CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

nemolizumab (TBC)

(Galderma Canada Inc.)

Indication: For the treatment of moderate-to-severe atopic dermatitis (AD) in patients aged 12 years and older who are candidates for systemic therapy.

March 10, 2025

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

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CADTH

CADTH Reimbursement Review
Patient Input Template

Name of the Drug and Indication	**NEMOLIZUMAB** **Manufacturer Requested Reimbursement Criteria:** For the treatment of moderate-to-severe AD in patients aged 12 years and older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable, and/or who are refractory to or ineligible for systemic immunosuppressant therapies. **Indications:** For the treatment of moderate-to-severe atopic dermatitis (AD) in patients aged 12 years and older who are candidates for systemic therapy.
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

The information gathered for this submission was obtained through questionnaires, interviews with patients, caregivers and health care professionals, ESC-led surveys, and published available data and information. ESC has gathered survey data from more than 3000 Canadians who live with eczema on topics such as quality of life impact, experience with treatments, the patient journey, and experience with itch. These survey reports can be accessed at eczemahelp.ca.

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.

Other AD sufferers have expressed the following:

- Painful and itchy skin lesions, including rash, cracks, fissures, sore, and blisters that commonly bleed and weep fluid
- Persistent itching that disrupts sleep, rash, work, and overall quality of life
- Visible skin flare-ups that lead to embarrassment and social anxiety
- Chronic pain and discomfort, including sensations of burning and rawness
- Fear of side effects from long-term use of prescribed treatments, like potent steroids
- Increased vulnerability to skin infections, requiring additional treatments and care
- Emotional toll, including feelings of isolation, frustration, and despair over limited treatment success
- Struggles with mental health issues, such as anxiety, depression, and low self-esteem
- Challenges in maintaining both social and intimate relationships due to the condition's impact on confidence and comfort
- A sense of hopelessness about the future, as many feel trapped in a cycle of flare-ups with no lasting solutions

Severity

AD is a chronic skin 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. Patients with uncontrolled moderate or severe forms of AD commonly report significant suffering, discomfort, and negative quality of life impact.

Itch

The burden and impact of itch are well known in atopic dermatitis literature published around the world and specific itch-related data obtained by Eczema Society of Canada. Data from Eczema Society of Canada's Itch in Atopic Dermatitis report outlined the following data related to the impact of itch: 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.

Itch is frequently reported as the most burdensome symptom of AD. Patients report that itch is a persistent and distressing symptom of AD. The frequency and severity of itch varies greatly from patient to patient. The relentless itching is a daily struggle that no amount of scratching can relieve. Often described as feeling like thousands of mosquito bites, this constant discomfort disrupts falling asleep and staying asleep, concentration, and overall well-being, profoundly impacting their quality of life.

"Living with eczema has significantly impacted my life. Constant itchiness disrupted my sleep, making it hard to focus or do daily activities."

"I was itchy all the time. I couldn't sleep because of the constant itch. I wanted to play sports with my friends, but even the smallest amount of sweat triggered an unbearable itch. I missed out on so much. I couldn't do anything."

Sleep

ESC survey data revealed that loss of sleep and poor sleep quality are reported as significant impacts on quality of life 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 noted that the itch and 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."

"Sleep for someone with eczema isn't just about rest—it's about battling relentless itchiness, discomfort, and the frustration of waking up to find your skin scratched raw and bloody."

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.

"I had fresh, open wounds all over my arms and legs. I couldn't walk straight; the wounds behind my knees made it difficult to, and even just stretching or straightening my legs caused excruciating pain."

"I hated the doctor visits when my eczema was at its worst. I always felt embarrassed to show my eczema."

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.

"During a terrible flare, my skin was weeping —on my face, on my chest and arms. I couldn't sleep from the stinging, and the social isolation was so difficult."

"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."

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.

"I would cry in the shower because even that simple daily task was a huge struggle."

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 factors, and patients interviewed reported experiencing painful splitting of the skin during regular daily activities.

"As a teenager, my eczema covered my whole body, including my face. That period in my life was my lowest point as I was overwhelmed with severe depression and anxiety while trying to cope with the demands of life."

