Canada's Drug Agency
L'Agence des médicaments du Canada

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

bimekizumab (Bimzelx HS)

(Sponsor's Name)

Indication: For the treatment of adult patients with moderate to severe hidradenitis suppurativa.

November 4, 2024

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CDA-AMC 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. **If your group has submitted input that is not reflected within this document, please contact Formulary-Support@cda-amc.ca.**

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CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: Bimzelx (bimekizumab)
Indication: Hidradenitis suppurativa
Name of Patient Group: Canadian Skin Patient Alliance (CSPA), Hidradenitis and Me Support Group
Author of Submission: Sabrina Ribau (CSPA), Dana Gies (CSPA), Latoya Palmer (Hidradenitis and Me Support Group), Chevonne Smellie (Hidradenitis and Me Support Group)

1. About Your Patient Group

This submission is supported through a collaboration between The Canadian Skin Patient Alliance (CSPA) and Hidradenitis and Me Support Group. CSPA is a national charity organization that improves the health and well-being of people across Canada affected by skin, hair, and nail conditions through collaboration, advocacy, and education. Hidradenitis and Me Support Group fosters self-care and a safe space for people with HS to connect with other individuals with HS, express their struggles, and gain knowledge about this skin condition.

2. Information Gathering

2.1 Data gathering

Data for this hidradenitis suppurativa (HS) treatment submission was gathered and compiled from the survey results from the 2020 National Report of Patients' Experiences Living with HS, The Health Policy Partnership's 2024 Call to action: improving the lives of people with hidradenitis suppurativa in Canada, and a patient survey hosted on CSPA's, HS Heroes', and HS & Me Support Group's communications channels from March 28 to May 23, 2023 in both English and in French. In this submission we report on combined English and French survey responses from the 2023 survey. A total of 15 survey responses were received, all in English. In addition, HS & Me Support Group posted in a Facebook group of Canadian HS patients and supporters requesting patient experiences using the subject drug.

2.2 Regional data

The 2020 National Report of Patient's Experiences Living with HS was based on an HS Patient Experience Survey that had the goal of providing a baseline measure for the state of care for individuals with HS. This survey was completed by 537 individuals with HS, of which 73 (14%) were from Canada, 267 (50%) were from the United States, and 67 (12%) were from the United Kingdom. The greatest proportion of Canadian participants were from Ontario (41%), followed by Alberta (18%).

The Health Policy Partnership 2024 report, Call to action: improving the lives of people with hidradenitis suppurativa in Canada aims to raise awareness of the burden of HS and the barriers faced by Canadians with condition along the entire patient pathway. The report was guided by a steering committee comprising of a patient representative and healthcare professionals.

The 2023 patient survey contained respondents from Canada, with the majority being from Ontario (47%, n=7). A smaller proportion of respondents also came from Alberta (27%, n=4), Manitoba (13%, n=2), Northwest Territories (7%, n=1), and British Columbia (7%, n=1). There were no survey respondents from Yukon, Nunavut, Saskatchewan, Quebec, Nova Scotia, New Brunswick, Prince Edward Island, or Newfoundland and Labrador.

2.3 Survey Demographics

The average age of individuals completing the 2020 survey was 38 years (range: 14-73) with 85% being under the age of 50 years. Of all patients, 93% identified as biologically female. Of all the participants, 68% did not have private insurance coverage.

All respondents in the 2023 patient survey were between 25 and 44 years of age, with 50% (n=5) being 25-34 years old and 50% (n=5) being 35-44 years old. There were no individuals under 25 years or over 44 years old. Thirty-three per cent (n=5) of respondents lived with HS for 10-15 years, 27% (n=4) for 15-20 years, 20% (n=3) for longer than 20 years, and 7% (n=1) for less than 5 years. The majority of respondents had moderate HS (53%, n=8), with 33% (n=5) rating HS as severe, and 13% (n=2) as mild. The most common comorbidities were mental health conditions (e.g., depression, anxiety) in 43% (n=3) of respondents. Inflammatory arthritis, a different inflammatory condition, and gastrointestinal disease were reported by 1 respondent each (14%).

