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

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

nemolizumab (TBC)

(Galderma Canada Inc.)

Indication: For the treatment of moderate-to-severe prurigo nodularis (PN).

January 17, 2025

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CDA-AMC in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings. **If your group has submitted input that is not reflected within this document, please contact Formulary-Support@cda-amc.ca.**

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By filing with CDA-AMC, the submitting organization or individual agrees to the full disclosure of the information. CDA-AMC does not edit the content of the submissions received.

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

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Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: Nemolizumab
Indication: Prurigo Nodularis
Name of Patient Group: Canadian Skin Patient Alliance (CSPA)
Author of Submission: Sabrina Ribau, Programs Manager (CSPA), Zahra Rehan, MD, Dana Gies, Executive Director (CSPA)

1. About Your Patient Group

This submission is supported by the Canadian Skin Patient Alliance (CSPA). CSPA is a national charity organization that improves the health and well-being of people across Canada affected by skin, hair, and nail conditions through collaboration, advocacy, and education. For more information, please visit: https://canadianskin.ca/en/.

2. Information Gathering

2.1 Data gathering

Information for this submission was compiled from a patient and caregiver survey shared on CSPA's communications channels from September 12 to November 29, 2024, and on CSPA's website, in both English and in French. In this submission we report on combined English and French survey responses. A total of 9 survey responses were received, 8 in English and 1 in French. Personal experience from people living with prurigo nodularis involved in the project was also gathered and included for this submission. We had no survey respondents with experience with the drug under review.

2.2 Regional data

The patient and caregiver survey contained 9 respondents from Canada, with the largest number being from Ontario (55.56%, n=5). A smaller proportion of respondents also came from Alberta (11.11%, n=1), Northwest Territories (11.11%, n=1), Quebec (11.11%, n=1), and New Brunswick (11.11%, n=1). There were no survey respondents from Yukon, Nunavut, British Columbia, Saskatchewan, Manitoba, Nova Scotia, Prince Edward Island or Newfoundland and Labrador.

2.3 Survey Demographics

When asked about their age, the respondents (n=5) were all over 35 years old, with more than half of respondents being over 55. 20% (n=1) were 35-44 years old, 60% (n=3) were 55-64 years old, 20% (n=1) were over 65 years old. There were four individuals who did not provide their age for the survey. For those who answered the question (n=5), 100% (n=5) of respondents have had prurigo nodularis for less than five years. Most respondents reported having severe (75%, n=3) or moderate (25%, n=1) prurigo nodularis, no respondent reported their prurigo nodularis as mild.

The most common comorbidities were mental health conditions (e.g., depression, anxiety) in 100% (n=2) of respondents who completed that survey question. One respondent listed iron deficiency anemia, another autoimmune condition and hypothyroidism. The second respondent shared having diabetes and allergic rhinitis. Regarding sex and gender, 100% (n=5) reported being female, and none identified as male. One respondent reported that they were a caregiver. When asked how they best described themselves, 80% (n=4) described themselves as White/Caucasian and 20% (n=1) described themselves as Eastern European.

3. Disease Experience

Prurigo nodularis (PN) is a chronic skin condition characterized by the development of firm, itchy nodules on the skin. These nodules typically appear on the arms, legs, and trunk but can occur anywhere on the body. The intense itchiness associated with PN often

leads to repeated scratching, which can worsen the condition and result in secondary infections, scarring, hypopigmentation and hyperpigmentation of the skin.

For the areas of body affected, 100% of survey responses reported their arms and back being affected by their condition. 75% of respondents mentioned an impact on their legs. 50% of respondents shared that buttocks were an area impacted by PN.

In terms of skin symptoms and side effects experienced, all patients reported the following signs: itchy skin, itchy bumps (nodules), burning or stinging skin, scratching, pain, and hyperpigmentation (dark spots). Three patients (75%) reported skin symptoms of scarring because of PN. One patient (25%) reported experiencing side effects of flares and hypopigmentation (light spots).

"***Not realizing I'm itching my legs is the worst. I will wake myself up in the middle of the night scratching so bad that my legs will be bloody and feeling raw."***

PN is far more than a skin condition; it impacts patients' psychological well-being, social interactions, and day-to-day functioning. While the physical manifestation of prurigo nodularis may seem to be the primary issue from the outside, the reality is that the disorder can profoundly disrupt the emotional, mental, and social aspects of patients' lives. Persistent and severe itching (pruritus) is the predominant symptom, which significantly disrupts daily activities and sleep. The visible nodules and scars may lead to embarrassment and reduced self-esteem. The chronic nature of PN can result in emotional distress, anxiety and depression.