"I remember feeling so depressed that I didn't want to live anymore. Only recently, I realized that my depression is connected to my eczema."

"Eczema made everything much harder. The constant physical pain, the impact on my self-esteem, and dealing with infections — it was a lot."

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%.

"Growing up, eczema covered 90% of my body. It wasn't just about the itch; I missed so much school, and I was bullied. It was a cluster of emotions and pain."

"Eczema has been a part of my life since I was three months old. My skin was frequently covered in weeping, infected eczema, leaving me in constant pain. The trauma from the relentless suffering and the never-ending treatments stayed with me."

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 healthcare 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 a financial burden, with 30% of respondents reporting financial challenges related to managing their child's disease.

"My child's eczema impacted our family's daily life. It felt like we were constantly in crisis mode."

"Living with eczema isn't just about managing the skin - it's about managing the constant discomfort, emotional toll, and impact on daily life. As a parent, it's heartbreaking to watch your child struggle and not have the treatment to help."

"My teenager's eczema impacted his mental health. He was bullied at school; kids took pictures of his skin and posted them on social media, calling him snake skin. We tried homeschooling, but that was very isolating for him."

4. Experiences With Currently Available Treatments

Patients with moderate to severe atopic dermatitis (AD) face significant challenges when treating their disease, and they are seeking safe and effective treatments to manage their disease. For those with severe cases, the constant itching, pain, and skin damage are compounded by the emotional toll of living with a chronic condition that feels unmanageable.

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 accessible to all patients. The unmet need for treatments that are both effective and safe leaves patients trapped in a cycle of flares, frustration, and hopelessness. This gap highlights the urgency for innovative therapies that can offer long-term relief and improve quality of life. AD is a heterogeneous disease, and access to a variety of treatment options is critical to providing patients with the hope and healing they deserve.

Given the above, there is a need and opportunity to introduce new therapeutic options to patients to treat their AD.

"Since childhood, I have been prescribed topical and oral steroids, anti-inflammatory and antibacterial creams, and ointments. You named it, and I've tried it."

"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."

"When we have severe eczema – all over our skin – everywhere – it is impossible to apply an ointment from head to toe. And they often don't even work after applying them twice a day every single day for weeks. We need something that actually works to stop the itch and clear the rash."

Patients report frustration with the trial-and-error process of cycling through currently available treatments. Patients interviewed have tried many therapies with little success. They 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 pathophysiology of atopic dermatitis shows that it is a heterogenous disease; therefore, multiple treatment options are needed. AD is recognized as a complex disease to manage, and new therapies offer another option for patients who can't get relief from other treatments currently available to them, either through their private or public drug plans.

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

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 nemolizumab 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 helps me heal from the trauma of living with this disease."

"It can be incredibly painful to simply care for your skin – applying treatments, even showering and putting on moisturizers is painful when your eczema is severe. My doctor gives me topical medications, but they don't understand that this is not helpful when the skin is in excruciating pain when you apply anything to it, AND when you have these rashes from literally your face to your feet. We need something that targets why the flares are starting in the first place."

6. Experience With Drug Under Review

Nemolizumab offers a new biologic option to treat moderate to severe AD. It gives patients rapid itch relief and, shortly after that, skin symptom relief. Patients report a significant reduction in itch, which also provides skin symptoms improvement, healed skin, and improved sleep, the ability to return to work and increased work productivity, and improved self-esteem and mental health.

Systemic treatments for AD offer an important option for patients in need. Nemolizumab 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.

Patients treated with nemolizumab reported significant reductions in itch and noticeable improvements in skin clearance from symptoms such as rashes, lesions, sores, and open wounds. Additionally, many patients also report improvement in their ability to sleep, enhanced work performance, and improved mood. Patients who previously failed approved and off-label medications also reported significant success clearing their skin and alleviating their itch after using nemolizumab.

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 manage, and there remains a gap in treatment for some patients.

In addition to seeking access to new therapies, AD patients also seek equity. When we look at other disease states, such as psoriasis for example, they have multiple systemic treatment options with multiple mechanisms of action and AD patients deserve the same. Not only are we seeking equity across disease states but across provinces in Canada and when compared to similar countries around the world.

