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

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

Iebrikizumab (Ebglyss)

(Eli Lilly Canada, Inc.)

Indication: For the treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years of age and older with a body weight of at least 40 kg, whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

November 14, 2023

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.**

Disclaimer: The views expressed in this submission are those of the submitting organization or individual. As such, they are independent of CDA-AMC and do not necessarily represent or reflect the views of CDA-AMC. No endorsement by CDA-AMC is intended or should be inferred.

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CDA-AMC does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no identifying personal information or personal health information is included in the submission. The name of the submitting group and all conflicts of interest information from individuals who contributed to the

Patient Input

Name of Drug: **Lebrikizumab**

Indication: For the treatment of adult and adolescent patients 12 years of age and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

Name of Patient Group: **Canadian Skin Patient Alliance**

Author of Submission: **Canadian Skin Patient Alliance**

1. About Your Patient Group

The Canadian Skin Patient Alliance (CSPA) is a national non-profit organization with a mission to improve the health and wellbeing of people across Canada affected by skin, hair, and nail conditions, through collaboration, advocacy, and education. For more information, please visit www.canadianskin.ca.

2. Information Gathering

Information for this submission was compiled from that shared in previous submissions to CADTH about patients' experiences living with atopic dermatitis (AD). Many of those submissions were prepared in collaboration with Eczéma Québec. This submission also includes data from the Canadian Institute for Health Information (CIHI) on AD-related emergency room (ER) visits and hospitalizations from 2016 to 2020, to gain a fuller understanding of healthcare utilization associated with this condition. This data, and our analysis of it, was included in the 2022 report *The Skin I'm In, 2022 Update: A National Report of the Patient and Caregiver Experience with Atopic Dermatitis*, www.canadianskin.ca/advocacy/advocacy-reports/eczema-report. This report was also developed in collaboration with Eczéma Québec, and supported through unrestricted funding from AbbVie, Leo Pharma, Pfizer and Sanofi.

Additionally, the information gathered in this submission also includes material from the current literature on guidelines and management of AD. Reference material is provided in the appendices.

3. Disease Experience

Atopic dermatitis (AD), also commonly known as eczema, is a chronic, inflammatory, and debilitating skin condition that causes dry, and itchy skin. The eczematous lesions can present practically anywhere on the body and have a significant impact on patient quality of life, beyond their physical presentation. Moderate to severe AD can result in the development of increasingly painful lesions, with the burden of disease extending beyond the impacts on the skin. Conditions associated with AD include asthma, seasonal allergies, environmental allergies, food intolerances, sleep disorders, anxiety, and depression. This condition not only results in a chronic burden on the patient, but also places an increased burden on the caregiver and the healthcare system due to frequent medical visits and the need for specialized treatment and ongoing care.

Patients often perceive living with AD as a daily battle that revolves around the management of the relentless itch/discomfort, and care for broken and bleeding skin when the drive to scratch becomes uncontrollable. Patients report that living with AD in itself can be as demanding as a full-time job, involving meticulous attention to and management of various factors, including skincare, product choices (e.g., soaps and detergents), and diet. If not considered thoroughly, each of these factors can worsen or trigger a new flare of the disease. Moreover, the dietary options that many patients are limited to in order to prevent flares can also impact their nutrition and health, adding an additional layer of stress to their everyday lives.

Although AD has impacts beyond cosmetic concerns, the visibility of the disease only amplifies the emotional toll and mental health struggles that patients experience. This makes it increasingly difficult for patients to manage both professional commitments and

social engagements. Many caregivers corroborate the impact of AD on patient quality of life by recalling the many missed activities, sick leaves, and postponed outings that have been precipitated by patients experiencing unmanageable flares. Caregivers further share that this disease also impacts their own emotional wellness as witnessing their loved ones experience these devastating symptoms can be both scary and distressing. These feelings can be exacerbated by a sense of helplessness and a lack of control over the situation. Further, the cost of treatment and other skincare products needed to manage the condition can place financial stress not only on the patient but also on the family who cares for them.

Patients directly share with us the following personal reflections on living with AD:

> **Physical and Social Impact:** *"I would take off my bra and the whole skin on my nipple would come off and get stuck to the fabric. My wounds would stick to anything I was wearing. When undressing, my skin would completely rip and bleed. The scabs on my back would get stuck on my bed sheets at night. And I would get infections from the textile fibers that would get in my scabs. It was horrible. During the day, my lesions would ooze and because of my clothing they would take forever to heal. Even though I am now controlled, and I use a treatment that manages most of my symptoms, my body is covered in brownish scars. To this day I never wear shorts or a bathing suit, and I still get comments on the way my skin looks when I do expose my scars."* (Eczéma Québec community member)
>
> **Emotional Impact:** *"As I grew up, my disease got worse and worse, until it got to the point where I frequently had to miss school, and had trouble sleeping at night. On days when I could attend school, I was teased because of the way my skin looked, and people stared or made comments on my appearance. I was not able to skip gym class even though the sensation of burning from sweat on my lesions would make me cry in front of my classmates. I felt as though no one understood what it was like living in my skin."* (Eczéma Québec community member)
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> **Sleep Impact:** *"My sleep is disturbed. I am disturbed in my daily life by uncontrollable itching for which I have to stop what I do (work, [driving a] car) to scratch myself."; "Some nights, it's like there's bugs crawling all over me. I know there's nothing there, but the itching is so intense, I can't help but check under the sheets."* (Eczéma Québec community members)
>
> **Professional Impact:** *"By May 2020, my doctor put me on medical leave. Even without washing my hands, they didn't improve. Plus, I couldn't sleep due to the itch and pain. I was suffering round the clock. I even thought about suicide because I felt so hopeless and didn't see a way out."; "I've lost count of the number of jobs I've lost due to the sick leaves I needed because of my AD. Each job starts out with hope, but eventually, I hit a bad phase where I start coming in late because of the lack of sleep or the unpredictability of the mornings. I have to get excused from shifts to get to appointments. It's heartbreaking to feel like a failure because of something you have no control over."*
>
> **Caregiver Impact**: *"That was the worst part for me. It was unbearable to see my child suffering and not being able to do anything about it. I spend many nights crying after I put her to bed because I thought I was not doing my job right. I prayed that I could take some of her pain away."* (Eczéma Québec community member)

While the disease course of AD for each individual may be unique, it is evident that many patients share a common lived experience characterized by the dual burden of coping with both the physical and psychosocial challenges of the disease. Data obtained from the Canadian Institute for Health Information (CIHI) was also reviewed and provides an additional layer of context for patient's disease experience. These reports highlight a considerable burden of disease with significant numbers of emergency room visits and hospitalizations associated with AD. (The patient group input refers to the figures titled "Number of ER Visits per Age Group and Sex, with AD as the main problem", and "Hospitalizations by gender and age with dermatitis and eczema as main diagnosis", available on page 39 and 42, respectively, of The Skin I'm In: 2022 Update, publicly accessible here).

Manion, R., Ribau, S., Bouchard, C., Isola, G., Jack, C., Lebo, D., & Pereira, J. The skin I'm in: 2022 update. Ottawa (ON): Canadian Skin Patient Alliance, Eczéma Québec, McGill University Health Center – Center of Excellence for Atopic Dermatitis, JRL Research & Consulting Inc.; 2022: https://www.canadianskin.ca/advocacy/advocacy-reports/eczema-report

Emergency room visits for AD were determined to be the main issue for the 0-11 and 18-64 age groups, reflecting the prevalence of this disease in both childhood and adulthood. The incidence of hospitalization for atopic dermatitis was also greater for females as compared to males, an interesting data point that can help better characterize the impact of the disease.

4. Experiences With Currently Available Treatments

Non-medical interventions: Skin hydration is a critical practice in managing AD. Individuals suffering with AD are typically advised to apply generous amounts of moisturizer or emollients to help protect their skin barrier. Moisturizers range from simple creams to more complex formulas advertised to be especially soothing for patients with AD, albeit at an increased price point. Notably, these moisturizers, which are becoming increasingly expensive, are not eligible for financial reimbursement and their annual cost can amount to a substantial expense. Patients with AD often also have to avoid generic products that contain high amounts of fragrances and harsh chemicals, which can trigger disease flares. As a result, most patients must exert greater care in finding or selecting alternative products that avoid these harsh soaps and irritating materials, something that may also contribute to the financial burden of managing this disease.

> Beyond trigger avoidance, applying moisturizing creams, and following nuanced self-care regimes, patients living with AD typically trial numerous medical treatment options, often with limited long-term success. Many patients have felt that "*NOTHING WORKS*" or when a treatment does work it is "*alright for a while but had side effects so [is] discontinued*". **One specific patient shared: "I've spent months on a waiting list, hoping to see a specialist. The wait is excruciating. And even when I get an appointment, there's always the anxiety over whether the prescribed treatment will work or if I'll have to start the process all over again. The treatments can be expensive, adding financial stress to an already challenging situation. The constant waiting - for appointments, for answers, for relief is emotionally and physically draining. I often wonder if I'll ever find lasting relief from this condition that so deeply affects my daily life." (Eczéma Québec community member)**

Below we share an overview of the medical treatment options available for AD and patient's experiences with these medications:

Topical Corticosteroids (TCS): TCS are typically the first-line treatment for AD. TCS are anti-inflammatory creams or ointments that reduce inflammation, itching, and redness by suppressing the immune response in the skin. While they are effective in reducing redness and itching, prolonged use has numerous side effects including thinning of the skin, skin discolouration, stretch marks, and pimples. More serious adverse effects include increased intraocular pressure, cataracts, and hormonal disturbances. The topical nature of this drug can result in a messy application that requires more caution of use to not affect nearby materials such as furniture and clothes.

- *"I use steroid creams, and sure, they work to an extent, but they have this side effect of thinning out your skin. Over time, I've noticed my skin's become super delicate. I'm not kidding when I say that even the slightest scratch can cause bleeding. And once you have a wound, it takes forever to heal."* (Eczéma Québec community member)

Topical Calcineurin inhibitors (TCI): TCIs are a non-steroidal treatment option typically used when TCS are ineffective or unsuitable. TCIs inhibit immune cell activity in the skin to reduce inflammation and are particularly effective for sensitive areas such as the face. This treatment option also has a decreased risk of causing skin thinning. Still, TCIs may take longer to take effect and are not free from side effects, which include itching at the application site, redness, stinging, rashes, and more rarely, skin infection, lymphoma, and skin cancers. Application of this drug can also be quite messy, staining things like glasses and clothes.

- *"I use [a TCI] for maintenance as part of my routine, but it's not always easy. There are days when it stings so badly on application, feels like it's just aggravating my skin rather than soothing it. And that's tough because I rely on it to keep my eczema in check."* (Eczéma Québec community member)

Phosphodiesterase 4 inhibitors (TPDE4i): TPDE4is are a relatively new class of medications used for moderate to severe AD, which help reduce the inflammatory response of the skin. Side effects include irritation at the application site, redness, and rashes. This drug can also be quite messy, staining clothes and bedding.

Off label oral systemic medications: These medications are typically reserved for severe atopic dermatitis or cases that have been poorly managed by other treatment options. They can also be used when other treatment options are contraindicated or evoke side effects. Cyclosporine, methotrexate, and azathioprine are immunosuppressant medications that provide relief for itching and rashes by reducing inflammation. Whilst they typically provide rapid relief for symptoms, potential side effects include high blood pressure, kidney problems, liver damage, nausea, fatigue, and increased risk of infections. As a result, use of these medications often requires routine blood work to monitor for potential side effects and are often reserved for extenuating circumstances.