3. Disease Experience

HS is a chronic inflammatory skin condition with physically and emotionally debilitating symptoms, such as painful boils and abscesses in skin folds (i.e., armpits, groin, under breasts, between buttocks). During a flare, these lesions produce purulent and malodorous discharge followed by healing of lesions with significant scarring and formation of fistulas. Fistulas are abnormal connections between two surfaces, with a common example being a connection between the anal canal and perianal skin leading to uncontrollable leakage of stool. Consequently, more than 80% of respondents to the 2020 National Report of Patient's Experiences Living with HS survey reported that HS negatively impacted their work performance (81%), social interactions, and intimacy with their partner. Fifty-nine percent of respondents missed at least 2 days of work every month and spent a median of 14 hours per month on HS-related tasks, such as wound care. Patients constantly worry about the odor, staining of clothes, and the unpredictable onset of disease flares, which are often very painful. These anxieties make social life challenging, with symptoms also impacting physical activity levels. For 68% of survey respondents, family life is also affected, and intimacy in 87%. As a result of a wide variety of stressors, nearly 70% of respondents reported feelings of depression. Moreover, one of the major manifestations of HS is debilitating pain associated with the lesions in the skin folds that persist for many years on a daily basis. Nearly all patients experience some degree of pain daily that is moderate on average (5.3 out of 10) as per the 2020 National Report. Pain is difficult to control in patients with HS making physical activity and wearing comfortable clothing very challenging. Most patients still report not having a successful pain management regimen, with only 11% of all respondents considering pain well-controlled and 46% reporting poorly controlled pain. It is also troubling that 51% of patients report self-managing with difficulty accessing prescriptions. There is therefore much room for improvement in pain control.

Respondents to the 2023 patient survey identified severe impact of HS on day-to-day life with drainage, severe pain, lesions that make it challenging to walk, challenges to find clothes. The costs of wound care and treatments are high, anxiety and irritation from living with HS are high. All patients report that HS lesions are chronic with the majority of patients constantly having active HS lesions. New lesions persist for months.

Patients with HS often remain undiagnosed and not correctly managed for a prolonged period. Canadian respondents reported a median of 7 years from symptom onset to HS diagnosis, with an average age of diagnosis being 30 years. During these 7 years, 97% of respondents have visited a family physician or a walk-in clinic for their symptoms, and 59% visited the Emergency Department at least once for HS symptoms (e.g., pain management). Eleven per cent visited ER more than 10 times and were treated by more than 10 different ER physicians. Unfortunately, 83% of individuals received at least 1 misdiagnosis prior to identification of HS, with an average of 3 misdiagnoses per person. Delayed diagnoses often translate into worse symptoms and more advanced disease when patients reach the moment of being offered a treatment plan. There were HS-related hospitalizations reported in several provinces, either as HS as a pre-admission comorbidity or as a most responsible diagnosis. The greatest number of hospitalizations were reported in Ontario, with over 60 hospitalizations for over 1200 days in 2018 for HS as a pre-admit comorbidity and over 70 hospitalizations with over 300 days with HS as the most responsible diagnosis. For HS as a pre-admission comorbidity, the length of stay was highly dependent on the severity of the main indication for admission.

The HS community in Canada faces many unmet needs, as indicated by survey respondents. As one respondent told us, improving treatments for HS "would be a miracle! This condition is so painful, so disgusting, and so life-altering. Talking with others, there is so much depression and pain associated with HS that it would be impossible not to show improvement with our well-being if all of our goals were met."

4. Experiences With Currently Available Treatments

HS is managed with a combination of medications, surgical procedures, wound care practices, and lifestyle modifications. In the 2020 National Report of Patient's Experiences Living with HS survey, respondents tried an average of 15 different medications, surgical procedures, home treatments, or lifestyle modifications to help manage symptoms, with only a few finding any significant improvement. The number of management strategies tried reflects the severity of the condition and the desire to decrease the burden of symptoms.

Respondents trialled numerous at-home therapies and lifestyle modifications that are more affordable (although there is no insurance coverage for these) and easier to access than some prescription medications and surgical treatments. However, overall, these offered either no or slight improvement in HS symptoms. Of all described non-drug therapies, stress management and diet modifications were the most successful treatment, reported by 20% of respondents for each. Avoiding tight-fitting clothing was also helpful with comfort and reducing exacerbation of lesions. Fifty-three percent of Canadian respondents had at least 1 corticosteroid injection, while 18% had this performed more than 10 times. Additionally, 74% had at least 1 boil or cyst incised or drained, and 19% underwent this procedure more than 10 times.