In summary:

1- For patients who have tried other treatments and failed, access to new treatments like nemolizumab 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, including following treatment plans, working closely with their health care professionals, educating themselves about their condition and are still in need to achieve management of their disease.

4- New treatments offer great hope to patients, but patients need 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.

"There's a misconception that eczema is just a rash or an itch. But it's so much more. I've seen people really struggle. It's important to realize that eczema can also affect your mental health, social life, and overall health."

"Even the government doesn't understand the severity of eczema. Many people feel lost trying to navigate their eczema, and we need access to treatments that work – and lots of options because one treatment doesn't work for everyone."

"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."

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
Galderma Canada Inc.				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: March 3rd, 2025

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CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: SR0869-000
Generic Drug Name (Brand Name): nemolizumab
Indication: Atopic dermatitis
Name of Clinician Group: Dermatology Association of Ontario AND Atlantic Dermatology Group
Author of Submission: <Enter Response here>

1. About Your Clinician Group

Please describe the purpose of your organization. Include a link to your website (if applicable).

The Dermatology Association of Ontario (DAO) (https://www.daontario.com) provides broad representation for dermatologists practicing in Ontario. Representing over half of the country's registered dermatologists, the DAO provides a unified voice for Ontario dermatologists in promoting better patient care, promoting dermatology in Ontario and supporting research and education within the community. The DAO membership consists of community dermatologists as well as national and internationally recognized experts in the treatment of acne.

The Atlantic Provinces Dermatology Group is a group of Dermatologists practicing in the Atlantic provinces, some of which are hospital based and others who have academic positions in the medical schools located in the Atlantic provinces. We do not have a website.

2. Information Gathering

Please describe how you gathered the information included in the submission.

Information for this submission was gathered from clinical trial data, available literature retrieved through PubMed, and Canadian clinical trialist experience on nemolizumab use.

3. Current Treatments and Treatment Goals

Please describe the current treatment paradigm for the disease.

- Focus on the Canadian context.
- Please include drug and non-drug treatments.
- Drugs without Health Canada approval for use in the management of the indication of interest may be relevant if they are routinely used in Canadian clinical practice. Treatments available through special access programs are relevant. Are such treatments supported by clinical practice guidelines?
- Do current treatments modify the underlying disease mechanism? Target symptoms?
- What are the most important goals that an ideal treatment would address?
- **Examples:** Prolong life, delay disease progression, improve lung function, prevent the need for organ transplant, prevent infection or transmission of disease, reduce loss of cognition, reduce the severity of symptoms, minimize adverse effects, improve health-related quality of life, increase the ability to maintain employment, maintain independence, reduce burden on caregivers.

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by pruritus (itch), skin barrier dysfunction, and recurrent flares. The management approach in Canada follows a stepwise approach based on disease severity, treatment response, and patient preference, integrating both non-drug and drug-based interventions.

For mild AD, first-line management focuses on basic skin care and trigger avoidance, emphasizing regular use of hypoallergenic emollients to restore skin barrier function and reduce transepidermal water loss. Patients are advised to avoid known irritants and allergens, and short, warm (not hot) bathing with gentle, fragrance-free cleansers are encouraged. If symptoms persist, topical anti-inflammatory therapies are introduced, including topical corticosteroids (TCS) and topical calcineurin inhibitors (TCIs; tacrolimus, pimecrolimus), which are effective for long-term maintenance in sensitive areas. Topical JAK inhibitors (ruxolitinib) and phosphodiesterase-4 inhibitors (crisaborole) are also available options in Canada.