When asked to list all aspects impacted by a PN diagnosis, survey respondents included the following: family relationships, intimate relationships), work life, mental health, social life, daily activities, sleep, self-esteem, finance and sex life. All respondents (100%) reported that PN affected their intimate relationships. 75% of respondents shared a disturbance in their family relationships, mental health and sleep. Fifty (50%) of respondents recounted an impact on their social life and daily activities.

"My sex life has been declining and my social life has become non-existent. Also, I can't wear shorts during the hot summer months because of the scared looks I get like I'm nasty and contagious."

The psychological impact of PN is profound, as the chronic nature and intense symptoms of this condition significantly affect mental health and emotional well-being. The psychological impact can include sleep disruption, emotional distress, body-image issues and experiencing social isolation or stigma. Particularly, constant itching and discomfort can lead to feelings of frustration, irritability and embarrassment. Compounding the psychological impacts with the impacts of constant itching and discomfort, PN has profound physical, emotional, mental, and social impacts on patients and their loved ones.

One patient quoted the following when asked how their PN experience has affected their family or caregiver: "Agitation, annoyed by my scratching, embarrassment"

Regarding impact on daily activities, 25% of respondents shared missing work 5-10 times monthly due to PN. Twenty-five percent (25%) of patients surveyed reported missing work 1-5 times monthly. Fifty percent (50%) of survey respondents communicated not missing work due to PN or missing work as a non-applicable factor in their situation.

Caregivers are also impacted, often witnessing their loved ones endure emotional pain, insecurity, and social withdrawal. The psychological burden on caregivers can be immense, as they provide ongoing emotional support and encouragement, while often feeling helpless themselves.

The caregiver responding to our survey observed their loved one being impacted in the following areas by PN: family balance/relationships, mental health and intimate relationships. For their loved one who lives with PN, the caregiver relayed their intimate relationships are impacted by PN. Additionally, the caregiver shared it is difficult to encourage their loved one to continue to use and take treatments for PN.

4. Experiences With Currently Available Treatments

Currently, PN patients and their caregivers navigate a range of treatments with varying degrees of effectiveness and accessibility challenges. Many patients report limited success with existing therapies, highlighting the need for new and more effective treatments. In our survey, all respondents indicated trying multiple treatments to manage their PN; 100% have tried topical corticosteroids, 80% have tried topical capsaicin, oral antihistamines and methotrexate, and 60% have tried topical calcineurin inhibitors, narrowband UVB phototherapy (NBUVB), and medical cannabis. The responses emphasize the limited efficacy of these treatments: despite all five having used topical corticosteroids in the past, none of the surveyed patients found them to work "well" or "very well". Instead, patients rated their experience as "did not work very well" (60%) or "no change" (40%). As topical corticosteroids are often the first-

line therapy for many skin conditions, including PN, this underscores the need for new and effective treatments that are accessible to patients.

Other treatments such as topical capsaicin, oral antihistamines and methotrexate also showed minimal effectiveness, with all respondents noting they “did not work very well” or there was “no change”. Further, there were two patients (40%) who reported having used all the treatments included in the survey in the past, including intralesional corticosteroids, topical vitamin D derivatives, psoralen plus UVA photochemotherapy (PUVA), oral cyclosporine, Dupixent, thalidomide, tricyclic depressants and anticonvulsants. Both patients shared that these treatments were minimally effective and there was “no change” in their condition. An interesting thing to note with both patients is that they currently use topical corticosteroids, oral antihistamines and topical capsaicin for their PN, despite both sharing these treatments are minimally efficacious with “no change” or do “not work very well”. This demonstrates the fatigue and frustration among patients, further underscoring the importance of new and effective treatments becoming available for patients so that they are able to have more and better options for managing their condition.