The most commonly used treatment at the time was a long course of antibiotics (82% of survey participants). In dermatology, antibiotics are often used for their anti-inflammatory properties rather than their antimicrobial properties. However, only 11% reported improvement in symptoms. Other treatments reported were CO_2 lasers (26% effective), radiotherapy (33%), incision and drainage (23%), and surgical therapies other than incision and drainage (39%). Only 27% of respondents used biologics, with 38% reporting symptomatic improvement. Overall, only 13% of respondents were satisfied with the current treatments being able to control HS symptoms, cure HS or enjoy social activities. Some contributing factors were side effects such as back pain, headache, intestinal problems, and fatigue. Additionally, procedures such as surgery have long wait times.

Pain is an important hallmark of HS (just as itching is for atopic dermatitis or psoriasis). Despite currently available treatments, only 11% of respondents consider their pain well controlled, with 46% reporting poor pain control.

Although some of the treatments may be effective for some proportion of users, less than 35% of respondents used any of them, suggesting access and affordability challenges. For those who do not have any insurance, monthly HS-related expenses were $158 for prescription drugs (excluding biologics) and non-prescription items (e.g., soaps, bath products, creams, wound care, non-prescription treatments/therapies, etc.). Those with private insurance that did not cover any HS treatments spent an average of $262 monthly (85% on non-prescription items and 15% on non-biologic prescription drugs). Those with private insurance that covered at least some HS-related expenses spent an average of $65 monthly, with approximately $48 on non-prescription items—the drug manufacturer's financial aid program sponsored patients using biologic therapy. One respondent without any private insurance reported that they spend $1,200 out-of-pocket every month on biologics. In contrast, two respondents with some private coverage reported paying $17 to $150 monthly for biologics.

There is much room for improvement in HS treatment with a strong need for safe, effective and accessible treatments to help manage this condition physically and emotionally.

One survey respondent noted in 2020 that "although we have come a long way from even 10 years ago to help manage HS, more needs to be done via research and making more biologics available (especially to us in Canada as adalimumab is the only one currently). Antibiotics are not the answer unless there is actual infection; we need to find why our bodies are doing this to us so we can tackle it and if not cure it, at least make HS way more manageable." Since the 2020 report, one other biologic, secukinumab (Cosentyx), has become available in Canada. However, there's still significant need for more treatment options to help patients effectively manage and treat a painful and debilitating condition like HS.

5. Improved Outcomes

The main treatment goals of participants in the 2020 National Report of Patient's Experiences Living with HS survey were to control HS symptoms (90%), cure HS completely (71%), and be able to enjoy personal relationships (69%). The majority of respondents (61%) were dissatisfied with the ability of currently available treatments and therapies for HS. The main reasons for the dissatisfaction included side-effects, such as back pain, headache, intestinal problems, and fatigue. For the surgical options, respondents found the long waiting time and a challenging recovery process made it impossible to work and care for family. Respondents reported that satisfaction with the therapy would significantly improve depression and anxiety, allow to live a happy life,

not feel judged when people stare, return hope and energy, and make them thrilled to participate in family life again. With effective therapy, participants felt they would derive emotional, physical and daily life benefits. Emotionally, they would have less worry and anxiety, would feel normal, not worried about shame during sexual activities, and would feel attractive. Physically, effective therapy would allow patients to be more active parents to their children, able to exercise, hike and walk more, wear clothing without worry, and have full range of motion. This would all translate to improvement in daily life, allowing patients more time to manage other people's challenges instead of being focused on self, be less dependent on others, able to have children, and return ability to eat without worrying about triggers for a flare.

6. Experience With Drug Under Review

Of the respondents to the Facebook post requesting experiences using bimekizumab for hidradenitis suppurativa, we found 4 patients have been on the treatment. At least 2 were introduced to the drug via clinical trial, and at least 1 used private insurance. Three of the four respondents reported that the treatment helped their symptoms. Two of the four respondents have stopped using the treatment due to the side effects, with one patient naming the fatigue they experienced on the treatment as their reason for stopping, despite it helping their symptoms a bit – this patient is now using a "sister medication." One out of the four patients is currently still using the treatment and is "doing very well on it." The respondent who accessed it via private insurance shared that they were on it for 1.5 years. They also shared that their flare ups became less intense while using the treatment, and when they did experience a flare up, the number of abscesses was reduced to one abscess instead of three in each affected area of the body. These varying experiences, including one patient who is still on the treatment after two years, highlight the diverse needs of HS patients and the need for more HS treatments for health care providers to have in their toolkit so that every person living with HS can access affordable and effective treatments to help manage their care. People impacted by HS, an extremely painful and burdensome condition, would benefit from new, effective treatments like bimekizumab being made available and affordable so that patients' symptoms can be improved, leading to better health outcomes and an improved quality of life for patients and their loved ones.