For moderate-to-severe AD, where topical treatments alone are insufficient, phototherapy (narrowband UVB) can be beneficial, but its accessibility is limited due to the need for frequent clinic visits (3x/week for at least 12 weeks), making adherence challenging for working adults and school-aged children. When phototherapy is impractical or ineffective, systemic treatments are introduced. The biologic therapies approved in Canada—IL-4/IL-13 inhibitors (dupilumab) and IL-13 inhibitors (tralokinumab, lebrikizumab)—are ideally the next therapy post-topical or phototherapy as per their product monographs as well as favorable safety profile and minimal need for lab monitoring. However, they generally require 4-12 months to achieve full efficacy, particularly for controlling itch and sleep disturbances, which are the most distressing symptoms for patients. In cases where biologics are inaccessible due to cost or payer restrictions, off-label immunosuppressants (e.g., cyclosporine, methotrexate, mycophenolate mofetil, azathioprine) are sometimes used, although they require frequent lab monitoring due to risks of nephrotoxicity, hepatotoxicity, and immunosuppression. Oral JAK inhibitors (abrocitinib, upadacitinib), approved for AD in Canada, provide rapid symptom relief, particularly for pruritus and sleep disruption, but require ongoing monitoring.

Treatment Goals & Ideal Therapy Characteristics

The most pressing treatment goals in AD include rapid and sustained relief from pruritus, improved sleep, and enhanced quality of life (QoL) to minimize the cumulative life impairment of the disease. Uncontrolled AD is associated with increased absenteeism and presenteeism at work and school, sleep disruption, and mental health burdens, making effective management crucial. Ideally, a treatment would:

- Rapidly alleviate itch and sleep disturbances (a limitation of current biologics).
- Reduce inflammation and skin lesions, leading to fewer flares and long-term disease control.
- Be safe and well-tolerated, with minimal lab monitoring requirements.
- Improve functional outcomes, including reducing time missed from work/school.

Nemolizumab represents a novel therapeutic option that aligns with these goals, as it targets IL-31, a key driver of pruritus and inflammation in AD, and has demonstrated JAK inhibitor-like speed of action without the need for ongoing lab monitoring. This differentiates it from existing biologics (slow onset) and oral JAK inhibitors (rapid but require monitoring), potentially filling an important gap in the Canadian AD treatment landscape.

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.

Please describe goals (needs) that are not being met by currently available treatments. Examples of unmet needs:

- Not all patients respond to available treatments
- Patients become refractory to current treatment options
- No treatments are available to reverse the course of disease
- No treatments are available to address key outcomes
- Treatments are needed that are better tolerated
- Treatments are needed to improve compliance
- Formulations are needed to improve convenience

Please describe limitations associated with current treatments (e.g., adverse events, administration, etc., if applicable).

Despite significant progress in the management of atopic dermatitis (AD), many patients continue to experience suboptimal disease control, treatment resistance, and a high symptom burden, highlighting the need for additional therapeutic options. One of the most pressing unmet needs is the speed of symptom relief, particularly for pruritus and sleep disturbance. Current biologic therapies, such as IL-4/IL-13 inhibitors, are effective at reducing inflammation but often take 4 to 12 months to reach full efficacy. During this period, patients continue to experience severe itching, disrupted sleep, and impaired daily functioning, leading to frustration and, in some cases, treatment discontinuation. While oral JAK inhibitors provide rapid relief, they require frequent laboratory monitoring due to risks of thromboembolism, infections, and hematologic abnormalities, which limits their accessibility for certain patient populations.

Another major gap in treatment is the limited options for patients who do not respond to or lose efficacy with existing therapies. Studies suggest that 40-50% of patients treated with IL-4/IL-13 inhibitors do not achieve an EASI-75 response, and some may experience secondary treatment failure over time (Silverberg JI, Wollenberg A, Reich A et al; ARCADIA 1 and ARCADIA 2 Study Investigators. Nemolizumab with concomitant topical therapy in adolescents and adults with moderate-to-severe atopic dermatitis (ARCADIA 1 and ARCADIA 2): results from two replicate, double-blind, randomised controlled phase 3 trials. Lancet. 2024 Aug 3;404(10451):445-460). For these individuals, treatment options are often limited to oral JAK inhibitors or off-label immunosuppressants such as cyclosporine, methotrexate, and mycophenolate mofetil, which come with significant safety concerns, including nephrotoxicity, hepatotoxicity, and immunosuppression. These agents also require regular laboratory monitoring, further adding to the treatment burden. Phototherapy is another option, but its requirement for clinic visits three times per week for at least 12 weeks makes it impractical for most working adults and students.