At this time, there are only two Health Canada approved treatments for prurigo nodularis: Dupixent and Nemolizumab. For PN, these treatments are not covered/approved on public or private insurance plans. In our survey, two patients reported trying Dupilumab in the past but both patients found there to be “no change” in their condition. It is difficult to conclude that Dupixent is not an efficacious treatment due to the small sample size of survey respondents. Dupilumab is also an expensive biologic medication, and our survey results demonstrate financial cost can be a barrier to accessing medications. When asked about aspects of a new PN treatment that are most important to patients, survey respondents indicated the top three factors to be effectiveness, affordability and lack of side effects. Other less important aspects included the treatment being easy to take or apply and conducive to the patient’s schedule. In our survey, the caregiver disclosed that the cost of medication is the most important aspect of a new treatment for them.

One patient quoted the following price for a treatment recommendation: “One recommendation was 12,000.00!?!?!”

Regarding side effects, patients reported experiencing a racing heart (n=1), skin irritation (n=3), nausea (n=2), vomiting (n=1), hypopigmentation (n=1) and hyperpigmentation (n=2). Only one respondent shared that they stopped treatment for PN because of side effects and three respondents shared that they stopped treatments because of a lack of efficacy. This highlights the importance of new treatments that are effective and have minimal side effects to better support patients in their treatment goals.

The psychological toll of repeatedly undergoing ineffective treatments cannot be overstated. Many respondents expressed frustration and emotional distress from trying multiple therapies with little to no improvement. When asked, participants overwhelmingly strongly agreed that they would be interested in a new treatment for PN (4 out of 5 respondents) and that they wish there was a better PN treatment option for them (4 out of 5 respondents). On the other side, three respondents (3/5) disagreed, and two respondents (2/5) strongly disagreed that they felt satisfied with their current treatment for PN. These patient experiences highlight the need for new, effective, accessible treatments for patients so that they can manage their condition and reduce the mental health burdens so often experienced by people impacted by prurigo nodularis.

5. Improved Outcomes

When asked about what aspects of a new treatment for prurigo nodularis are important to them, patients shared that effectiveness (4/5), affordability (3/5), lack of side effects (3/5) were their top priorities. They are also looking for treatments that are easy to take/apply (2/5) and are conducive to their schedule (2/5). Four of five patients who responded to the survey question reported that they strongly agreed that they would be interested in a new treatment for prurigo nodularis and that they wish there was a better PN treatment option for them, and one disagreed. All five patients felt that they strongly disagreed or disagreed that they felt satisfied with their current treatment for PN, highlighting a need for new, effective treatments. When asked about their reasons for stopping their treatments, ¾ who replied to the question shared that it was being it was not effective, and the fourth shared it was due to side effect, further emphasizing the desire for safe, effective, affordable treatments. A treatment that is simple to administer and integrates smoothly into daily life reduces the logistical and psychological burden on patients. This is particularly relevant for individuals managing the emotional and burdensome weight of prurigo nodularis, as well as any coexisting conditions or family responsibilities.

Patients also shared that they have experienced financial challenges that have affected their access to PN treatments, with one patient sharing that “paying for over-the-counter anti-itch, moisturizers, ointments, etc.” contributed to the burden of disease, and this patient used a public drug plan for their insurance coverage for their medications. Another shared that they had received the following suggestion, “one recommendation was 12,000.00!?!?” and this patient did not have insurance coverage and paid out of pocket for treatments, highlighting the financial burden of living with PN when there are not affordable options indicated for PN. When

paired with some of the other quality of life impacts reportedly experienced by patients and their loved ones living with PN, including negative impacts on intimate relationships, family relationships, mental health, work life, social life, daily activities, and sleep, it's instrumental that new therapies indicated for PN are accessible and affordable to improve health outcomes and the quality of life of patients and their caregivers.

In addition to managing itch, psychological and social relief are underlying motivations behind these desired outcomes. With a treatment that offers tangible improvement and restores a sense of normalcy, patients anticipate a significant enhancement in quality of life, self-confidence, and social participation. Ultimately, our survey responses reveal that patients desire treatments that are not only clinically effective but also supportive of their holistic well-being. Effective, accessible treatments like Nemolizumab have the potential to address the physical and emotional gaps in the current treatment landscape, allowing patients to regain a sense of agency over their condition and their lives.

6. Experience With Drug Under Review

No survey respondents had used the drug under review.

As a national patient organization, CSPA recognizes and emphasizes the importance of providing access to effective and affordable treatments to people across Canada. As there are no currently available treatments indicated for PN covered by public drug plans in Canada, it's incredibly important that more treatments tailored to PN become available, accessible, and affordable for patients.