7. Companion Diagnostic Test

Not applicable.

8. Anything Else?

Given such significant impact of HS on the lives of individuals living with the condition, it is important to explore effective and safe treatment options to alleviate the suffering and improve health outcomes. There remains a need for additional treatment options. Access to new and promising treatment is critical to helping patients gain a sense of control over their disease and begin to regain their quality of life. In the words of one respondent in the 2020 HS Report, "It took 15 years of suffering to finally get told what it is. Then I got told there's nothing you can do about it. You can only treat the symptoms."

Individuals with HS have often attempted numerous treatments and therapies to manage the debilitating symptoms of their condition. In particular, very few HS patients are treated by a pain management specialist. When their HS is well-treated, it becomes more manageable, and the pain they experience because of this disease is reduced.

The nature of this disease requires ongoing care and a constellation of different approaches. Individuals with HS incur considerable expenses on HS-related items, including those required for daily wound care.

For more information about the challenges of living with HS, please see the following resources:

- CSPA information page for HS
- Hidradenitis and Me Support Group information page

CADTH

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.

   No. CSPA and Hidradenitis & Me Support Group worked with staff and volunteers to complete this report. No funding was received to complete this submission.

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.

   As mentioned above, this submission draws on evidence in CSPA's 2020 HS Report, for which funding was received from a pharmaceutical company. That company did not see any data or drafts prior to its publication by the CSPA. For that report, data was purchased by CSPA from the Canadian Institute for Health Information.

   No funding or other support was received to complete this submission.

3. 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
UCB			X	
Novartis			X	
AbbVie				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: Dana Gies
Position: Executive Director
Patient Group: Canadian Skin Patient Alliance
Date: October 31, 2024

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Novartis			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: Latoya Palmer
Position: Founder
Patient Group: Hidradenitis & Me Support Group
Date: October 31, 2024

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: SR0856-000
Generic Drug Name (Brand Name): Bimekizumab
Indication: Hidradenitis suppurativa
Name of Clinician Group: Atlantic Dermatology Specialist Group
Author of Submission: Dr. Tracey Brown-Maher, Dr. Wayne Gulliver, Dr. Irina Turchin, Dr. Ashley Sutherland

1. About Your Clinician Group

Atlantic Dermatology Specialist Group is a group of physicians that includes dermatology-certified specialists practicing general dermatology with vast experience managing various skin conditions including hidradenitis suppurativa. Members of this group previously provided clinician input for a review on the treatment of hidradenitis suppurativa. Several members are engaged in clinical research and have extensive experience in managing hidradenitis suppurativa.

2. Information Gathering

Group members gathered relevant scientific and clinical information which was further compiled and circulated for comments and discussion. All members had an opportunity to provide their feedback and opinions. The final document includes group expert clinician input.

3. Current Treatments and Treatment Goals

Hidradenitis suppurativa (HS) is a chronic inflammatory disabling disease characterized by painful inflammatory nodules, abscesses, and tunnels which usually involve intimate places such as pubic area, groin, inframammary area, and axillae. In addition to significant pain, the lesions can also have malodorous discharge, leading to significant scarring and disability. Lesions may also occur in other areas including head and neck, trunk, and limbs. Hidradenitis suppurativa is much more common in females (approximately 2/3) with increased prevalence in Canadian Indigenous population and the African Canadian population. Hidradenitis Suppurativa usually starts in the teens or early twenties, and on average there is a delay of diagnosis up to eight years. This delays treatment and increases the risk of progression and scarring. Its prevalence is estimated at approximately 1%, but the global range may vary from <0.1% to as high as 4%. The median age of onset is early twenties, and the disease has been reported in children as well as post-menopausal women. Hidradenitis Suppurativa has a significant genetic factor with as many as 30% of patients having a positive family history. Hidradenitis suppurativa is associated with multiple comorbidities including obesity, smoking, metabolic syndrome, autoimmune disorders including Crohn's disease and inflammatory arthritis, malignancies such as squamous cell carcinoma (SCC), and multiple psychological comorbidities including depression and anxiety. (Reference Miller et al dermatology clinics 34 (2016) 7-16).

The approach to Hidradenitis Suppurativa must be multidisciplinary and includes medical, surgical, and lifestyle interventions. The multidisciplinary team includes dermatology, general and plastic surgery, primary care providers, and depending upon comorbidities may also include general internal medicine, rheumatology, gastroenterology, psychiatry to name a few.