- *"I tried methotrexate for 18 weeks, but it didn't help."* (Eczéma Québec community member)

Oral Corticosteroids: Oral corticosteroids are an off-label treatment option for AD that provides rapid symptom relief by reducing the immune response throughout the body. However, side effects are quite serious and include weight gain, mood changes, diabetes, and osteoporosis. This medication requires close medical supervision and cannot be used for extended durations. As a result, it is not an effective long-term solution for managing the chronic course of AD.

- *"In times where I experienced severe, full-body flares, it was like my body was on fire, from head to toe. During these periods, the doctors would put me on prednisone. It helped short term, but once the medication was stopped, the intense itch and inflammation would come back."* (Eczéma Québec community member)

Phototherapy: Phototherapy is a treatment option that uses UV light and is often considered for moderate to severe AD in adults and adolescents. Although phototherapy is regarded as one of the safest treatment options, it requires administration in the clinic, on average, two to three times per week, which is impractical for majority of the working population. Beyond time restraints, expensive and inaccessible travel is another barrier to receiving this treatment. Moreover, although at home units have previously been used, they are increasingly expensive and insurance coverage is variable.

Biologics (e.g., Dupilumab/Dupixent): Biologics are a newer class of drugs that help manage redness, itching, and skin legions by mitigating inflammation through targeting various molecules involved in the immune response. Biologics have shown promise within dermatology as they have been able to improve symptoms with reduced systemic side effects, requiring less monitoring. However, regular injections may be necessary, which can be difficult for certain patients. Reported side effects also include injection site reaction and conjunctivitis.

- *"I started Dupixent. It changed my life. Within the first few weeks, the itchiness decreased significantly. Gradually, my eczema almost entirely disappeared, and I was able to return to work. Unfortunately, the medication has lost some of its effectiveness, so some eczema has returned, but it's still manageable without the itch, so for now, I'm sticking with Dupixent. However, I had to change jobs because even with Dupixent, if I wash my hands too much, the eczema flares up on them. So, while Dupixent helps a lot, I still have to follow a routine of using mild soaps, unscented moisturizing creams, cortisone creams, and so on. I had no difficulty getting Dupixent because I was able to prove that I had tried other treatments without success, and I had a DLQI score of 22/30"* (Eczéma Québec community member)

Janus Kinase Inhibitors (JAKi): JAKis are prescribed as daily oral medications typically reserved for treatment of AD when other options have been exhausted. JAKis work by targeting the JAK signaling pathway, which is involved in immune and inflammatory reactions, to reduce inflammation and itch. Given that these medications are relatively new in the context of treating AD, their long-term effects remain a concern among some patients. Side effects may include upper respiratory tract infections, headache, and mild gastrointestinal symptoms.

Despite the apparent advancements in AD treatments, there are numerous barriers that remain, which impair patients from being able to effectively manage this disease. These barriers include travel to and from appointments, availability of medication, time involved in receiving the medication, and cost of medications. Patients share the following quotes with regards to their experiences with managing their atopic dermatitis:

- With regards to why a treatment was not immediately started:*"Yes. Because of the cost of injections, the dermatologist wants to see if my condition gets worse before using it".* (Eczéma Québec community member)
- *""Sometimes nothing works to manage this beast of a disease, and we are left feeling hopeless and helpless. We NEED more options in Canada to treat this."* (Eczéma Québec community member)

As a result, there remains a need for more effective and accessible treatment options for patients living with AD in Canada, which will help them manage a disease that is otherwise detrimental to their physical wellness and overall quality of life.

5. Improved Outcomes

In considering new therapies, patients, caregivers, and their families have expressed a hope for a range of desired outcomes that future medications may target to improve the management of their AD beyond what is currently achievable with existing treatment options. Many patients highlight the following outcomes as important considerations for the development of new treatments:

manages itch, reduces flare, manages redness and inflammation, gives fast relief, addresses thickening of the skin, is easy to use, is covered by insurance/affordable, allows them to stop using topical treatments, and does not require injections.

Below is a summary of survey responses by patients living with AD with regards to what factors they value in new treatments:

Outcome	Strongly agree	Somewhat agree	Neither agree nor disagree
Manages the itch	27/28	1/28	0
Reduces flares	24/27	2/27	1/27
Manages the redness and inflammation	23/27	3/27	1/27
Gives fast results	19/28	7/28	2/28
Addresses lichenification (thickening) of the skin	18/27	7/27	2/27
Is easy to use	20/28	5/28	3/28
Is covered by insurance / is affordable	19/27	4/27	4/27
Allows me to stop using topical treatments	19/28	4/28	5/28
Does not require injections (by myself or someone else)	16/28	3/28	9/28

Safety: Patient safety is a primary priority for new treatment options. Both patients and their caregivers seek therapies with minimal short-term and long-term side effects.

- *“First and foremost, I'd love a treatment that could control the itching without causing more harm to my skin.”* (Eczéma Québec community member)

Symptom Management: Effective symptom management is a critical consideration for patients contemplating novel treatment options. This includes providing relief to: itch, redness, skin lesions, dryness, pain, bleeding, and flares. Direct improvements to these aspects of the disease would allow for improved physical skin health as well as sleep and overall wellbeing. Patients also hope that the medication’s effect in managing these symptoms provides more than temporary relief, allowing for long-term management of their disease.

- *“The persistent itch was, by far, the most incapacitating aspect.”* (Eczéma Québec community member)
- *“I would love a treatment that would give me more than just temporary relief. Something that could help break the itch- scratch cycle, so I could have a good night's sleep, or focus on my work without constant discomfort.”* (Eczéma Québec community member)

Ease of Use: Many patients report that difficult-to-use treatments pose a barrier in their journey to effectively managing their disease. Many feel that the layers of cream they have had to apply several times a day not only requires a reliance on help from their caregivers, but is uncomfortable, and transfers to their clothes and home environment. For these reasons, many patients value alternate treatment options such as oral medications.

- *"The time I need to put into my skin routine often feels like a part-time job."* (Eczéma Québec community member)

Affordability: Given the chronic nature of the disease, patients living with AD are burdened with increased financial expenses that can span their entire lives. For this reason, affordable treatment options or ones that are covered by healthcare/insurance are invaluable, decreasing the financial stress for patients, caregivers and their families.

- *“The costs associated with the trial-and-error nature of treatment regimens is very frustrating.”* (Eczéma Québec community member)

Ultimately, an ideal drug would be one that is safe, easy to use, affordable, and offers significant long-term symptom relief, which will allow patients to regain their quality of sleep, increase their productivity, and improve their psychosocial wellbeing.

6. Experience With Drug Under Review

We did not hear from any patients or caregivers who had direct experience with the drug under review.

7. Companion Diagnostic Test

N/A

8. Anything Else?

Despite the number of atopic dermatitis treatments in Canada, a considerable number of patients still find themselves underserved by the available options. The burden of this disease, unmanageable side effects of current treatment options, and lack of accessibility (both financial and physical) of available medications highlight key concerns for the patient population.

We extend our gratitude to CADTH for considering this submission.

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.

CSPA is grateful to our volunteer who developed this submission. As noted above, this submission includes information that was shared in previous patient input submissions that CSPA completed in collaboration with Eczéma Québec. It refers to data obtained from CIHI and patients' experiences shared in *The Skin I'm In, 2022 Update* report. That report was developed in collaboration with Eczéma Québec and was supported through unrestricted funding from AbbVie, Leo Pharma, Pfizer and Sanofi.

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.

Please see the notes above.

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
AbbVie				X
Eli Lilly		X		

Leo Pharma			X	
Incyte			X	
Pfizer			X	
Sanofi				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: Rachael Manion

Position: Executive Director

Patient Group: Canadian Skin Patient Alliance

Date: November 15, 2023

Appendix: References

Weidinger, S., & Novak, N. (2016). Atopic dermatitis. The Lancet, 387(10023), 1109–1122. https://doi.org/10.1016/s0140-6736(15)00149-x (Weidinger & Novak, 2016)

UpToDate. Retrieved November 13, 2023, from Uptodate.com website: https://www.uptodate.com/contents/treatment-of-atopic-dermatitis-eczema?search=atopic%20dermatitis&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=1#H1841273735 ("UpToDate," 2023)

CADTH Reimbursement Review Patient Input Template

Name of the Drug and Indication	**(TBC) Lebrikizumab** **Manufacturer Requested Reimbursement Criteria:** As per proposed indication; for the treatment of adult and adolescent patients 12 years of age and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Lebrikizumab injection can be used with or without topical corticosteroids **Indications:** For the treatment of adult and adolescent patients 12 years of age and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Lebrikizumab injection can be used with or without topical corticosteroids.
Name of the Patient Group	Eczema Society of Canada
Author of the Submission	Eczema Society of Canada
Name of the Primary Contact for This Submission	Amanda Cresswell-Melville Executive Director, Eczema Society of Canada
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

Eczema Society of Canada (ESC) is a registered Canadian charity dedicated to improving the lives of Canadians living with eczema with a mission of support, education, awareness, and research. To learn more, visit www.eczemahelp.ca.

2. Information Gathering

ESC has gathered survey data from more than 3000 Canadians who live with atopic dermatitis (AD) on topics including quality of life impact, experience with treatments, the AD patient journey, and experience with itch related to AD. Respondents included Canadians living with AD and their caregivers/family members. Information for this submission was also gathered via questionnaires and one-on-one interviews.

3. Disease Experience

About AD

AD, the most common type of eczema, is a chronic, inflammatory skin disease. It is characterized by dry, itchy, inflamed skin that can crack, ooze, and bleed. AD patients experience “flares,” which are periods of worsening of the disease and its symptoms. AD flares can be extremely itchy and painful, and can lead to psychological distress and negatively impact the individual and their family.

Severity

AD is a spectrum disease ranging from mild to severe. AD patients experience periods of flare, and periods of remission, but patients with moderate to severe AD often never experience periods of clear skin, and that is often compounded with widespread disease and lesions/rash covering large body surface areas. As noted, some patients never experience relief from these life-altering symptoms, which is more likely among uncontrolled moderate to severe patients. Significant suffering, discomfort, and negative quality of life impact are commonly reported by patients with uncontrolled moderate or severe forms of AD.

Itch is frequently reported as the most burdensome symptom of AD. Adult survey respondents reported feeling itchy multiple times each day (reported by 72% of respondents with moderate AD and 95% of respondents with severe AD). As the severity of AD increases, so does the frequency of itch, as 44% of survey respondents with severe AD reported feeling itchy all the time. 71% of adult survey respondents with moderate or severe AD rated their overall itch as 7 out of 10 or greater, and at its worst, 42% of survey respondents rated it as 10 out of 10 – the worst itch imaginable. More than half (54%) of adult survey respondents with severe AD report rarely being able to control their urge to scratch their skin.

Sleep

ESC survey data revealed that loss of sleep and poor sleep quality are reported as significant quality of life impacts due to AD. 63% of survey respondents with moderate AD and 86% of survey respondents with severe AD reported that itch negatively impacted their sleep. 50% of survey respondents with severe AD reported experiencing sleep loss eight nights per month or more. Patients interviewed shared that the urge to itch is more pronounced at night, and the ability to sleep can be significantly affected. One patient interviewed reported they would scratch themselves all night long, and another reported that not only the itch, but the pain from scratching themselves so severely would interrupt their sleep.

“The indescribable itch was a constant torment, robbing me of peaceful sleep. People often advised me to stop scratching, but it's incredibly challenging to resist.”

“At one point, I was covered with an itchy rash from head to toe [and] I literally didn’t sleep for three days straight and went to the emergency room. I was a mess, and nothing I was doing was helping.”

“Falling asleep can be nearly impossible.”