One thing that was consistent across survey respondents was that patients and their loved ones shared their frustration with a lack of treatments available in Canada for PN and the need for safe, effective, and affordable options. "It is very disappointing that there Is a medication for prurigo nodularis, a devastating skin condition, but is unavailable for patients," shared one patient in the survey. Another simply implored, "Please approve it so I can afford it," highlighting the significant need for treatments that are affordable and covered under drug plans across the country so that PN patients can seek effective care for their condition. One other patient shared, "I need to find a treatment that actually works long term and that is effective and has little side effects," echoing the feelings of the other PN patients and caregivers who participated in the survey. Nemolizumab is one of only two treatments approved for use in prurigo nodularis in Canada. Of the two treatments, access to both is currently costly and difficult (both nemolizumab and dupilumab are currently under review for recommendation by CDA), impacting the ability for PN patients and their families to seek treatment via medications that are both indicated and covered under public drug plans for their incredibly uncomfortable condition.

7. Companion Diagnostic Test

Not applicable.

8. Anything Else?

Given such a significant impact of prurigo nodularis on the lives of individuals living with the condition, it is important to explore effective and safe treatment options to improve the quality of life of those affected by prurigo nodularis. There remains a great need for effective treatment options for prurigo nodularis. Access to new and promising treatments is critical to helping patients gain a sense of control over their disease and begin to regain their quality of life. Presently, there are no treatments indicated for PN covered under public drug plans in Canada, leaving a significant need for new treatments for.

Individuals with PN have often attempted numerous treatments, therapies, and other strategies off-label to manage the signs of their condition. When their PN is well-treated, it becomes more manageable, and the physical, psychological, and social impacts they experience because of this disease are reduced.

The nature of this disease requires ongoing care and a constellation of different approaches. Individuals with prurigo nodularis incur considerable monetary expenses on products and treatments to manage their condition, as well as significant psychosocial costs of living with or being in a family with someone who has a debilitating condition like PN, considerably impacting mental and physical health and wellbeing for the individual and their family. CSPA supports the advancement of treatments for PN and is encouraged by the possibility of improving access to new, effective treatments for PN patients and their families to improve their health outcomes and quality of life.

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.

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

   No. CSPA worked with staff and volunteers to complete this report. No funding was received to complete this submission.

6. 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. CSPA worked with staff and volunteers to complete this report. No funding was received to complete this submission.

7. 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
Sanofi			X	
Galderma		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: Sabrina Ribau
Position: Programs Manager
Patient Group: Canadian Skin Patient Alliance
Date: January 10, 2024

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: SR0861-000
Generic Drug Name (Brand Name): Nemolizumab
Indication: Prurigo Nodularis
Name of Clinician Group: Atlantic Dermatology Group
Author of Submission: Wayne Gulliver

1. About Your Clinician Group

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. Some of the group members are investigators with extensive experience in clinical trials and research. We do not have a website.

2. Information Gathering

Information gathering included attending sessions related to prurigo nodularis at the recent European Academy of Dermatology and Venerology in Amsterdam September of 2024, as well as a literature search was conducted by WG. Galderma provided a synopsis of the clinical research related to nemolizumab.

3. Current Treatments and Treatment Goals

There are no treatment guidelines for prurigo nodularis. New therapies are needed in order to improve the signs and symptoms of this relentless difficult-to-treat dermatological disease. On July 17, 2023 Sanofi-Aventis Canada Inc. announced that Health Canada had issued notice of compliance for Dupixent (dupilumab injection) for the treatment of patients with moderate-severe prurigo nodularis (PN) when disease is not adequately controlled with topical prescription therapies or when those therapies are not available. It can be used with or without topical corticosteroids. In the Liberty-PN Prime and Prime-2 studies patients receiving dupilumab reported that 58.8% of the dupilumab treated vs. 19% of the placebo treated patients achieved clinically meaningful improvement in itch (decrease of 4 points on the NRS scale), while 46.4% of the dupilumab treated patients vs. 17% of the placebo treated patients had clear or almost clear skin; 35.3% of dupilumab treated patients vs. 8.9% of placebo treated patients had both clear or almost clear skin and a clinically meaningful improvement in itch. Although dupilumab has been approved for prurigo nodularis, it is experience of this group that some patients with PN do not respond to dupilumab and many patients have difficulty accessing this drug as their drug plans do not cover this indication.

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.