The first guidelines for the treatment of hidradenitis suppurativa were comprised and published by the European Academy of Dermatology and Venerology and published in the JEADV in 2015 (Zouboulis et al JEADV 2015; 29:619-44). In 2016 an evidence-based approach to the treatment of hidradenitis suppurativa/acne inversa based on the European Hidradenitis Suppurativa Guidelines was published in 2016 (Gulliver et al Reviews in Endocrinology Metabolism Disorders 2016 17(3:343-351)). Further guidelines including the North American Guidelines for the Management of Hidradenitis Suppurativa were published in 2019 (Alikhan et al JAAD 2019 July; 81(1:91-101)).

The current treatment approach combines both medical and surgical management, management of comorbidities, lifestyle, and supportive therapy. Present goals of therapy are to clear lesions and improve symptoms such as pain, drainage, odor, pruritus and to prevent progression to tunnels or scarring. In all patients, no matter what the stage, there is discussion of pain management, mental health issues, wound care, avoidance of triggers, along with implementation of programs of tobacco cessation and weight reduction. Use of antiseptic washes and warm compresses may also be implemented. In patients with mild disease (Hurley Stage I) topical clindamycin may be used. If this is not helpful, then patients are considered for treatment with oral tetracyclines such as Doxycycline 100mg PO daily for twelve weeks or a combination of clindamycin 300mg PO BID and rifampicin 300mg PO BID for twelve weeks. For mild disease, hormonal therapy such as oral contraceptive pills (Diane 35), topical or oral retinoids, laser hair removal, local excision, intralesional steroids, incision and drainage, topical resorcinol, and deroofing may be implemented. For more severe disease and disease progressing to Hurley stage II or III, biologic therapies including Adalimumab and Secukinumab may be initiated. Other options of treatment include a combination of antibiotics such as moxifloxacin, rifampin, and metronidazole. Occasionally IV ertapenem is considered for rescue. Off-label biologic treatment include the use of Infliximab, ustekinumab, or anakinra. Antibiotic and biologic therapy are also combined with lifestyle intervention, pain control, wound care, hormonal treatment, retinoids, local or wide surgical excision.

With respect to the current treatments, our goals are to improve symptoms and prevent progression of hidradenitis and significantly improve the quality of life. We also hope to improve symptoms by reducing pain and pruritus as well as eliminating the drainage. Although the current treatments (i.e. Adalimumab and Secukinumab) target inflammatory cytokines associated with HS including TNF and IL17, in clinical trials only 40-60% of patients achieve the primary outcome of greater than 50% reduction of inflammatory lesion count (abscesses + inflammatory nodules) and no increase in abscesses and draining fistulas when compared to baseline (no progression) i.e. HiSCR $\geq$ 50. Very few patients achieve 100% clearance and in most clinical trials this number is not reported. Both Adalimumab and Secukinumab do improve patient symptoms such as pain, drainage, and as mentioned prevent disease progression. It should be noted that with prolonged treatment the number of patients achieving HiSCR 50 may increase and in real world studies does reach as much as 70% by 52 weeks. When it comes to the ideal treatment, we would like to observe 90-100% of patients achieve HiSCR 50, along with a significant proportion of patients achieving HiSCR 90 or 100. The ideal treatment should improve symptoms, quality of life, prevent disease progression, reduce the need for surgical intervention, prevent or treat comorbidities such as inflammatory arthritis, anxiety/depression, and metabolic syndrome. Another important treatment goal is to have patients gain full employment/or return to the workforce; many patients with moderate/severe Hidradenitis Suppurativa are under-/unemployed.

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 are currently only two on-label treatment options commercially available in Canada for hidradenitis suppurativa. The response to these medications is variable. Based on pivotal trials for adalimumab (PIONEER I and PIONEER II), 42% and 59% of patients, respectively, reached the primary endpoint of HiSCR50 at week 12. In the pivotal trials for secukinumab (SUNSHINE and SUNRISE), 38.3% to 44.5% of patients reached the primary endpoint of HiSCR50 at week 16. Neither treatment can reverse the course of the disease or improve the permanent anatomical disruption seen with HS scarring, which can happen early in the disease course. While the available treatment options improve symptoms for some patients with HS, response may not be complete and many patients still struggle with draining, painful, scarring lesions in intimate and sensitive anatomical locations even while on therapy. There are many that fail these current treatments or have intolerable side effects. Injection site reactions and pain occur more often with adalimumab injections. Paradoxical psoriasis and eczema are also seen more often with anti-TNFs. Secukinumab often has a waning effect in psoriasis over time and may have the same issue in HS. Currently approved treatments are given more often (adalimumab weekly); secukinumab is every four weeks currently. Bimekizumab was studied at both two- and four-week dosing intervals, and fewer injections often leads to better adherence. Any amount of active HS disease causes significant distress to patients and has impact on