Family Burden

The burden of AD also extends to caregivers and family members. Partners and spouses reported loss of sleep due to their partner’s sleep disruption, such as waking and scratching through the night. Family members have also reported feelings of helplessness, guilt, and frustration as it relates to the patient’s disease. Intimacy, family dynamics, and relationships are affected by the disease, and many report experiencing feelings of anxiety and depression in addition to sleep loss.

“Family vacations had to be carefully planned, with my parents ensuring that accommodations had hardwood floors to avoid triggering my eczema. My eczema’s influence was felt throughout my family.”

Skin Impacts

AD is not only itchy and painful, but the visible skin symptoms are also distressing. Patients reported skin damage, bleeding, scarring, and pigment changes due to rashes and scratching of the skin, with 62% of survey respondents with moderate AD and 87% of survey respondents with severe AD having scars or marks on their skin from scratching. Others reported that they experienced deep cracks and blistered skin that would break or split from movements as minor as walking or signing their name. Patients report

they have bled through their clothing and needed to change their sheets daily due to blood stains. Others reported they needed to vacuum daily to remove the dead skin that would flake from their bodies. These outcomes can be embarrassing and significantly affect patients' confidence, sexual relationships, and intimacy. Episodes of itch can also be difficult for a non-AD sufferer to fully appreciate or understand. The intensity and drive to scratch the skin is described as overwhelming and uncontrollable.

"Having severe eczema as an adult was like having a brand-new disease. I wasn't prepared for the secondary infections. It was an immense struggle."

"People don't understand how bad it is and how much it's hurting you, and yet you're constantly trying to keep up with everyone else despite it."

Flares

The unpredictable patterns of flares and/or exacerbations, along with the physical symptoms of AD, can significantly impact mental health and cause stress (69% of survey respondents with moderate AD and 87% of survey respondents with severe AD reported that itch negatively impacts stress). Patients reported that the mental health impact of AD is a significant aspect of the disease and is often not understood by others, nor prioritized by health care providers. Feelings of depression and anxiety, as well as poor self-esteem, low energy, and, in some extreme cases, suicidal thoughts, can be common among the more severe patients with AD. Itch can also be debilitating, with 46% of adult survey respondents with moderate or severe AD reporting this experience.

"Tasks as simple as bathing can be excruciating."

"Eczema has had a significant impact on my body image. The visible wounds on my face, which turned brown rather than red, made me feel and look scary. I often felt unclean and strange."

"People don't understand the reality of living with eczema. It affects how you operate as a human being.

Hygiene

AD patients also report that their AD negatively impacts their hygiene, as bathing and hand washing can be excruciatingly painful. This cycle of poor hygiene is not only uncomfortable and socially disruptive, but it also perpetuates the cycles of infection and the need for additional options of antibiotics and treatments.

"It can be incredibly painful if the soap contains ingredients that irritate my skin. Balancing water temperature can also be painful, and even washing and drying myself can trigger distressing reactions, giving me a mere 30 seconds before the venomous itch strikes."

Social impact

AD can negatively impact mood, work, school, and social interactions. 32% of adult survey respondents with moderate or severe AD have missed work events due to their disease, and 30% have had to change careers or give up certain activities. Patients report that their disease also impacts work, including both productivity and contributions while at work. Pain and discomfort are a factor, and patients interviewed reported experiencing painful splitting of the skin during regular daily activities.

"I missed so much school due to my AD that I never graduated high school."

"Eczema deprived me of joy."

"I was in such bad shape that daily tasks became almost unbearable. I couldn't work and wasn't able to play with my children without breaking my skin."

Impact on Youth

Adolescents with AD can suffer significantly with itch and pain, however, the impact goes far beyond those symptoms. The daily life of 52% of the families in ESC survey data of moderate-to-severe disease is negatively impacted by AD. In the same moderate-to-severe disease data, 70% of youth experience loss of sleep. 30% experience difficulty participating in sports or physical activities,

and 21% avoid social activities. 30% of teenagers experience anxiety related to their AD. The disease also impacts the child at school. 20% of adolescents with moderate-to-severe disease miss school days specifically due to their AD, with 23% of those respondents missing ten or more days of school per year and 12% missing 20 or more days of school per year. The caregiver-reported rate of bullying of children related to moderate-to- severe AD is 14%.

Caregivers

55% of caregivers to a teenager with moderate-to-severe AD also experience sleep loss. 69% of caregivers report experiencing anxiety related to managing a youth with moderate-to-severe AD, and 25% reported experiencing depression related to their child's moderate-to-severe AD. Caring for a child with moderate-to-severe AD can also take a toll on the caregiver's lifestyle, with 23% reporting having little or no time for social activities, 23% reporting having little or no time for intimacy, and 29% reporting having little or no time for exercise and physical activity. Additional challenges reported by caregivers include time management, stress, and feeling that they lack support to manage their child's disease. 62% report that time management is a challenge when trying to care for their child with moderate-to-severe AD, and 63% report experiencing physical, mental, or emotional stress. Caregivers of children with moderate-to-severe disease also report feeling a lack of support, with 36% reporting feeling a lack of support from the health care system and 19% feeling a lack of support from family members and friends. Caring for a child with moderate-to-severe AD can also cause financial burden, with 30% of respondents reporting financial challenges related to managing their child's disease.

"*When our child went into high school, the bullying started. The name-calling, isolation, and nasty rumors about him being "contagious" all took an immense toll. It broke our hearts. It got so bad, we decided to keep him home while we desperately searched for something to save him, to give him hope."*

"It took me a very long time to not be ashamed of having eczema. As a teenager, the mental strain is hard, and a seemingly harmless comment can completely ruin your day. Physically, you're left restricted in how much you can push your body to mitigate sweating and that's without even thinking about infections."

4. Experiences With Currently Available Treatments

For some patients with moderate to severe uncontrolled AD, current available therapies do not manage their disease and these patients are in desperate need of solutions.

According to ESC survey data, 87% of adult respondents living with moderate AD report their disease is not well-controlled. Additionally, nearly three-quarters (74%) of respondents have been suffering for more than a year without adequate treatment, and a third (33%) report that they have lived six years or longer without adequate treatment. Sadly, nearly one in four (24%) report having lived a decade or longer without adequate treatment. Despite a number of systemic therapeutic options being available, there still remain patients in need of new options.

For uncontrolled moderate to severe AD patients, systemic treatments may be offered. Until recently, systemic treatments have been very limited for AD patients, including phototherapy and the use of off- label immune-suppressing medications (such as methotrexate and cyclosporine). Oral corticosteroids are commonly used as "rescue medications" for significant AD flares, and were the most frequently used systemic treatment for AD, according to a recent ESC survey. Recently, new systemic therapies have become available and are life-changing options for some patients; however these may not work for all patients, and many are not be accessible to all patients. AD is a heterogenous disease, and a variety of therapies are required to help as many patients as possible.

"The side effects of medications were among the most severe I've ever experienced. Insomnia, acne, and weight gain were all part of the package, and they took a significant toll on my physical and mental well- being. I'd look in the mirror and not even recognize myself."

"Living with eczema isn't easy, and searching for an effective treatment is a frustrating and difficult process. Improved access is a crucial step forward. Having access to proper treatment can help improve many facets of your quality of life."

"My dermatologist kept prescribing me harsher and harsher creams, but my skin just kept getting worse. I tried phototherapy, but it was more than 30 minutes away, and my schedule couldn't keep up. You have to go often for it to work, and I just couldn't."

"I've tried everything – literally everything – even phototherapy, which made me feel hot and sweaty and made my disease worse."

Patients report having suffered, often for decades and commonly report now having little hope and low expectations when it comes to finding a treatment that will help to control their disease and bring them relief. This significant challenge highlights the need for improved and additional treatment options.

5. Improved Outcomes

The primary desired outcome is better control of the disease, as patients report that with current therapies, while they may achieve some temporary relief, there is still a constant cycling on and off of medications as their disease flares. In addition to better disease control, patients are seeking relief from itch and would like therapies that are simple to adopt into their lifestyle and care routines.

In additional detail, patients interviewed expressed wanting a treatment that helped reduce symptoms like itch, dryness, flaking, inflammation, blistering, and cracked skin. Individuals who live with uncontrolled AD are seeking a long-term solution that allows them to sleep, to heal, and to avoid the relentless and debilitating cycle of flares. They also are seeking relief from the pain, discomfort, and psychological burden they live with each day. They want the ability to carry out simple daily activities, such as bathing, contributing at work, and exercising. They want to feel comfortable in their skin, establish and maintain intimate relationships, and reduce or eliminate potential complications and secondary infections that often arise as a result of living with uncontrolled forms of the disease. Innovative treatments such as lebrikizumab can offer these patients hope that they can experience control of their disease and achieve a better quality of life.

“I'd constantly hear stories of people who miraculously got rid of their eczema, leading to immense pressure and self-doubt. I found myself questioning what I was doing wrong.”

“I would want something that is safe, effective, and help me heal from the trauma of living with this disease.”

6. Experience With Drug Under Review

Lebrikizumab offers a new biologic option to treat moderate to severe AD and has been shown to be effective at clearing the skin, reducing itch, and improving quality of life. Systemic treatments for AD offer an important option for patients in need. Lebrikizumab was reported to be an excellent treatment to break the chronic flare cycle of AD. AD is a heterogenous disease and requires a variety of treatments to be available to fill gaps in therapeutic options. Lebrikizumab was also reported as well tolerated.

"I experienced such a noticeable improvement [during the clinical trial for Lebrikizumab] that I knew I was likely in the treatment arm."

"While taking Lebrikizumab, I remember thinking, 'Wow, my skin hasn't ever felt so clear and normal."

Having additional systemic treatment options for AD patients gives the patient community a better chance to manage this burdensome and debilitating disease.

7. Companion Diagnostic Test

N/A

8. Anything Else?

AD can be an unrelenting, painful, and frustrating disease to live with and to manage, and there remains a gap in treatment for some patients.

In summary:

1. For some patients access to new treatments like lebrikizumab can be life changing.
2. Patients with moderate or severe AD suffer greatly due to constant itch, and skin symptoms such as rash, lesions, sores, blisters, scaling, crusting, and infections.
3. Many patients have diligently exhausted all treatment options, and are still in need, failing to achieve management of their disease.
4. New treatments offer great hope to patients, but patients needs access to these potentially life changing treatments.

5. AD is a heterogeneous disease. No single treatment option will be able to meet the needs of all patients.

“Canadians deserve equitable access to therapies that are shown to be safe and effective.”

“I would like for doctors and politicians to realize the painful effects of severe AD are debilitating and chronic, but with the help of new drugs and therapies for people suffering with AD life can be great.”

“I wish a better system could support patients in managing their treatments**.”**

“It would be wonderful if everyone in Canada had the same access to treatment.”

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.

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.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Eli Lilly 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: Amanda Creswell-Melville

Position: Executive Director

Patient Group: Eczema Society of Canada

Date: November 17th, 2023

Name of the Drug and Indication	**Lebrikizumab for the treatment of moderate-to-severe atopic dermatitis (AD)**
Name of the Patient Group	**Eczéma Québec**
Author of the Submission	**Charlie Bouchard, Director, Eczema Quebec**
Name of the Primary Contact for This Submission	**Charlie Bouchard**
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

Eczéma Québec, established in 2020 as a non-profit organization in Québec, stands as the sole entity in the region devoted exclusively to enhancing the understanding, education, and advocacy for eczema patients in the province of Québec. Our endeavors are rooted in elevating public consciousness about eczema, enriching educational avenues, and staunchly advocating on behalf of those suffering from this skin condition. Our collaborative approach involves forming alliances with individuals living with atopic dermatitis, encompassing both adolescents and adults, healthcare professionals, and experts, to uplift the quality of care in Québec. Discover more about our initiatives and efforts at our website, www.eczemaquebec.com.