The need for safe, well-tolerated treatments that require minimal monitoring is also critical. While biologics have a favorable safety profile compared to oral JAK inhibitors and traditional systemic immunosuppressants, their slow onset and reliance on reducing inflammation rather than directly targeting itch leave a treatment gap for rapid symptom relief. Patients need an effective therapy that provides rapid itch relief and improves sleep without the need for extensive laboratory monitoring. Additionally, while IL-4/IL-13 inhibitors primarily target inflammation, they do not directly address the neuroimmune component of pruritus, which remains a key driver of disease burden in AD.

Another key unmet need in AD treatment is the frequency of administration required for existing biologic therapies. Dupilumab, tralokinumab, and lebrikizumab all require biweekly dosing after an initial loading dose, which can be burdensome for patients who prefer less frequent injections or who struggle with adherence to more frequent dosing schedules. In contrast, nemolizumab is administered once monthly from the start of treatment, providing a lower injection burden while still delivering rapid and sustained symptom relief. This reduced dosing frequency may improve adherence, enhance patient convenience, and minimize treatment fatigue, making nemolizumab a more attractive option for patients who prioritize ease of use alongside efficacy.

Nemolizumab has the potential to fill these critical gaps by offering rapid and sustained itch relief with minimal safety concerns. In clinical trials, nemolizumab demonstrated significant pruritus reduction as early as Day 2 and sleep improvement by Day 3, with these benefits continuing to increase through Week 16 (Silverberg JI, Pinter A, Alavi A et al. Nemolizumab is associated with a rapid improvement in atopic dermatitis signs and symptoms: subpopulation (EASI ≥ 16) analysis of randomized phase 2B study. J Eur Acad Dermatol Venereol. 2021 Jul;35(7):1562-1568). This JAK inhibitor-like speed of action without the need for frequent lab monitoring represents a major advancement in the treatment landscape.

5. Place in Therapy

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

Is there a mechanism of action that would complement other available treatments, and would it be added to other treatments?

Is the drug under review the first treatment approved that will address the underlying disease process rather than being a symptomatic management therapy?

Would the drug under review be used as a first-line treatment, in combination with other treatments, or as a later (or last) line of treatment?

Would the drug under review be reserved for patients who are intolerant to other treatments or in whom other treatments are contraindicated?

Is the drug under review expected to cause a shift in the current treatment paradigm?

Please indicate whether or not it would be appropriate to recommend that patients try other treatments before initiating treatment with drug under review. Please provide a rationale for your perspective.

Nemolizumab would represent a significant addition to the current treatment paradigm for moderate-to-severe AD, particularly for patients who experience persistent pruritus despite other systemic therapies. Unlike IL-4/IL-13 inhibitors, which primarily target inflammation, nemolizumab directly blocks IL-31 signaling, interrupting the itch-scratch cycle at its root. This unique mechanism of action makes it a complementary therapy that can be used alongside existing treatments or as an alternative for patients who have failed biologics or cannot tolerate JAK inhibitors.

The ideal placement for nemolizumab would be in patients who have inadequate response to topical treatments, particularly those seeking faster symptom relief than what current biologics provide. It would also be a preferred option for individuals who need a rapid-acting systemic agent but have contraindications to JAK inhibitors, such as patients with a history of cardiovascular disease, thromboembolism, or immunosuppression concerns. Additionally, patients who have failed IL-4/IL-13 inhibitors or those with persistent, severe pruritus despite biologic therapy would benefit from nemolizumab as an alternative pathway targeting pruritus directly.

Not only should nemolizumab be included with IL-4/IL-13 inhibitors as a first-line systemic option, it could shift the treatment paradigm by providing a faster-acting alternative for patients whose primary symptom burden is driven by itch and sleep disturbance. Given its monthly dosing schedule and lack of requirement for lab monitoring, it is expected to improve patient adherence and convenience compared to oral JAK inhibitors or traditional immunosuppressants.

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?

Which patients are most likely to respond to treatment with drug under review?

Which patients are most in need of an intervention?

Would this differ based on any disease characteristics (e.g., presence or absence of certain symptoms, stage of disease)?

