease Activity Score (PASDAS), but are not practical for daily practice. In contrast, the Minimal Disease Activity (MDA) is a feasible tool that is easy to apply in clinical practice and also commonly used in clinical trials (LC Coates. Ann Rheum Dis 2010;69:48–53). Patients achieve MDA when 5 of the following 7 criteria are met: tender joint count ≤ 1; swollen joint count ≤ 1; Psoriasis Area and Severity Index ≤ 1 or body surface area ≤ 3%; patient pain visual analog score (VAS) ≤ 15; patient global disease activity VAS ≤ 20; Health Assessment Questionnaire (HAQ) Disability Index ≤ 0.5; tender entheseal points ≤ 1.

For skin disease, the Psoriasis Area and Severity Index (PASI) score is commonly used in RCTs. In practice, the body surface area (BSA) involvement of psoriasis is the most practical measure. Patients with severe skin disease are likely to be co-managed with a dermatologist.

For axial disease, the most frequently used outcome measure for disease activity in Canada is the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). This is also commonly used for insurance and reimbursement purposes.

Figure of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) on an NRS, from the slide deck of the Assessment of SpondyloArthritis International Society and originally from Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol.* 1994;21(12):2286-2291.

Rheumatologists in Canada consider an improvement in the BASDAI score of 2 points or 50% reduction from baseline to be a meaningful improvement. This is also what payers (insurance companies and provincial payers) consider to be a meaningful response to treatment.

This questionnaire assesses several domains of the patient's experience with axial disease, including pain, fatigue, and morning stiffness. A score of 4 or higher is considered to be high disease activity and would be considered candidates for therapy with bimekizumab.

Clinical trials often use an ASDAS response as an outcome measure instead of a BASDAI score. ASDAS has the advantage of incorporating CRP to the more subjective questions included in BASDAI and has been shown to be superior in predicting future damage in axial spondyloarthritis (S Ramiro. Ann Rheum Dis 2014;73:1455–61. D Poddubnyy. Ann Rheum Dis 2016;75:2114–8).

Figure of Quick ASDAS-CRP Calculation Form, from the open-access slide deck of the Assessment of SpondyloArthritis International Society, and originally from Calin A, Garrett S, Whitelock H, et al. A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. *J Rheumatol.* 1994;21(12):2281-2285.

However, it is mostly not feasible to have the CRP at the time of the clinical visit, so it is often not used in "real life" outside of clinical trials. It is important to note that, neither BASDAI nor ASDAS were established for axial psoriatic arthritis. They were both developed for assessing disease activity in axial spondyloarthritis and have been borrowed to be used in axial psoriatic arthritis. One trial that compared the BASDAI and ASDAS in axial psoriatic arthritis failed to show the superiority of ASDAS (L Eder. Ann Rheum Dis 2010;69:2160-2164). Therefore, BASDAI is the most commonly used index to monitor axial psoriatic arthritis in clinical practice. Since the BASDAI is driven by patient-reported outcomes, it should not vary from physician to physician.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

- Lack of response to therapy.
- Adverse events (in particular, fungal infections, serious infection, newly presented inflammatory bowel disease).
- Patient preference, as part of the shared decision-making process, for example, if they have difficulty using the treatment or prefer another way of administration.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

Bimekizumab is provided as subcutaneous injections, that would allow for self-administration by the patient.

A specialist (rheumatologist) will be required to prescribe bimekizumab and to monitor for adverse events. Regular bloodwork will need to be monitored by the rheumatologist for any adverse events.

6. Additional Information

The addition of a dual mechanism of inhibition for IL17a and f and rapid response to treatment provides potentially an additional option for treatment. Due to the limited amount of advanced therapeutics, it will be a welcome addition for both clinicians and patients.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

   This document was drafted by Drs. Peter Tugwell and Sibel Aydin, and verified by Dr. Carter Thorne.

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   Jordi Pardo Pardo run the searches and assisted adding references and with the final editing.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for <u>each clinician</u> who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Peter Tugwell

Position: Professor

Date: 30-09-2023

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Reformulary Group	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Sibel Aydin

Position: Professor

Date: 8/10/2023

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
UCB		X		
Abbvie			X	
Pfizer		X		

Novartis			X	
Janssen		X		
Fresenius- Kabi	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Carter Thorne

Position: Community Rheumatologist, Assistant Professor

Date: 9/10/2023

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Abbvie	X			
Biogen	X			
Nordic	X			
Pfizer	X			
Roche	X			
Sandoz	X			

* Place an X in the appropriate dollar range cells for each company.