2. Information Gathering

In preparation for this patient input submission to CADTH on lebrikizumab, Eczéma Québec has engaged in a multifaceted information gathering process. Our approach was designed to capture a broad spectrum of patient and caregiver perspectives on atopic dermatitis and their experiences with Lebrikizumab. The following methods were employed to ensure a comprehensive and representative collection of data:

1. **Review of Scientific Literature**: We analyzed recent studies, including the pivotal work by Silverberg et al. (2023), published in The New England Journal of Medicine, which provided critical insights into the efficacy and safety of lebrikizumab for moderate-to-severe atopic dermatitis.

2. **Informal Conversations with Patients**: Our team engaged in informal dialogues with patients within our network. These discussions offered real-world insights into the daily challenges faced by those with atopic dermatitis and their experiences with various treatments.

3. **Analysis of 'The Skin I'm In' Report**: Insights were also extracted from the previously published report 'The Skin I'm In', a collaborative effort between Eczéma Québec and the Canadian Skin Patient Alliance (CSPA). This report sheds light on the broader impacts of atopic dermatitis on patients' lives.

4. **Collaboration with the MUHC Center of Excellence for Atopic Dermatitis**: Data and expert opinions were sourced from the McGill University Health Centre's Center of Excellence for Atopic Dermatitis, renowned for its research and patient care in the field of atopic dermatitis.

5. **Patient Testimonials and Interviews**: Our submission is further enriched by direct patient accounts, including 9 written testimonials, 14 patient interviews, and feedback from 3 patient group discussions. These personal narratives provide invaluable insights into the lived experiences of individuals managing atopic dermatitis.

The data gathering process took place between February and October 2023, primarily within Canada, ensuring the relevance and applicability of the insights to the Canadian context. The demographic distribution of our respondents spanned various ages, genders, and ethnic backgrounds, reflecting the diversity of the atopic dermatitis patient

population in Canada. Our aim was to capture a comprehensive view of patient experiences, focusing on both the impact of atopic dermatitis on daily life and the potential benefits of lebrikizumab as a treatment option.

This multi-dimensional approach to information gathering allows for a nuanced understanding of the patient perspective, which we believe is crucial for informing CADTH's reimbursement review process for lebrikizumab.

3. Disease Experience

Atopic dermatitis (AD) is a chronic, relapsing skin disorder characterized by an array of symptoms that significantly disrupt daily living. These symptoms, ranging from parched, inflamed skin to severe itching and possible skin thickening or infections, extend their impact beyond the skin. AD is commonly accompanied by co-morbid allergic conditions such as asthma and seasonal allergies, and is often linked with sleep disturbances, anxiety, and depression.

The prevalence of AD in affluent nations is estimated at about 20% among children and 10% among adults, indicating that in Canada, approximately 3.2 million individuals over the age of 15 live with AD. Not limited to childhood, AD also presents in adults, underscoring its complex manifestation.

> *"From the earliest days I can remember, I have been locked in an unyielding battle against AD. As a child, brief periods of peace were punctuated by the mild eruptions of my symptoms, usually in response to moments of heightened stress. But, as I transitioned into adulthood, my eczema resurfaced with an unheralded intensity, a severe onslaught that infiltrated every facet of my existence. The persistent itch was, by far, the most incapacitating aspect." – 26-year old female AD patient*

Patients' narratives capture the essence of living with AD. One 26-year-old recounts her lifelong struggle, noting the escalating severity in adulthood, with the relentless itch being the most debilitating symptom. Adults and adolescents with moderate to severe AD often face such intense symptoms that normal life activities, including sleep and concentration, are severely affected. The physical manifestations of AD, such as rashes, not only cause pain but also contribute to psychological distress through stigmatization, impacting self-esteem and social interactions.

> *"The itch is the last thing I feel before sleep and the first thing I notice when I wake up."* – 38-year old female AD patient

> *"Some nights, it's like there's bugs crawling all over me. I know there's nothing there, but the itching is so intense, I can't help but check under the sheets."* – 67-year old male AD patient

> *"I've had to stumble out of bed at 2am, desperate for relief, and practically scald myself in a hot shower just to numb the itch."* - 25-year old female AD patient

The emotional and psychological burden of AD is profound, with 89% of survey respondents in the 'The Skin I'm In Report: 2022 Update' acknowledging a significant impact on their quality of life. The necessity for comprehensive treatment strategies that consider both physical symptoms and psychological well-being is critical.

> *"There are mornings when I wake up to find my eyes sealed shut. It's terrifying. The process of prying them open is beyond painful. It feels like I've been thrust into some gruesome horror film. The ordeal often results in my eyelids bleeding, so before I can even manage a good morning to my husband, I'm rushing off to the bathroom to apply a compress. It just makes everything difficult. And these thing happen way too frequently to call off work or take time off. So I've just learnt to push through it. But in bad periods, I cry myself to work most days."* – 26-year old female AD patient

AD's influence on professional life is tangible, with patients reporting frequent work absences due to the condition. The report from the MUHC COE-AD indicates that such absences are common, with nearly 38.1% of patients missing work

days in the past year. The narratives highlight the despair and disruption caused by AD, with stories of job loss, medical leaves, and the humiliation and frustration associated with the condition.

> *"By May 2020, my doctor put me on medical leave. Even without washing my hands, they didn't improve. Plus, I couldn't sleep due to the itch and pain. I was suffering round the clock. I even thought about suicide because I felt so hopeless and didn't see a way out."* – 42-year old female AD patient

> *"I've lost count of the number of jobs I've lost due to the sick leaves I needed because of my AD. Each job starts out with hope, but eventually, I hit a bad phase where I start coming in late because of the lack of sleep or the unpredictability of the mornings. I have to get excused from shifts to get to appointments. It's heartbreaking to feel like a failure because of something you have no control over."* – 46-year old female AD patient

> *"I remember having to call in sick because my flare-up was so bad I couldn't wear clothes, let alone step outside. But I don't know how to explain it, it's like humiliating and hard to explain to someone that your skin feels like it's burning and that that's the reason you can't make it."* – 48-year old male AD patient

Access to healthcare presents another challenge, with Canada's low ratio of dermatologists to the population making specialized care difficult to obtain, particularly in remote areas. The anxiety surrounding healthcare access, the efficacy of treatments, and the financial burden of care compound the adversity faced by patients.

> *"I've spent months on a waiting list, hoping to see a specialist. The wait is excruciating. And even when I get an appointment, there's always the anxiety over whether the prescribed treatment will work or if I'll have to start the process all over again. The treatments can be expensive, adding financial stress to an already challenging situation. The constant waiting - for appointments, for answers, for relief - is emotionally and physically draining. I often wonder if I'll ever find lasting relief from this condition that so deeply affects my daily life."* – 25-year old female AD patient

In an analysis of Canadian Healthcare system usage data conducted in the context of the Skin I'm In Report – 2020 Update, Eczéma Québec and the Canadian Skin Patient Alliance found a significant disease burden, with numerous emergency room visits and hospitalizations linked to AD. The data suggest a higher frequency of hospitalizations among adults compared to children and indicate that women are hospitalized more often than men for AD-related conditions. (The patient group input refers to the figures titled "Number of ER Visits per Age Group and Sex, with AD as the main problem", and "Hospitalizations by gender and age with dermatitis and eczema as main diagnosis", available on page 39 and 42, respectively, of The Skin I'm In: 2022 Update, publicly accessible here).

Manion, R., Ribau, S., Bouchard, C., Isola, G., Jack, C., Lebo, D., & Pereira, J. The skin I'm in: 2022 update. Ottawa (ON): Canadian Skin Patient Alliance, Eczéma Québec, McGill University Health Center – Center of Excellence for Atopic Dermatitis, JRL Research & Consulting Inc.; 2022: https://eczemaquebec.com/resources/reports/

AD's impact extends to family life, where caregivers endure emotional and psychological challenges. Financial burdens, sleep disruption, and the emotional toll of caring for a loved one with AD are profound. Caregivers report feelings of despair and guilt, with their health affected by stress and exhaustion.

In conclusion, the day-to-day reality for those with moderate to severe AD is one of psychological and socio-economic strain, limiting engagement in normal activities and diminishing quality of life. The unpredictability of AD, the need for strict skincare routines, and the dietary vigilance required pose constant challenges for patients, emphasizing the necessity for personalized and multifaceted management strategies.

> *"I used to love the gym, but now sweating is painful. Not being able to exercise messes with my head. It feels like my body is against me."* – 50-year old male AD patient

"I found myself withdrawing from the physical activities that I once reveled in." – 26-year old female AD patient

4. Experiences With Currently Available Treatments

Individuals with atopic dermatitis (AD) frequently use a regimen that includes intensive moisturization to maintain the skin barrier, but these essential creams are not eligible for reimbursement, leading to significant out-of-pocket expenses. Beyond the daily use of topical treatments, patients often have to modify their environment and personal care habits, avoiding common irritants like certain fabrics, perfumes, and soaps.

Topical Corticosteroids (TCS) are commonly prescribed as an initial treatment for AD due to their efficacy in reducing inflammation and itch. Yet, their prolonged application can cause adverse effects such as skin thinning, discoloration, and hormonal imbalances. Patients have expressed concerns about the delicate nature of their skin after long-term TCS use, with even minor abrasions leading to injury.

"I use steroid creams, and sure, they work to an extent, but they have this side effect of thinning out your skin. Over time, I've noticed my skin's become super delicate. I'm not kidding when I say that even the slightest scratch can cause bleeding. And once you have a wound, it takes forever to heal." – 32-year old female AD patient

Calcineurin Inhibitors (TCI) are alternatives when TCS are unsuitable or ineffective. Despite their utility, patients report stinging sensations upon application, and there are concerns about the potential long-term risks like skin infections and cancers, causing some to discontinue use.

"I stopped using [my TCI] when I saw that it could cause skin cancer" – 40-year old male AD patient

"I use [a TCI] for maintenance as part of my routine, but it's not always easy. There are days when it stings so badly on application, feels like it's just aggravating my skin rather than soothing it. And that's tough because I rely on it to keep my eczema in check." – 19-year old female AD patient

Phosphodiesterase 4 inhibitors (TPDE4i) address moderate to severe AD symptoms but are not without drawbacks, such as irritation at the application site and the inconvenience of product residue that can stain personal items and clog drains.

"it's not just about the skin anymore, it's also the mess that comes with it. My clothes are always catching stains, and the shower can get all blocked up because of the product buildup. Everything I touch seems to get a greasy smudge, from my glasses to my cellphone." – 38-year old female AD patient

Patients resort to **off-label oral systemic medications** like cyclosporine, methotrexate, and azathioprine, particularly when topical treatments are inadequate. While these can suppress an overactive immune response, they carry risks to organ function and heightened infection susceptibility, reserving their use for severe AD cases.

"I tried methotrexate for 18 weeks, but it didn't help." – 42-year old female AD patient

Oral corticosteroids are powerful anti-inflammatory agents providing short-term relief. However, their substantial side effects limit long-term utility, leading to a cyclical pattern of symptom flare-ups post-treatment.

"In times where I experienced severe, full-body flares, it was like my body was on fire, from head to toe. During these periods, the doctors would put me on prednisone. It helped short term, but once the medication was stopped, the intense itch and inflammation would come back." – 67-year old male AD patient

IL-blockers Monoclonal Antibodies have emerged as a life-changing option for some, reducing itchiness and improving skin condition significantly. Yet, of the approved options, not all patients maintain long-term efficacy, and some experience side effects such as severe conjunctivitis.