quality of life, sexual health, and employment. Bimekizumab is the only treatment to reduce draining tunnels and show higher improvements in HiScr (90-100), skin pain and QOL. Bimekizumab formulation can also be left out of the refrigerator for longer periods which would be more convenient for most patients, especially with travel (thirty days as opposed to fourteen days for adalimumab and four days for secukinumab before being discarded as unsafe).

Alexa B. Kimball, M.D., M.P.H., Martin M. Okun, M.D., Ph.D., David A. Williams, M.D, M.P.H., Alice B. Gottlieb, M.D., Ph.D., Kim A. Papp, M.D., Ph.D., Christos C. Zouboulis, M.D., Ph.D., April W. Armstrong, M.D., Francisco Kerdel, M.D., Michael H. Gold, M.D., Seth B. Forman, M.D., Neil J. Korman, M.D., Ph.D., Evangelos J. Giamarellos-Bourboulis, M.D., Ph.D., Jeffrey J. Crowley, M.D., Charles Lynde, M.D., Ziad Reguiai, M.D., Errol-Prospero Prens, M.D., Ph.D., Eihab Alwawi, B.S., Nael M. Mostafa, Ph.D., Brett Pinsky, Ph.D., Murali Sundaram, Ph.D., Yihua Gu, M.S., Dawn M. Carlson, M.D., M.P.H., and Gregor B.E. Jemec, M.D., D.M.Sc. Two Phase 3 Trials of Adalimumab for Hidradenitis Suppurativa. N Engl J Med 2016;375:422-434

Alexa B Kimball, Gregor B E Jemec, Afsaneh Alavi, Ziad Reguiai, Alice B Gottlieb, Falk G Bechara, Carle Paul, Evangelos J Giamarellos Bourboulis, Axel P Villani, Andreas Schwinn, Franziska Ruëff, Larisha Pillay Ramaya, Adam Reich, Ines Lobo, Rodney Sinclair, Thierry Passeron, Antonio Martorell, Pedro Mendes-Bastos, Georgios Kokolakis, Pierre-Andre Becherel, Magdalena B Wozniak, Angela Llobet Martinez, Xiaoling Wei, Lorenz Uhlmann, Anna Passera, Deborah Keefe, Ruvie Martin, Clarice Field, Li Chen, Marc Vandemeulebroecke, Shoba Ravichandran, Elisa Muscianisi. Secukinumab in moderate-to-severe hidradenitis suppurativa (SUNSHINE and SUNRISE): week 16 and week 52 results of two identical, multicentre, randomised, placebo controlled, double-blind phase 3 trials. Lancet 2023; 401: 747–61

5. Place in Therapy

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

Bimekizumab is a monoclonal IgG1 antibody that selectively inhibits Il-17F in addition to Il-17A. It has a unique mechanism of action that reduces inflammation, nodules, abscesses, skin pain, and draining tunnels. It would be used as a stand-alone biologic but could be used in combination with oral antibiotics, intralesional steroids, topicals for maintenance and/or flares. Bimekizumab ultimately reduces IL-17 more effectively and decreases the inflammation that leads to HS. Early treatment seems to decrease progression. It is currently the only agent shown to reduce draining tunnels. Therefore, IL-17 appears to be one of the pathways for HS.

Bimekizumab, due to its higher efficacy and durability of treatment, should be used as a first-line treatment. Because hidradenitis suppurativa is an effervescent disease, it may at times require combination with other rescue therapies such as topical and oral antibiotics, intralesional corticosteroids, or surgery. This is the current treatment paradigm. However, bimekizumab has been shown to reduce the need for any rescue interventions (10.8 in treatment group compared to 15.1 placebo) and decrease the incidence of medical intervention (7.6 in treatment group vs 12.3 placebo), BE HEARD pooled data from week 0-16.Time to first procedural intervention was numerically longer with bimekizumab as compared to placebo, 65.3 days (SD 36.3) compared to 30.4 days (SD 17).

We would expect that bimekizumab would be approved as a first-line option for moderate-severe hidradenitis suppurativa. It should not be used as a second line biologic and can be used in any patient that does not have active inflammatory bowel disease (in whom an IL-17 would be contraindicated). It would also be considered first-line biologic for those with hidradenitis suppurativa that also have multiple sclerosis and systemic lupus erythematous, in whom anti-TNF therapy (adalimumab) would be contraindicated.