Since the underlying disease mechanism is thought to be a type-2 inflammatory response (regulated by IL 4, 13, and 31) Dupilumab does target 2 of the cytokines linked to prurigo nodularis. It should be noted that nemolizumab targets IL 31, known as itch cytokine, important in pathophysiology of prurigo nodularis. For patients who do not respond to dupilumab or are unable to access dupilumab, a number of appropriate and inappropriate therapies are being utilized by Canadian clinicians; these include topical corticosteroids, intralesional corticosteroids, high dose non-sedating antihistamines, phototherapy including narrowband UVB, bath and topical PUVA. Oral immunosuppressants have also been used including cyclosporin, methotrexate, azathioprine, cyclophosphamide, tacrolimus, intravenous gamma globulin, treatments such as thalidomide, lenalidomide, serotonin uptake inhibitors, tricyclic antidepressants, naloxone, naltrexone, and neurokinin-1 receptor antagonists including aprepitant, serlopitant have been employed. The majority of these therapies are neither approved nor effective over the long term.

The most important treatment goals and ideal therapy would address the primary outcomes of the nemolizumab and dupilumab clinical trials i.e. clinically significant reduction in itch ideally itch score 0 and clear (or almost clear) physician global assessment of skin lesions along with improved quality of life with a dermatology life quality index (DLQI) of 0 or 1. In a recent study, it was reported that many patients receive potentially inappropriate medication for the treatment of prurigo nodularis. This was well studied by Taylor et al of Johns Hopkins school of Medicine (Journal of American Academy of Dermatology September 2023 ab209 abstract 44486). This study concluded that 43.8% of patients receiving potentially inappropriate medications including first generation antihistamines, antidepressants, and gabapentinoid use. This was prominent in elderly patients for which prurigo nodularis is more common. In a systematic review of systemic and non-systemic medications for the treatment of prurigo nodularis, Ranpariya et al reported that topical corticosteroids demonstrated a 51% improvement rate in a retrospective study while UV phototherapy a 78% response rate, in cases resistant to topical. As mentioned, dupilumab showed significant response rate in 44.9% compared to 15.9% in the placebo group at 24-weeks. Drugs such as cyclosporin and methotrexate displayed positive responses with less adverse effects than thalidomide, but patients relapsed after withdrawal of therapy. Thalidomide was shown to be effective in some patients but had significant adverse events related to muscle and nerve related side effects. They concluded that phototherapy, corticosteroids, cyclosporin, methotrexate offer viable options, but the potential benefits are limited because of the risk of relapse and potential side effects. Dupilumab is highly effective with a good side effect profile but disease control is only achieved in 44.9% of patients.

5. Place in Therapy

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

With the drug under review, under the current treatment paradigm nemolizumab targets IL 31 which is an important cytokine in prurigo nodularis. It would be a stand-alone treatment.

Nemolizumab would be the first drug that targets IL 31 which is thought to be the major cytokine in prurigo nodularis. Dupilumab which targets IL 4 and 13 is approved and targets two other cytokines related but less prominent in the pathoimmunology of prurigo nodularis.

Nemolizumab could be considered either as first line or used after failure of topical corticosteroids, or failure or non-availability of phototherapy. Nemolizumab should be indicated in all patients who have failed topical corticosteroids or for which phototherapy is not available or is not effective. Nemolizumab will cause a shift in the current treatment paradigm as it can be used as first line therapy in patients with prurigo nodularis or in patients who have failed or who are intolerant to dupilumab, topical corticosteroids, or phototherapy.

As previous stated no placebo controlled double blind clinical trials have been conducted in topical corticosteroids or phototherapy, these treatments may be considered and used prior to initiation of nemolizumab. In our opinion, there is not enough data to support the consideration of cyclosporin, methotrexate, leflunomide, or other systemic therapies.

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?

Patients most likely to benefit from treatment with nemolizumab are patients with prurigo nodularis who have a pruritus score measured by NRS of ≥ 7 and who have moderate to severe prurigo nodularis as diagnosed by the 5-point investigators global assessment (IGA scale range 0-4) and who have 20 or more nodules bilaterally distributed on the arms, legs, and trunk.

Patients in most need and best suited for treatment are the patients with moderate to severe prurigo nodularis with an itch score ≥ or equal to 7 with at least 20 lesions.