> *"I started Dupixent. It changed my life. Within the first few weeks, the itchiness decreased significantly. Gradually, my eczema almost entirely disappeared, and I was able to return to work. Unfortunately, the medication has lost some of its effectiveness, so some eczema has returned, but it's still manageable without the itch, so for now, I'm sticking with Dupixent. However, I had to change jobs because even with Dupixent, if I wash my hands too much, the eczema flares up on them. So, while Dupixent helps a lot, I still have to follow a routine of using mild soaps, unscented moisturizing creams, cortisone creams, and so on. I had no difficulty getting Dupixent because I was able to prove that I had tried other treatments without success, and I had a DLQI score of 22/30"* - 42-year old female AD patient

Janus kinase inhibitors (JAKi) offer a novel oral treatment option with promising results, yet their recent introduction means long-term safety is not fully understood, and there are concerns about their risk profile.

> *"Starting [a JAKi] was a game-changer for me, honestly. I was scared at first, had some side effects right out of the gate, but I stuck with it. And let me tell you, I'm so glad I did. My skin has cleared up more than I ever thought possible, and within the first week, I started feeling less and less itchy".* – 46-year old female AD patient

Despite advancements, a considerable proportion of patients report ongoing moderate to severe symptoms under current treatment regimes, with many expressing dissatisfaction. The restrictive reimbursement criteria and the high cost of newer therapies pose further barriers, rendering some treatments inaccessible without substantial financial strain.

> *"Management wise, I found a promising ally in Dupilumab in 2019. My skin improved, the itching subsided, and my nights were filled with restful sleep. Yet, two years later, I faced a setback. Severe conjunctivitis and eczema on my eyelids began a cycle of unending inflammation. I found myself caught in a disconcerting position - should I trade the known for the unknown, considering the other available options came with more risks and uncertain long-term safety?"* – 26-year old female AD patient

Patients navigate a complex array of treatments with varying efficacy and side effects, emphasizing the need for new therapies that could address these gaps. The experiences shared highlight a landscape where managing AD is as much about mitigating side effects and handling practical treatment challenges as it is about symptom relief. It is imperative that patient have access to a wide pool of options and don't feel in a state of last resort when an option fails.

> *"Now my treatment regimen includes Dupixent and an immunosuppressor. But despite this, my AD is still very much present. I can still see the patches of dry, inflamed skin peeking out from under my sleeves. And the itch, it's always there, a constant reminder. It continues to impact my daily life; from the clothes I choose to wear to the activities I can engage in. It feels like a never-ending challenge."* – 67-year old male AD patient

5. Improved Outcomes

In the context of evaluating new therapeutic options, individuals affected by atopic dermatitis (AD), along with their caregivers and families, prioritize a spectrum of outcomes not sufficiently addressed by existing medications.

Safety Profile: Paramount to patients is the safety of new treatments. There is a strong preference for therapies with fewer adverse effects, both in the short and long term. This is especially pertinent given that many discontinue treatments due to safety concerns for prolonged use.

"First and foremost, I'd love a treatment that could control the itching without causing more harm to my skin." – 35-year old female AD patient

Symptom Relief: The ultimate goal is to find a therapy that offers substantial and enduring symptom management. Patients express a strong desire for treatments that can alleviate the pervasive itching, improve skin integrity, and thus reduce sleep disturbances and enhance mental well-being.

"I'm really hoping for something... something that gives real, long-lasting relief, you know? Not just a band-aid on the problem, but something that truly helps my skin heal. […] . I just want a chance to be in control again, not always feeling like my skin is calling the shots. That's what I'm really looking forward to in a new treatment." – 67-year old male AD patient

Sleep Quality: A significant expectation is for treatments to provide relief from the itch-scratch cycle that disrupts sleep. Improved sleep quality is anticipated to bolster daily functioning and mood.

"I would love a treatment that would give me more than just temporary relief. Something that could help break the itch-scratch cycle, so I could have a good night's sleep, or focus on my work without constant discomfort." – 32-year old female AD patient

"The primary thing I'd hope for is an effective treatment that controls her severe itchiness and soothes her skin. It's heartbreaking to see her suffering from the constant irritation." – Caregiver to a 63 year old AD patient

Productivity and Stability: An effective treatment is seen as one that allows for uninterrupted focus on daily and professional tasks, potentially reducing the frequency of work or school absences due to AD flares.

"I had to change jobs because even with Dupixent, if I wash my hands too much, the eczema flares up on them. So, while Dupixent helps a lot, I still have to follow a routine of using mild soaps, unscented moisturizing creams, cortisone creams, and so on. I find it challenging that people don't know much about severe eczema, so they show little empathy." – 42-year old female AD patient

Life Normalization: A lessened overall impact of AD is sought so that individuals can more freely engage in social activities, work, and leisure without the constant intrusion of their condition.

"My symptoms got worse, so much so it feels like I'm dealing with a whole new disease. I've always loved the outdoors, travelling, hiking, camping. But now, with the unpredictability of my skin and the demands of treatment, it's hard to enjoy these things..[…] Now, it's just a reminder of how my skin holds me back. I can't even think about staying in a hotel without worrying about staining their clean white bedsheets with blood from scratching. It's embarrassing and makes me incredibly self-conscious. I'm hoping things will get better, but for now, it's tough." – 56-year old male AD patient

Emotional Well-being: Better control over AD is expected to alleviate the psychological impact of the disease, thereby enhancing personal relationships and social interactions. Increased self-esteem and reduction in the stigma associated with visible skin conditions are key outcomes.

"Every comment on "how bad" it looked or "how painful" it seemed when referring to my raw patches of skin all over would only draw me back to the itching, stinging, burning, boiling feeling of my skin. Every well-meaning yet misguided advice confronted me with the thought of me failing to manage my condition. Alienation was profound and painful." – 26-year old female AD patient

Treatment Usability: Ease of use is critical. Treatments that are simple to apply, with manageable side effects, will likely see higher adherence. The ideal therapy would integrate seamlessly into patients' lives without feeling burdensome.

Treatment Flexibility: Patients seek treatment options that do not impose on their daily routines, preferring those that do not require frequent applications or special considerations during use.

> *"The time I need to put into my skin routine often feels like a part-time job."* – 19-year old female AD patient

Durability of Treatment Effect: There is a desire for treatments that offer long-term relief, reducing the cycle of symptom recurrence and the need for constant retreatment.

Cost-effectiveness: Financial accessibility is a pressing concern. An optimal treatment would balance efficacy with affordability, easing the financial burden of managing AD.

> *"I've had severe AD since I was around 15. Since moving out of my parents' home, it has become increasingly difficult to afford everything I need to manage my skin. Between the volumes of creams, the special soaps, cleaning products, unscented laundry detergent, cotton sheets, clothes that I ruin, the costs add up. I currently use dupilumab and it's helping so much, but it's another expense and with the current cost of living, it's hard for me to keep up."* – 22-year old female AD patient

Lebrikizumab, as a new treatment option, is being evaluated by patients and caregivers through the lens of these desired outcomes. If lebrikizumab can effectively address these areas where current treatments fall short, it could markedly enhance the quality of life for patients and their families. This includes a potential reduction in the day-to-day management of AD, increased participation in social and professional activities, and overall improved physical and emotional health.

Trade-offs in therapy choice are also a critical consideration. While efficacy remains a primary concern, the implications of side effects, treatment burden, and cost are also weighed heavily in decision-making. The hope is that lebrikizumab will offer a favorable balance, meeting the nuanced needs of the AD community.

6. Experience With Drug Under Review

While direct patient experiences with Lebrikizumab within our community are currently unavailable, insights can be gleaned from its phase 3 clinical trials and the experiences of patients using similar IL-blocker monoclonal antibodies, such as tralokinumab and dupilumab. These medications have shown life-altering improvements in the management of atopic dermatitis (AD), and we anticipate that lebrikizumab could offer comparable, if not enhanced, benefits due to its specific mechanism of action and the promising results from clinical studies.

Patients who have used similar therapies have reported significant advancements in disease control, symptom relief, and overall quality of life. Benefits have included reduced itching, better sleep quality, and improved skin health, which collectively translate to a more normal daily living experience. From the clinical data available, lebrikizumab has shown a favorable efficacy profile, with the potential to improve upon these outcomes, especially for those who may not have achieved optimal results with other treatments.

Access to lebrikizumab for patients has primarily been through clinical trial participation. However, we foresee that upon approval, private insurance coverage could be a viable pathway for many. The possibility of adding another therapeutic option like lebrikizumab is significant for patients who have had limited success with existing treatments, offering hope for better disease control and an improved quality of life.

While we do not have accounts of disadvantages or side effects specific to lebrikizumab from our network, we acknowledge the importance of monitoring for potential adverse effects as observed in clinical trials and managing them

as necessary. The ease of use, often a deciding factor for treatment adherence, is another aspect where we expect lebrikizumab to be favorable, given the trends in administration and dosing schedules seen in similar biologic treatments.

There may be specific subgroups within the AD patient population, such as those with a particular biomarker profile or those who have not responded to other IL-blockers, for whom lebrikizumab might be particularly beneficial. The sequencing of therapies is critical, and for some patients, lebrikizumab might serve as a first-line biologic treatment or as an alternative when others have not provided sufficient control.

In summary, the key values important to patients and caregivers with respect to lebrikizumab or any new drug include efficacy, safety, ease of use, and accessibility. The community looks forward to more personalized treatment options that can be seamlessly integrated into their lives without compromising safety or efficacy.

7. Companion Diagnostic Test

There is no companion test.

8. Anything Else?

As CADTH reviews lebrikizumab, it is crucial to understand the broader context in which this therapy will operate. Despite an increasing number of treatments for atopic dermatitis (AD) in Canada, there is a substantive patient population for whom existing therapies are insufficient. The reasons are multifaceted:

- **Comprehensive Disease Impact**: AD transcends a mere dermatological ailment, exerting profound effects on physical, emotional, and social well-being. The condition can severely disturb sleep, mental health, and the capacity to function effectively in work or educational settings.
- **Limitations of Current Therapies**: While current treatment options for AD have advanced, they are not without significant drawbacks. Side effects may rival the severity of AD symptoms, and accessibility issues due to cost or logistics remain significant barriers to effective disease management.
- **Need for Personalized Treatment**: The heterogeneity of AD symptoms and responses to treatment necessitates a personalized approach to therapy. Not all patients respond to existing medications, and for some, the side effects are untenable.

Lebrikizumab's review comes at a critical juncture where the need for new, effective, and patient-friendly treatment options is high. Preliminary data on the efficacy and safety profile of lebrikizumab are encouraging and could represent a pivotal addition to the AD treatment paradigm. It is essential to consider that for a subset of patients, particularly those who have not found relief with current treatments, lebrikizumab could offer a significant improvement in disease control and life quality. But don't just take it from us — our community members, deeply affected by atopic dermatitis, are the true voices of lived experience and hope. One such member's testimony encapsulates the collective sentiment:

> *"Today, I hold out hope that this testimony will lead to significant advancements for everyone who suffers from atopic dermatitis like me. I want to emphasize the importance I place on Eczema Quebec! They are actively involved in shaping the future of atopic dermatitis treatments. They make our needs heard by the Canadian Agency for Drugs and Technologies in Health so that it is possible for us to access treatments like 'lebrikizumab' without too much expense. I hope that this testimony will bring about significant progress for all those who suffer from atopic dermatitis like me and that this medication will be made accessible to all patients who need it."* – Member of Eczéma Québec's Patient Community

We urge CADTH reviewers and the expert committee to recognize the individuality of patient experiences with AD and the urgency for expanding the therapeutic arsenal with drugs like lebrikizumab that potentially offer improved outcomes. The decision to include lebrikizumab in the list of reimbursable medications could be a decisive factor in altering the lives of those burdened by AD, providing them with renewed hope and the possibility of a better quality of life.