Bimekizumab is expected to cause a shift in the current treatment paradigm as it is more efficacious than current treatments. It is the only treatment to look at higher endpoints, such as HiSCr 90 and 100 and meet these; about 32% met HiSCr 90 and about 24% met HiSCr 100 at week 48 (BE HEARD pooled data mNRI). HiSCr 75 responses at week 16 were double than placebo (34% q4w group vs 17% placebo) and improved to 47.6% at week 48. Patients that had a response at week 16 tended to maintain their response at week 48 (approximately 80% for HiSCr 75, 65% for HiSCr 90; as observed). Response rates were similar no matter the age, BMI, duration of disease, and sex. While bimekizumab worked well for moderate and severe patients, those with moderate disease did slightly better. This supports the idea that earlier intervention may help prevent progression of disease.

It is the only biologic thus far to show improvement in draining tunnels. At week 48, BE HEARD pooled data, 54.6-57.9% of patients achieved zero draining tunnels. It also showed that of those with more than five draining tunnels at baseline, about 30% had no draining tunnels at week 48 (as observed data). There is no medical treatment currently approved that has shown improvement in

draining tunnels, which has a huge impact on quality of life. BE HEARD pooled data also demonstrated higher changes from baseline in HiSQOL scores (HS quality of life scale) in treatment groups compared to placebo group at week 16 (-11.0 vs -5.8; MI). Adverse events were low in treatment groups, and most were mild-moderate and resolved with time/treatment and there was no signal for IBD. There was a low incidence of candidiasis which in most patients was mild and there was lower incidence over treatment periods. Bimekizumab was well tolerated.

Currently patients with hidradenitis suppurativa need to fail three months of oral antibiotic (doxycycline or combination of clindamycin and rifampin) and have three active lesions in two areas to move on to a biologic treatment. We strongly recommend that patients be able to start bimekizumab after meeting this criterion as well. Patients should not have to try less effective biologic options before going on to bimekizumab (adalimumab HiSCr 50 41.8% at week 16; secukinumab HiSCr 50 45% at week 16)) due to the risk of progression, scarring and impact on quality of life for patients, especially those in younger age groups.

Kimball et al 2024. Lancet 403;10443:P2504-2519. Efficacy and safety of bimekizumab in patients with moderate-to-severe hidradenitis suppurativa (BE HEARD I and II): two 48 week, randomised, double-blind, placebo controlled, multicentre phase 3 trials.

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?

Any patient with moderate to severe HS who had failed topical therapies (antibacterial wash, topical antibiotic) and systemic antibiotics (tetracycline class or Clindamycin with rifampin) would be a candidate for bimekizumab treatment.

Moderate to severe HS is defined as total abscess/nodule count of 5 or greater and lesions are present in at least 2 distinct anatomical areas. Genital area should be considered as a special site due to significant impact on QoL(impact on relationships and sexual health) and long-term disease sequelae unique to this site (lymphedema, scarring, risk of SCC). Patients with three abscess/nodules in the genital area should be considered to have moderate to severe disease. Tunnels/fistulae are considered late disease sequelae that are preventable by effective medical therapy. Patients with moderate to severe disease with no tunnels should still be considered for bimekizumab biologic therapy. HS is easy to clinically diagnose by PCPs, general surgeons, ER physicians, obstetrics/gynecologists, plastic surgeons, gastroenterologists and dermatologists and does not require a diagnostic test . It may be underdiagnosed by NPs and some other PCPs. The only time there is a small issue with diagnosis is distinguishing perianal HS from fistulizing perianal Crohns. Here multidisciplinary collaborations are used along with colonoscopy, MRI and clinical judgement. Any patient on bimekizumab that has at least a 25% improvement at twelve weeks should continue to improve with time. Those with no response whatsoever or worsening at sixteen weeks should discontinue treatment.

Bimekizumab would not be suitable for any patient who is unable to tolerate injections or has contraindication to IL-17 inhibitor such as active inflammatory bowel disease or immune deficiency associated with chronic candidiasis. Bimekizumab has not been studied in population younger than 18 years of age and in pregnant or breastfeeding women. Bimekizumab treatment should not be combined with other biologics.

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?