How would patients best suited for treatment with drug under review be identified (e.g., clinician examination/judgement, laboratory tests (specify), diagnostic tools (specify))

Are there any issues related to diagnosis?

Is a companion diagnostic test required?

Is it likely that misdiagnosis occurs in clinical practice (e.g., underdiagnosis)?

Is it possible to identify those patients who are most likely to exhibit a response to treatment with drug under review?

The patients best suited for nemolizumab are those with moderate-to-severe AD who have failed topical treatment. Additionally those patients experiencing persistent, severe pruritus and sleep disruption, including those who have not achieved sufficient symptom relief with IL-4/IL-13 inhibitors or who require faster-acting treatment are also suited for nemolizumab therapy. Patients with contraindications to JAK inhibitors, such as those with a history of cardiovascular disease, thromboembolic risk, or concerns about immunosuppression, would also be strong candidates.

In contrast, nemolizumab may not be necessary for patients with mild AD who can be managed effectively with topical treatments alone.

Nemolizumab does not require a companion diagnostic test, and patient selection would be based on clinical judgment, severity of pruritus (PP-NRS), sleep impairment, and previous treatment history. Since misdiagnosis of AD can occur, particularly in adult-onset cases, clinician expertise in differentiating AD from other eczematous conditions (e.g., contact dermatitis, seborrheic dermatitis, cutaneous T-cell lymphoma) is essential to ensure appropriate patient selection.

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?

Are outcomes used in clinical practice aligned with the outcomes typically used in clinical trials?

What would be considered a clinically meaningful response to treatment? Consider the magnitude of the response to treatment. Is this likely to vary across physicians?

Examples: improved survival; reduction in the frequency/severity of symptoms (provide specifics regarding changes in frequency, severity, etc.); attainment of major motor milestones; ability to perform activities of daily living; improvement of symptoms; and stabilization (no deterioration) of symptoms.

In clinical practice, treatment response is typically assessed using patient general satisfaction as well as physician global assessment. Other standardized measures of disease severity, pruritus, and QoL impact could be included as well. The most relevant other standardized outcomes include:

- Physician/Investigator's Global Assessment (IGA) 0/1: Achieving clear or almost clear skin is a standard goal for systemic therapy.
- Pruritus reduction: A ≥4-point improvement in Peak Pruritus Numerical Rating Scale (PP-NRS) is considered clinically meaningful, and this was achieved by ~68% of nemolizumab-treated patients in Phase 2b trials (Silverberg JI, Pinter A, Alavi A et al. Nemolizumab is associated with a rapid improvement in atopic dermatitis signs and symptoms: subpopulation (EASI ≥ 16) analysis of randomized phase 2B study. J Eur Acad Dermatol Venereol. 2021 Jul;35(7):1562-1568).
- Sleep improvement: A ≥4-point improvement in Sleep-NRS, achieved by ~76% of nemolizumab-treated patients in clinical trials, is a key marker of treatment benefit (Silverberg JI, Pinter A, Alavi A et al. Nemolizumab is associated with a rapid improvement in atopic dermatitis signs and symptoms: subpopulation (EASI ≥ 16) analysis of randomized phase 2B study. J Eur Acad Dermatol Venereol. 2021 Jul;35(7):1562-1568).
- EASI-75 response: A ≥75% improvement in Eczema Area and Severity Index (EASI) is an important benchmark, and nemolizumab showed statistically significant improvements over placebo in Phase 3 trials **(**Silverberg JI, Wollenberg A, Reich A **et al**; ARCADIA 1 and ARCADIA 2 Study Investigators. Nemolizumab with concomitant topical therapy in adolescents and adults with moderate-to-severe atopic dermatitis (ARCADIA 1 and ARCADIA 2).

Patients should be reassessed every 4-12 months to determine whether continued treatment is warranted.

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

Examples: disease progression (specify, e.g. loss of lower limb mobility); certain adverse events occur (specify type/frequency/severity); or additional treatment becomes necessary (specify).