We thank CADTH for their thorough review and careful consideration of all aspects of lebrikizumab's potential impact on patients with atopic dermatitis.

Appendix: Patient Group Conflict of Interest Declaration

Eczéma Québec is committed to maintaining the integrity and objectivity of the CADTH reimbursement review process. We acknowledge the importance of transparency in declaring any real, potential, or perceived conflicts of interest.

1. **Assistance in Submission Completion:** For this submission, Eczéma Québec did not solicit or receive assistance from any entities outside of our patient group. The content, perspectives, and conclusions presented herein were developed independently by Eczéma Québec, based on our members' insights, the experiences of our community, and our comprehensive analysis of available scientific literature and clinical trial data relevant to lebrikizumab.

2. **Assistance in Data Collection or Analysis:** No external assistance was sought or obtained for the collection or analysis of data used in this submission. All data referenced have been sourced from publicly available scientific studies, including phase 3 clinical trial results for lebrikizumab, and have been interpreted solely by Eczéma Québec without external influence.

Eczéma Québec operates with the utmost respect for the principles guiding CADTH's decision-making process. We strive to provide input that reflects the unmet needs and collective voice of patients with atopic dermatitis, without bias or external influence. Our focus is on advocating for access to new, effective treatments that could significantly improve the quality of life for individuals affected by this condition.

Table 1: Financial Disclosures

Companies or organizations that have provided Eczéma Québec with financial payment over the past two years AND who may have direct or indirect interest in 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
AbbVie Canada				X
Leo Pharma			X	
Sanofi				X
Pfizer			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.

On behalf of Eczéma Québec
Name: **Charlie Bouchard**

Position: **Director**

Patient Group: **Eczéma Québec**

Date: **2023-11-14**

Clinician Input

CADTH Project Number: SR0819-000

Generic Drug Name (Brand Name): **Lebrikizumab**

Indication: **Moderate-to-severe atopic dermatitis in adults and adolescents**

Name of Clinician Group: **Dermatology Association of Ontario (DAO)**

Author of Submission: **Dr. David N. Adam**

1. About Your Clinician Group

The DAO is the provincial association for Dermatologists. Membership consists of dermatologists from all areas of the specialty including academic and community-based practitioners. We are proud to include both regional, national, and international experts in atopic dermatitis amongst our membership.

2. Information Gathering

Published data from pivotal trials, existing literature on the topic and expert opinion of our members formed the basis for the data presented in this summary.

3. Current Treatments and Treatment Goals

The treatment of atopic dermatitis consists of lifestyle modification (avoidance of irritants, frequent use of moisturizers, avoidance of known allergens), prescription topical therapies (steroids, calcineurin inhibitors, phosphodiesterase-4 inhibitors), phototherapy and systemic therapy. Moderate to severe atopic dermatitis is almost always inadequately managed by topical therapy. This is in large part due to the larger body surface area involved in this severity of the disease. Therefore, patients with moderate to severe dermatitis almost invariably will require phototherapy or a systemic agent to manage their illness.

Phototherapy while sometimes effective is difficult to access for many patients as they must attend clinics that are limited in number and operate during regular business hours. Therefore, to successful attend treatment significant absenteeism from school and work would be required thereby limiting access. Furthermore, many areas of Ontario do not even have a phototherapy unit that is accessible within a reasonable commute.

Systemic therapies include off-label treatments that historically have been used (cyclosporine, methotrexate, azathioprine and others) however these treatments are limited largely by their limited efficacy and significant toxicities. Due to their long list of potential side effects and adverse effects these therapies are often contraindicated in many patients or provide limited efficacy.

A welcome addition to the armamentarium has been biologics including dupilumab and tralokinumab as well as Janus Kinase (JAK) inhibitors. These medications have delivered significantly better efficacy with better tolerability and overall, significantly improved safety profile for the treatment of this chronic disease. These therapies are utilized when patients require systemic treatment and in the case of publicly covered patients have failed other off-label systemic agents.

Currently available JAK inhibitors include abrocitinib and upadacitinib. These molecules are approved for public patients for the treatment of moderate to severe atopic dermatitis when conventional systemics have failed. JAK inhibitors offer the advantage of superior efficacy particularly in the first 24 weeks when compared to traditional systemic agents as well as biologics. This has been examined in head-to-head studies against biologics. Importantly however both clinical trials and real-world experience seem to indicate that these curves approach each other in the long term delivering similar long term efficacy. JAK inhibitors, like traditional systemic do require regular bloodwork and based on their mechanism and clinical trial data are not appropriate for all patients thus necessitating a black box warning in the product monograph.

Available biologics on the market currently include dupilumab and tralokinumab and soon lebrikizumab. These agents are used for patients with moderate to severe disease after having failed or have contraindications to conventional systemic agents for publicly covered patients. Biologics offer the advantages of being generally well tolerated and do not require any laboratory monitoring.

Dupilumab is a monoclonal antibody that targets the common IL-4 and IL-13 receptor. Tralokinumab is a monoclonal antibody that targets soluble IL-13. Lebrikizumab, a novel molecule that targets soluble IL-13 has completed phase III studies and will soon be on the market as well. Lebrikizumab and tralokinumab are distinct molecules with a distinct mechanism of action that differentiates them from dupilumab. This mechanistic difference has clinical relevance as patients that fail or cannot tolerate dupilumab can be switched to lebrikizumab. The safety profile of lebrikizumab is also superior to that of dupilumab in that the rate of conjunctivitis is lower in lebrikizumab treated patients.

Goals of treatment can be defined with outcome measures from clinical trials like the eczema area and severity index (EASI) and/or the investigator global assessment (IGA) however on a more practical level these measures serve as a proxy for whether or not the disease is sufficiently controlled that it no longer limits the patients life.

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 many patients that either fail or have contraindications to traditional systemic therapies and cannot access phototherapy. Of this population there are significant numbers of patients who have contraindications (namely, cardiovascular events, thrombosis, malignancy, and serious infections) to JAK inhibitors or simply are frightened by the black box warning on the medications and do not wish to start therapy. Of patients on JAK inhibitors there are those that develop side effects (including acne, herpes infections, GI upset) and must stop therapy. Finally, dupilumab while effective in a significant proportion of patients does not deliver adequate response rates in close to half of patients as judged by EASI 75 response in the pivotal trials. Finally, there are a significant number of patients who develop side effects, namely conjunctivitis, while on dupilumab and need alternate therapies that can deliver efficacy with a lower risk of side effects.

5. Place in Therapy

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

Lebrikizumab would fit into the current treatment paradigm as another treatment option for patients alongside dupilumab, tralokinumab or JAK inhibitors. For patients with private insurance these medications are often available as first line therapy however for public patients they are second line behind traditional systemics. Importantly, only dupilumab and JAK inhibitors are currently accessible to publicly covered patients as advanced therapies. There is a pressing clinical need for more biologic molecules, like lebrikizumab to be covered for publicly covered patients for the reasons elaborated upon in the previous section.

Evidence from clinical trials of lebrikizumab strongly supports in place in the treatment algorithm for moderate to severe atopic dermatitis. Entry into clinical trials were based on patients that had failed topical therapies so there is rationale for allowing this medication even as a post topical intervention, without the need for failure of traditional systemic therapies.

Specific outcome measures from the pivotal clinical trials for lebrikizumab demonstrate robust efficacy with a reassuring safety profile. The EASI 75 and IGA 0/1 target in the lebrikizumab studies is comparable to that of dupilumab at all time points. Further, NRS values demonstrate a significant impact on itch as measured by NRS scores as well. These results are clearly seen at the primary endpoint at week 16 and are maintained out to week 52 and beyond. These dramatic improvements in disease control and itch translate into measurable improvements in other patient reported outcomes like the DLQI.

Lebrikizumab offers another potential attractive advantage for prescribers, patients, and payors. Recently released 52-week data show that there is only a slight difference between responders when they were randomized to either q2 weekly maintenance dosing versus q 4 weekly dosing. This offers obvious benefits for patients that wish to decrease their needle burden and for payors with obvious cost saving.

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?

Lebrikizumab would be best suited for the treatment of adult patients with moderate to severe atopic dermatitis who have failed topical therapies and those that have failed or do not have access to phototherapy. While currently advanced systemic therapies

require patients to have trialed or have contraindications to traditional systemics ideally patients would be able to access safer and more effective therapies without having to trial less efficacious treatments that are known to be less safe.

Barring that kind of access, the DAO would hope and expect that lebrikizumab would be given the same considerations as other approved advanced therapies like dupilumab and JAK inhibitors. Particularly as there are patients that fail or have side effects with these advanced therapies and currently there are no other approved options.

Lebrikizumab would not be least suitable for patients with an allergy to the medication or an excipient in the injection itself. Lebrikizumab may be less suitable for patients with needle phobias however the side effect profile of oral medications often engenders some trepidation in patients that can outweigh their hesitancy for needles. Also oral medications will still require needle exposure in the form of blood monitoring.

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?

Patient response is assessed via:

1. IGA score of 0 or 1.
2. EASI improvement (75% by 12-16 weeks)
3. Itch NRS reduction of 4 or more points.
4. DLQI improvement of >4 points

Initial treatment response is typically assessed at 4-6 months and then annually thereafter.

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

Factors to be considered when deciding to discontinue treatment with lebrikizumab would be adverse events (this was exceedingly rare in the clinical trials) or lack of efficacy as judged at month 4-6.

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]?

Treatment with lebrikizumab would be appropriate in the community setting. Diagnosis, treatment and monitoring of patients on lebrikizumab should be limited to specialists trained in this area which would include dermatology, allergy/immunology or pediatricians.

6. Additional Information

It is the sincere hope of the DAO that CADTH will consider the points made in this application and extend a favorable opinion for lebrikizumab. While patients with psoriasis have over 10 approved and covered biologics, patient with atopic dermatitis, an equally crippling disease that ruins the lives of the patients and their family members only has one currently approved. This discrepancy is striking and needs to be rectified. Lebrikizumab offers a safe, effective and durable treatment for our patients with life altering disease and is sorely needed.

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.

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.