Baseline disease assessments should include location of disease (anatomical areas), presence of inflammatory lesions including abscesses and/or nodules, and presence of tunnels, and whether they are draining or not. PROs (patient reported outcomes) of DLQI (dermatology life quality index) and HiSCr QOL are indicative of affects of quality of life. Skin pain assessments are also relevant.

Initial patient reassessment should be done between four-six months with documentation of response of 50% improvement in inflammatory lesion count with no disease worsening as indicated by new abscesses or tunnels. Improvements in the QOL assessments would be relevant. Subsequent reassessments should be done every twelve months for patients responding to therapy and at any time if there is concern about adverse events or loss of treatment response. Response to treatment may differ depending on severity of disease at presentation, number of previous treatments, extent of concomitant comorbidities; HS responds slowly, and evaluation of treatment response should be done later than twelve weeks ideally.

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

If no treatment response has been achieved at four-six months, bimekizumab should be discontinued. Bimekizumab should be discontinued when patient experiences adverse events where continuation of bimekizumab would not be beneficial. Discontinuation may be considered in an event of special safety situation such as pregnancy.

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]?

Patient with HS may be diagnosed by any HCP and treated with first line conventional therapies including topical treatments, intralesional and oral steroids, systemic antibiotics. Biologic therapy initiation should be restricted to practitioners with advanced understanding of disease and biologic therapies such as dermatologists. Prescription renewal can be done by any practitioner able to assess disease severity and monitor treatment efficacy and adverse events including dermatologists, rheumatologists, gastroenterologists, and general practitioners with special interest in skin diseases.

References:
Alavi A, Adam DN, Alhusayen R, Boucier M, Brassard A, Coutts P, Gooderham M, Gulliver W, Hong CH, Lynde C, Marcoux D, Papp K, Poulin Y, Sibbald RG, Shear NH. Definition of Moderate to Severe Hidradenitis Suppurativa: A Position Paper by the Canadian Hidradenitis Suppurativa Foundation (CHSF). J Cutan Med Surg. 2016 Nov;20(6):613-615. doi: 10.1177/1203475416660296. PMID: 27821541.

6 Additional Information

Currently bimekizumab is only indicated for treatment of moderate to severe psoriasis and active psoriatic arthritis or axial spondyloarthritis in Canada. However, due to overlap of comorbidities, some of our patients treated on label with bimekizumab have concomitant HS. Our group has seen real world improvement in HS in those patients which provides hope to both those struggling with the disease and the clinicians trying to find an effective treatment. Currently with HS, there is no drug that fits all scenarios, and bimekizumab would add to our armamentarium in tackling this disabling chronic skin disease.

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.

   No, only the clinician group compiled this submission.

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.

   Data slides from phase III clinical trials for bimekizumab were provided by UCB for aid in submission, by Dale Yakutchik, MSL, Policy, HealthCare Ecosystems, UCB, Dieppe, NB

   There was no other input provided.

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: Irina Turchin
Position: Dermatologist, Fredericton, NB
Date: 08-Sep-2024

☒ **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**
Abbvie				x
Janssen			x	
Novartis			x	
Eli Lilly			x	
Incyte			x	
UCB			x	

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

Declaration for Clinician 2

Name: Dr. Wayne Gulliver
Position: Dermatologist, Professor of Dermatology, MUN, St. John's, NL
Date: 13/09/2024

☒ **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 2: Conflict of Interest Declaration for Clinician 2

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Abbvie			x	
Janssen			x	
Novartis			x	
Eli Lilly	x			
Incyte	x			
UCB	x			

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

Declaration for Clinician 3

Name: Tracey Brown-Maher
Position: Dermatologist, Principal Investigator, St. John's, NL
Date: 15/09/2024

☒ 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

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Abbvie			x	
Eli Lilly			x	
Pfizer			x	
Galderma		x		
Incyte			x	
Leo Pharma			x	
Sanofi			x	
Novartis			x	
Janssen			x	
BMS			x	
BioJamp		x		
Boehringer Ingelheim	x			
UCB			x	
Amgen		x		

Sun Pharma		x		
Bausch Health			x	

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

Declaration for Clinician 4

Name: Ashley Sutherland
Position: Dermatologist, Halifax, NS
Date: 10/09/2024

☒ 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 4: Conflict of Interest Declaration for Clinician 4

	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	
Janssen	x			
Novartis		x		
Eli Lilly		x		
Incyte	x			
UCB	x			
Pfizer	x			
Leo		x		
BMS	x			
Sun Pharma	x			
Arcutis	x			
Bausch Health	x			
Boehringer Ingelheim	x			
Sanofi	x			
Galderma	x			

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