Nemolizumab should be discontinued if a patient does not achieve a clinically meaningful response by Week 16. Specifically, discontinuation should be considered if:

- PP-NRS and Sleep-NRS do not improve by ≥4 points.
- EASI improvement is <50%, indicating insufficient efficacy.
- Severe injection-site reactions or hypersensitivity occur, though clinical trials have not reported significant safety concerns.

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]?

Examples: Community setting, hospital (outpatient clinic), specialty clinic

If a specialist is required, which specialties would be relevant?

Nemolizumab would be prescribed in outpatient dermatology or allergy/immunology clinics, where specialists in AD management can appropriately assess disease severity, treatment response, and patient eligibility. Patients can self-inject once trained or be injected in clinics. No specialized infusion center or monitoring infrastructure is needed, making it accessible in community settings.

Dermatologists and allergists are expected to be the primary prescribers, given their expertise in systemic AD treatments. Unlike oral JAK inhibitors and immunosuppressants, nemolizumab does not require extensive safety monitoring, reducing the burden on the healthcare system, healthcare providers and patients.

6. Additional Information

Is there any additional information you feel is pertinent to this review?

Nemolizumab represents a paradigm shift in AD treatment, offering rapid relief of itch and sleep disturbance, a unique mechanism targeting IL-31, and a favorable safety profile without lab monitoring requirements. Positioned as a next-line option for patients failing topical treatments or those requiring rapid symptom relief, it fills a critical gap in the AD treatment landscape.

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 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: Maxwell Sauder
Position: Dermatologist and secretary, Dermatology Association of Ontario
Date: 10-March-2025

☒ **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

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

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

Declaration for Clinician 2

Name: Sameh Hanna, MD, DABD
Position: Clinical Lead, Dermatology in Bloor, Toronto, ON Canada; Lecturer, Temerty School of Medicine, Iniversity of Toronto, Toronto, ON Canada
Date: 07 Mar 2025

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

Table 2: Conflict of Interest Declaration for Clinician 2

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Abbvie		X		
Amgen	X			
Eli Lilly	X			
Galderma	X			
LeoPharma	X			
Pfizer		X		
Sanofi		X		

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

Declaration for Clinician 3
Name: Geeta Yadav
Position: Dermatologist
Date: 07 March 2025

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

Table 3: Conflict of Interest Declaration for Clinician 3

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Abbvie			X	
Amgen			X	
Eli Lilly			X	
Galderma			X	
LeoPharma			X	
Pfizer			X	
Sanofi			X	

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

Declaration for Clinician 4
Name: Fiona Lovegrove
Position: Dermatologist
Date: 07 March 2025

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

Table 4: Conflict of Interest Declaration for Clinician 4

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

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

Declaration for Clinician 5

Name: David N. Adam
Position: Medical Director, Baywood Dermatology; Assistant Professor, University of Toronto; Lead Investigator, CCA Medical Research; President, Dermatology Association of Ontario
Date: 08 March 2025

☒ 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 5: 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
Abbvie			X	
Amgen		X		
Eli Lilly			X	
Galderma	X			
LeoPharma			X	
Pfizer		X		
Sanofi			X	

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

Declaration for Clinician 6

Name: Irina Turchin
Position: Dermatologist, Fredericton, NB
Date: 06-Mar-2025

☒ 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

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

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

Declaration for Clinician 7

Name: Ian David Rex Landells

Position: Dermatologist, Clinical Associate Professor Medicine and Pediatrics, Memorial University, St. John's, NFLD

Date: 2-Mar-2025

☒ 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

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Abbvie		X		
Amgen	X			
Eli Lilly	X			
Galderma	X			
LeoPharma		X		
Pfizer	X			
Sanofi		X		

Declaration for Clinician 8

Name: Tracey Brown-Maher

Position: Dermatologist, St. John's, NFLD

Date: 02-March-2025

☒ 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

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

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

Declaration for Clinician 9

Name: Nicole Maillet Lebel
Position: Dermatologist, Moncton, NB
Date: 06-March-2025

☒ 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

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

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

Declaration for Clinician 10

Name: Wayne Gulliver
Position: Dermatologist, St. Johns, NFLD
Date: 06-Mar-2025

☒ 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

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
CADTH	x			
Galderma			x	
Sanofi	x			

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