   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. **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: Dr David Adam

Position: Dermatologist

Date: 20 Sept 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**
Lilly			X	
Abbvie			X	
Pfizer		X		
Leo			X	
Sanofi			X	

Declaration for Clinician 2

Name: Dr. Lyne Giroux

Position: Dermatologist

Date: 20 Sept 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 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**
Lilly	x			
Abbvie		x		
Pfizer	x			
Leo	x			
Sanofi	x			

Declaration for Clinician 3

Name: Dr. Fiona Lovegrove

Position: Dermatologist

Date: 7 Oct 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 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
Lilly		x		
Abbvie			x	
Pfizer			x	
Leo			x	
Sanofi			x	

Declaration for Clinician 4

Name: Dr. Thanashan Rajakulendran

Position: Dermatologist

Date: 15 Oct 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 4

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Lilly	0			
Abbvie	x			
Pfizer	0			
Leo	x			
Sanofi	x			

Declaration for Clinician 5

Name: Dr. Jane Wu

Position: Dermatologist

Date: 15 Oct 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 5

Company	**Check appropriate dollar range***			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Lilly	x			
Abbvie		x		
Pfizer	x			
Leo	0			
Sanofi	x			

Declaration for Clinician 6

Name: Dr. Paul Adam

Position: Dermatologist

Date: 12 Nov 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 6

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

Abbvie	0			
Pfizer	0			
Leo	0			
Sanofi	0			

Declaration for Clinician 7

Name: Dr. Mohammed Bawazir

Position: Dermatologist

Date: 24 Oct 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 7

Company	**Check appropriate dollar range***			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Lilly	x			
Abbvie			x	
Pfizer	x			
Leo	x			
Sanofi		x		

Declaration for Clinician 8

Name: Dr. David Croitoru

Position: Dermatologist

Date: 26 Oct 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 8

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Lilly	x			
Abbvie			x	
Pfizer	x			
Leo	x			
Sanofi		x		

Declaration for Clinician 9

Name: Dr. Perla Lansang

Position: Dermatologist

Date: 29 Oct 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 9

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

Leo	x			
Sanofi				x

Declaration for Clinician 10

Name: Dr. Lara Gunton

Position: Dermatologist

Date: 30 Oct 23

☒ **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 10

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Lilly	x			
Abbvie		x		
Pfizer	x			
Leo	x			
Sanofi	x			

Declaration for Clinician 11

Name: Dr. Geeta Yadav

Position: Dermatologist

Date: 3 Nov 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 11

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Lilly	x			
Abbvie				x
Pfizer			x	
Leo		x		
Sanofi			x	

CADTH Project Number: CADTH Project Number: **SR0819-000**

Generic Drug Name (Brand Name): **Lebrikizumab**

Indication: **Moderate to severe atopic dermatitis ('msAD') in age 12 years and older**

Name of Clinician Group: **Canadian Dermatology Association (CDA)**

Author of Submission: **CDA Pharmacy and Therapeutics Advisory Board**

1. About Your Clinician Group

The Canadian Dermatology Association, founded in 1925, is the national medical specialty association that represents Canadian certified dermatologists. The association exists to advance the science and art of medicine and surgery related to the care of the skin, hair and nails; provide continuing professional development for its members; support and advance patient care; provide public education on sun protection and other aspects of skin health; and promote a lifetime of healthier skin, hair and nails.

Clinical review and oversight is provided by the Canadian Dermatology Association's Pharmacy and Therapeutics Advisory Board. Website Link: Canadian Dermatology Association www.dermatology.ca

2. Information Gathering

Information that was gathered from clinical experience, research and trial experience, medical literature, published trials and other research designs, and national and international meetings.

3. Current Treatments and Treatment Goals

Atopic dermatitis (often referred to as 'AD', commonly referred to as 'eczema') is a chronic, inflammatory skin condition that can range in levels of severity and burden and affects all ages, ethnicities and genders. The pathophysiology of AD is complex, involving genetic predispositions and environmental factors that can influence its nature and course. AD is fundamentally characterized by structural dysfunction of the skin barrier, and a dysregulated immune response (involving predominantly Th2 immune pathways and increased expression of Th2 cytokines such as IL4, 13, 31). AD is often the first step observed in the 'atopic march' which represents associations of progressive clustering of atopic and allergic diseases (eg. AD, asthma and allergic rhinitis). In Canada, AD may affect up to 3.5% of adults, and 8-15% of children (Barbarot et al., 2018; CPSA 2023). The majority of patients represent more mild-to-moderate spectrums of disease (~88%), and a minority of patients represent severe disease (Barabot et al., 2018). Mild to moderate cases generally can be managed with earlier stages of the therapeutic ladder (eg. lifestyle, over-the-counter, topical prescription therapies). However, those who fail these therapies and still have moderate to severe AD (msAD) with large burdens of impact including poor quality of life require treatment escalation.

The AD treatment ladder reflected in many guidelines followed by Canadian dermatologists firstly include non-prescription and lifestyle factors such as trigger avoidance, hypoallergenic skin care, bathing, and moisturizing which is recommended for all. If AD is not controlled, prescription topical therapy is considered in which topical steroids are most commonly employed as first-line since the 1950s. In Canada, the currently available three classes of topical prescription therapies for AD include: 1. Topical corticosteroids (TCS), 2. Topical calcineurin inhibitors (TCIs; tacrolimus 0.03% and 0.1%, pimecrolimus 1%), and 3. Topical PDE4 inhibitors (crisaborole 2%). For msAD, further options include phototherapy, traditional off-label systemic immunosuppressants (methotrexate, cyclosporine, mycophenolate, azathioprine, oral steroids). Newer, more targeted AD-disease mechanism on-label systemic agents for msAD currently available to prescribe in Canada include biologic therapy (dupilumab, IL4/13 inhibitor), tralokinumab (IL13 inhibitor; limited coverage), and oral small molecule inhibitors (eg. JAK1 inhibitors; upadacitinib and abrocitinib). Limitations of some of these therapies and unmet needs for new options are as reviewed in the below.

General important goals of AD therapy include maximizing efficacy and safety benefit. This includes treating signs and symptoms (eg. short and long-term management, addressing flares, itch), improving quality of life and mental health status associated with the condition (eg. sleep quality, anxiety, depression), keeping ability to function or 'normalized life' (eg. reduce presenteeism/absenteeism from work, school), and reducing adverse and serious adverse events. Some goals of therapy may be

difficult to address in those who face barriers to care (such as northern and remote populations, examples reviewed below). Many goals of therapy can be measured using the patient history and physical exam, supplemented by clinician and patient reported outcomes with ongoing follow-up.

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 a definite unmet need for new treatment options for moderate-to-severe (msAD) in general due to the high rates of uncontrolled disease and lack of currently available Health Canada approved therapies. Below reviews unmet needs as shown in recent literature and from clinical experience, and limitations of currently available therapies.

Three Canadian survey reports from the Eczema Society of Canada (Quality of Life Report for moderate-to-severe Atopic Dermatitis (2017), Itch in Atopic Dermatitis Report (2021), and Atopic Dermatitis Patient Journey (2023) highlight the following burdens: Signs and symptoms, challenges in access to care, high rates of poorly controlled disease, treatment failures, multi-tiered treatment regimens, significant quality of life impact, and others of the patient experience. Below includes a summary of findings:

Society of Canada: Quality of Life Report for Moderate-to-Severe Disease (2017):

Adult data:

- 41% of respondents indicated their treatment needs are not being met by current AD therapies
- 43% of respondents reported using 10 or more different treatments for AD, 29% reported using 15 or more different treatments to manage AD
- 63% reported that off-label traditional systemic immunosuppressant medications (Methotrexate, Cyclosporine) did not work well to manage their AD
- 98% of patients tried topical steroids, and 91% reported that their AD is not well controlled.
- 78% reported they have lived without adequate treatment for a year or more
- 42% of respondents visited a doctor four or more times in the past two years to manage their AD. Almost one-third waited 6 months or longer, resulting in patients visiting the ER for flares.
- Quality of Life Impact:
    - 87% of respondents indicated their daily life is negatively impacted by AD
    - Respondents reported:
        - § Loss of sleep (79%; 29% reported more than 14 nights per month, and 50% reported 8 nights or more of sleep loss per month)
        - § Anxiety (64%)
        - § Avoidance of social activities (48%), physical activities (47%), intimacy (40%)
        - § Missing work or important life events (32%),
        - § Needing to change careers or give up certain activities (30%).

Eczema Society of Canada Itch in Atopic Dermatitis (2021):

Most patients responding to this survey (87%) were in the moderate-to-severe AD category, representing 85% adults and 15% caregivers of children with AD.

- Adults with moderate or severe AD describe their itch as:
    - Unpredictable (78%)
    - Debilitating (46%)

    - Underestimated (71%)
    - 62% of moderate, and 87% of severe AD patients report scars or marks on their skin due to scratching

- **Mental health**: 45% of moderate AD, and 71% of severe AD patients report that itching negatively impacts their mental health.
- **Stress:** 69% of moderate AD, and 87% of severe AD patients report that itch negatively impacts stress.
- **Absenteeism/Presenteeism:** 27% of moderate, and 48% of severe AD patients report itch negatively impacts their work or school.
- **Sleep Disruption:** 18% of moderate, and 55% of severe AD patients report being woken every night due to itch

Findings from these Canadian-based surveys are similar to other recent literature on unmet needs in AD. Itch has been reported as the most burdensome symptom of AD (ESC, 2021, Fasseeh et al., 2002; CPSA/McGill 2022). Other common and burdensome symptoms reported in various studies include scratching, excessive dryness/scaling, red/inflamed skin, papulovesicular lesions, thickening of skin (lichenification), open sores or oozing, pain, anxiety, depression, and sleep disturbance (Silverberg et al., 2018; CPSA/McGill 2022; Fasseeh et al., 2022). A systematic review on 'Burden of Atopic Dermatitis in Adults and Adolescents' (Fasseeh et al., 2022) concluded that, 'the burden of AD is significant', and that 'the hidden disease burden is reflected in its high indirect costs and the psychological effect on quality of life. The magnitude of the burden is affected by severity level.' Updated information on the Canadian economic burden of AD in terms of direct or indirect costs is needed; in 2004, the annual total cost of AD was estimated to be 1.4 billion mostly attributed to indirect costs (Barbeau, 2004). This information taken together, especially in the Canadian context, shows that even though increasing treatment options are currently available for AD, many patients are still unable to manage or control their condition and continue to have significant disease burdens.

Over-the-counter moisturizers, emollients, hypoallergenic products and lifestyle modifications are first-line therapies. However, when first-line prescription treatment is required, currently, in Canada we have only three Health-Canada approved prescription topical therapies for AD: 1. Topical corticosteroids (TCS) - Various classes that have restrictions based on potencies, body site, formulation (delivery vehicle), and duration of use; 2. Topical calcineurin inhibitors (TCIs; Topical tacrolimus 0.03% or 0.1% ointment, pimecrolimus 1% cream); and 3. Topical PDE4 inhibitors (crisaborole 2% ointment). Generally, these topical options are used for those who have mild-to-moderate disease that failed non-prescription therapy, but can be used for all levels of disease. For those that fail topicals and the traditional (eg. guideline-based) therapeutic ladder and still have msAD, further options include phototherapy (often of limited success, burdensome for some patients to attend, or poorly accessible for rural, remote and underserviced populations), or traditional off-label systemic immunosuppressants (eg. Methotrexate, cyclosporine, mycophenolate, azathioprine, oral steroids). These more broad and non-specific immunosuppressants are also associated with a range of systemic side effects, some potentially severe such as cytopenias, hepatotoxicity, hypertension, renal damage, infection and malignancy and often aren't recommended for long-term use (eg. Cyclosporine). These therapies require consistent and regular safety monitoring (eg. clinical follow-up, recurrent labwork, baseline and ongoing chest X-rays, others like TB or quantiferon tests). Monitoring for and managing side effects of traditional systemic immunosuppressants can be challenging for patients without family physicians, or those who have lack of lab or healthcare facility access in rural and remote areas of Canada (many of these concerns are magnified in remote and northern Canadian Indigenous communities). On a practical level, paperwork and time required to coordinate safety monitoring and ongoing follow-up for msAD patients on such therapies can add to more human resource and overhead burdens (eg. nursing, admin time) on prescribing clinicians compared to other commonly encountered conditions; there also is a need to reduce these burdens.

Health Canada approved AD-targeted biologic and oral small molecule (eg. JAK1 inhibitors) are becoming increasingly available. These new options often still carry their own limitations with regards to safety and efficacy profiles, and access. Many patients fail, or are intolerant to the currently available systemic and biologic therapies. Oral JAK1 inhibitors demonstrate rapid pruritus responses and improvement in EASI scores, but carry a certain potential side effect profile and also carry a black box warning. The currently available biologic therapy for msAD, dupilumab, also comes with unmet needs with regards to therapeutic failures, and side effects such as conjunctivitis or recalcitrant facial erythema. Although the mechanism is not fully understood regarding dupilumab and ocular side effects, a meta analysis by Halling et al. (2021) estimated up to 26% of patients may get conjunctivitis. In clinical experience, patient impacts from ocular side effects like conjunctivitis can require discontinuation due to intolerance (even if the medication has greatly helped their AD).

A strong benefit to biologic therapy is labwork is not required, and safety profiles are generally more favorable relative to the currently available systemic alternatives needing regular safety monitoring. Safety profiles can be beneficial, especially as in rural, remote and underserviced areas, it has been increasingly difficult for patients to access both specialist and primary care should safety concerns arise or a generalist or specialist's involvement is required while on immunosuppressant therapy. Also,when requiring labwork or

other forms of safety monitoring (eg. Chest X-Ray, TB test, age-appropriate cancer screening), long travel distances may be challenging for some patients to access labs or other facilities on a regular basis for baseline and safety monitoring; in clinical experience this reflects in baseline and monitoring tests or labwork often being delayed or missed.

Biologic therapy has potential to address some of these barriers due to the favorable efficacy and safety profiles and lack of need for baseline workup or ongoing lab monitoring. Additional information includes that the safety profile of currently limited available options for biologic therapy has benefitted some populations who face intersectional barriers to care, and face higher risk for poor outcomes or challenges to optimizing therapeutic outcomes. An example of this includes rural, remote and northern Canadian Indigenous peoples who represent the most likely racial group to live rurally and remotely in Canada (OECD, 2022). Many of these communities lack healthcare practitioner and facility access, and face barriers to care and health disparities due to complex determinants of health linked to the Canadian historical, legal and social system. msAD and co-morbid bacterial skin infections has been shown to be a prevalent issue of unmet need in literature, and media, and in clinical experience (Asiniwasis & Chu, 2022; Forsey, 2014; Asiniwasis et al., 2021; Schreiber et al., 2023). Biologic therapy, including IL13 inhibitors such as lebrikizumab provides a safe and effective option for many of those facing barriers to care (eg. difficult lab and healthcare practitioner access for safety monitoring for systemic immunosuppressants) or uncontrolled comorbidities, or for those who have failed or

been intolerant to, or cannot access (eg. phototherapy). Also, IL13 inhibitors may decrease risk of skin infections (Lytvyn, 2023; Silverberg et al., 2023) which may help address the problem of secondarily infected AD.

5. Place in Therapy

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

Lebrikizumab would fall into the category of biologic therapy indicated for moderate-to-severe AD. Currently, dupilumab is available with limited availability of tralokinumab in this category in Canada. Referring to general AD treatment guidelines and where biologic therapy would fit within, lebrikizumab would fit as an option for first-line biologic therapy for msAD, similar to dupilumab. Lebrikizumab would likely adopt the same criteria for use as dupilumab which may vary depending on type of coverage plans (eg. fail topicals, phototherapy, off-label systemic therapy). Lebrikizumab can be used for msAD patients who fail to respond, or are intolerant of, systemic therapy, phototherapy, other biologics or oral JAK inhibitors. Also, due to the overall favorable safety profile and minimal contraindications to using lebrikizumab, comorbid patients with msAD could potentially be a candidate for lebrikizumab. These could include those who have comorbidities/contraindications to JAK inhibitors (eg. risk factors for DVT/PE, cancer, infection) or other systemic immunosuppressants.

Lebrikizumab contributes to an important shift in the current treatment paradigm towards a new era of focus on novel disease-mechanism targeting and disease modification with favorable safety and efficacy profiles. Also, with the overall well tolerated safety profiles and lack of need for lab/safety monitoring (as required for systemic immunosuppressants), it also can alleviate burdens on prescribers, patients and the healthcare system. It represents a fast-acting therapy targeted to IL13 that has reached meaningful primary and secondary endpoints as demonstrated in multiple RCTs. Significantly important and meaningful results are found in the lebrikizumab trials from 16 up to 52 week data across multiple trials involving adults and adolescents (age 12+) with msAD. Primary endpoints from ADvocate 1 and ADvocate 2 (monotherapy trials evaluating efficacy and safety outcomes for 16 weeks for msAD age 12+) at week 16 included: IGA score 0,1 at week 16 and $\geq$ 2 point improvement from baseline and EASI 75. EASI75 was reached in 58.8% of those in ADvocate-1, and 52.1% in ADvocate 2 (versus placebo 16.2%, 18.1% respectively). EASI90 was reached in up to 38%. Primary endpoints of IGA 0,1 were met by 43% at Week 16 versus 12.7% placebo (ADvocate 1), 33.2% versus 10.8% (ADvocate 2). Early separation from placebo in response rates, were seen. Also, less rescue therapy was required in the lebrikizumab versus placebo arm. In week 52 data, durable rates were seen at maintaining EASI75, IGA and pruritus NRS, and many patients continued to improve, reaching EASI 90 at both every 2 week and every 4 week dosing. The ADore study assessed 52 week efficacy and safety data of adolescents with msAD (age 12-18). IGA 0,1 was reached in 14.4%, 46.3%, and 62.6%, in weeks 4, 16 and 52 respectively. EASI 75 was reached by 28.6% at week 4, 73.2% of participants at week 16, and 81.9% at week 52 demonstrating excellent response. EASI50 was reached in 94.4% of patients, and EASI 90 in 61.4% of patients at week 52. In the ADvantage study, 16 week efficacy and safety combined with low or mid potency TCS in patients with msAD not adequately controlled or non-eligible for cyclosporine was assessed in Phase 3 ADVantage study. The primary endpoint EASI75% response 68.4% and secondary endpoint EASI90 represented 42.9% at week 16. IGA 0/1 was reached by 42% of patients, and half of patients reached a $\geq$4 point improvement in pruritus NRS at week 16, with a faster response observed in the lebrikizumab group. Lebrikizumab also has been associated with improved outcomes in msAD in age 12+ when in combination with TCS, as seen in the

ADhere study for 16 weeks. Results met statistical significance for primary endpoints and safety profile consistent with previous studies.

Overall, from an interpretation standpoint from what we currently have available, lebrikizumab demonstrates excellent safety and efficacy profiles and fills a gap in unmet needs. Ideal therapies are characterized by rapid itch reduction and improved, durable disease response. Lebrikizumab also demonstrates quick onset of action for signs and symptoms such as itch and inflammation, but also excellent efficacy (EASI75 and 90 response rates) and safety outcomes at weeks 16 and 52 compared to placebo. Many results are comparable, or potentially more advantageous, to currently available options such as dupilumab or tralokinumab. There also is an option to prescribe lebrikizumab as every 4 week dosing (as was demonstrated in ADvocate 1 and 2) where after week 16, responders could be re-randomized to every 4 week dosing while maintaining efficacy. This is favorable for patients and clinicians in terms of less frequent injections instead of the standard every 2 week injections. Also, lower rates of rescue therapy were seen in the lebrikizumab arms, and rates of adverse events remained low in the 52-week data. Safety overall been demonstrated consistent and generally favorable across all trials. Rates of conjunctivitis seem comparable to Phase III studies in currently available biologic therapies, or may be less than what is observed in duplilumab postmarketing studies although more information is needed. In clinical experience, patients who have recalcitrant conjunctivitis or facial erythema from dupilumab requiring discontinuation, IL13 inhibitors can be a safe and effective option without re-encountering recurrence of these adverse events. Additionally, patients may respond well to IL13 inhibition after failing dupilumab has been observed in practice, and improvement of special sites such as hands and face. Additionally, lebrikizumab responders have been seen in dupilumab failures in 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?

Refer to section 4.1 and 5.1 with regards to which patients are most in need of intervention. Patients best suited for treatment would be those with uncontrolled msAD who are candidates for systemic therapy or meet criteria for biologic therapy as identified by the diagnosing clinician who is familiar with AD. Special considerations include IL13 inhibitors are not indicated for those with other severe forms of atopic/allergic comorbidities (eg. severe asthma, eosinophilic esophagitis) as it is approved with dupilumab. Thus, dupilumab may be chosen for those with severe forms of these atopic comorbidities.

No specific diagnostic tools or companion diagnostic tests are required for lebrikizumab or currently available biologic therapies for msAD, should the diagnosis of AD be confirmed (eg. meeting currently accepted standards of diagnostic criteria supported by history and clinical exam). Misdiagnosis and under-diagnosis in AD would be considered uncommon for those that can recognize this condition, but there are some rare forms of skin conditions that may mimic disease morphologies. However, this is often ruled out through history, clinical exam and morphology, and skin biopsy/histology or other appropriate tests should concerns for alternate diagnoses arise. Currently, there is no regular bedside or biomarker tests that are used in msAD, but discussed in the academic literature. Treatment responses currently is identified from information gathered from patient history and physical exam, and clinician and patient-reported outcomes (eg. EASI, BSA, IGA, DLQI, etc) for msAD.

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?

For moderate-to-severe AD, clinical practice uses a combination of information gathered from patient history and exam, physician-reported clinical scoring systems and patient reported outcomes. Commonly used clinician scoring includes EASI (Eczema Area and Severity Index; calculated based on erythema, infiltration/papulation, excoriation, lichenification, and regional area involvement), BSA (body surface area), and IGA (Investigator's Global Assessment). Commonly used patient-reported outcomes include the DLQI and children's DLQI (Dermatology Quality of Life Index), and NRS scales (Pruritus Numeric Rating). Many of these scoring systems represent some used in clinical trials as primary and secondary outcomes, but in practice due to time limitations only some are used as above. Generally, a trial period of 3-12 months is used for biologic therapy to determine if an adequate or lack of acceptable response, with follow-up every 3-6 months which may be further extended should the patient be stable, tolerating well, and reach their optimized treatment benefit (eg. reassessment once yearly). A clinically meaningful response can widely vary, from more stringent definitions as in Phase 3 RCTs (eg. IGA 0,1 or meeting EASI75 as seen at certain time points in phase 3 trials), to those more relatively interpreted in practice; even a partial response (eg. EASI50 instead of EASI75, or IGA 2 instead of IGA 0,1) in therapy can be very meaningful for patients and clinicians if they are able to gain back function or have improved quality of life. Often, partial responses can be further improved to clear or almost clear (IGA 0,1) or at least much more manageable disease characterized by normalization of life by adding combination therapy (eg. topicals). The global context of patient response relative to their individual

situation, including support from clinician and patient reported outcomes, is ultimately what determines a clinically meaningful response in real-life practice.

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

General reasons for discontinuation include poor efficacy or inadequate response after adequate trial, recurrent flares or worsening of disease, or intolerance/side effects requiring discontinuation. Some details are discussed in the above sections.

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]?

Given the scope of practice, those who work with this population and have experience in treating msAD as prescribers could include dermatologists, allergists/immunologists, and pediatricians who are familiar with and manage msAD.

6. Additional Information

Thank you for considering our application. We have included in this review a discussion on unmet needs faced by clinicians and also considerations for our patients based on discussing clinical experience with a literature review focusing on unmet needs, and the need for new therapeutic options in msAD.

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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.

   N/A - Clinician inputs

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.

   N/A - Clinician inputs

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 each clinician 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: Rachel Asiniwasis, MD, FRCPC, DABD

Position: Dermatologist, CDA Pharmacy & Therapeutics Advisory Board Member

Date: Nov 11, 2023

X **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**

Lilly (regarding lebrikiumab)		x (AD,alopecia, psoriasis)		
Sanofi (dupilumab)		x		
Leo (tralokinumab)	x			

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

Declaration for Clinician 2

Name: Andrei Metelitsa, MD, FRCPC, DABD

Position: Dermatologist, CDA Pharmacy & Therapeutics Advisory Board Member<Enter currently held position>

Date: 12-11-2023

X 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

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

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

Declaration for Clinician 3

Name: Monica Li, MD, FRCPC, DABD

Position: Dermatologist, CDA Pharmacy and Therapeutics Advisory Board Chair

Date: 14-11-2023

X 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**
Add company name				
Add company name				
Add or remove rows as required				

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