There are no issues related to diagnosis. There's no companion diagnostic test as biopsy is not required as dermatologists experienced in the diagnosis and treatment of prurigo nodularis will confirm the diagnosis clinically. As these patients are managed by dermatologists it is unlikely that misdiagnosis will occur in clinical practice. Other diagnosis should be considered including pemphigoid nodularis, mastocytosis, lichen planus, nodular scabies, arthropod bites, lymphocytoma cutis, lymphomatoid papulosis, amyloidosis, reticulohistiocytosis and cutaneous T-cell lymphoma.

To date there are no clinical, pathological, or chemical markers that would identify patients that are most likely to exhibit response to treatment.

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

Clinical assessments outcomes in practice should be physician IGA clear or almost clear, as well as a 4 point improvement in patient peak NRS score. This should also be correlated with measurement of DLQI. It's also expected that patients would not only have improved quality of life but also improved peak pruritus NRS, and improvement in sleep disturbance numerical rating scale (NRS) as seen in phase 3 clinical trials. It is noted that these improvements in IGA, PPNRS, and DLQI continued or increased out to week 52.

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

In a pooled subgroup analysis patients between the ages of 18-65 tended to do better with nemolizumab . Patients should be treated with nemolizumab at the approved dose for at least 24-weeks; those patients not achieving a 4 point improvement in PP NRS or not achieving clear or almost clear after 6 months of therapy should be discontinued.

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]?

Prurigo nodularis should be managed by dermatologists experienced in the diagnosis and management of prurigo nodularis as well as experienced in the use of biologics. Dermatologists should also be experienced in measurement of DLQI, IGA, counting nodules, and PP NRS.

6. Additional Information

Please see attached references

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: Wayne Gulliver
Position: Dermatologist, St. John's, NFLD
Date: 11-Jan-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

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

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

Declaration for Clinician 2

Name: Irina Turchin
Position: Dermatologist, Fredericton, NB
Date: 11-Jan-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

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

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

Declaration for Clinician 3

Name: Tracey Brown-Maher
Position: Dermatologist, St. John's, NFLD
Date: 12-Jan-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
Galderma			x	
Sanofi			x	

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

Declaration for Clinician 4

Name: Nicole Maiillet-Lebel
Position: Dermatologist, Moncton, NB
Date: 14-Jan-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
Galderma		x		
Sanofi		x		

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

Declaration for Clinician 5

Name: Alana McEvoy
Position: Dermatologist, Halifax, NS
Date: 15-Jan-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
Galderma	x			
Sanofi		x		

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

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CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: SR0861-000
Generic Drug Name (Brand Name): nemolizumab
Indication: prurigo nodularis
Name of Clinician Group: Dermatology Association of Ontario
Author of Submission: Dr. Maxwell Sauder

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.

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.

Current Treatments and Treatment Goals for Prurigo Nodularis (PN)

In Canada, the treatment of prurigo nodularis (PN) lacks specific clinical practice guidelines, but international recommendations emphasize a multimodal approach targeting itch management, lesion treatment, and comorbidities.

Current therapies often begin with topical treatments such as corticosteroids and emollients, progressing to systemic options as needed. Dupilumab, an IL-4 and IL-13 inhibitor, is approved by Health Canada for PN; however, it is not yet publicly reimbursed. Other used off-label include systemic immunosuppressants (e.g., methotrexate, cyclosporine), JAK inhibitors, neurokinin 1 receptor antagonists, and monoclonal antibodies targeting IL-4 pathways. Non-drug treatments such as narrowband UVB phototherapy and psychosocial have been attempted with limited availability and success in addressing the significant psychological burden of PN and improving overall quality of life.

The primary goals of PN treatment are to provide rapid and sustained itch relief, reduce lesion severity, and promote healing while addressing the neuroimmune dysregulation underlying the disease. Ideal treatments aim to modify the disease process, breaking the itch-scratch cycle and reducing the risk of recurrence. They should also alleviate psychological comorbidities, improve sleep, and enhance the patient's ability to perform daily activities; thus, reducing the cumulative life course impairment. Given the high disease burden, treatments must be both effective and accessible, with a focus on minimizing adverse effects and ensuring long-term disease control. However, challenges persist, including limited access to systemic therapies and the absence of standardized care pathways in Canada. A truly effective PN therapy would address both symptomatic relief and the underlying mechanisms of the disease, ultimately improving patients' quality of 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.

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).

Current treatments for prurigo nodularis (PN) in Canada fail to fully address critical disease management needs, particularly for moderate to severe cases. While first-line treatments like topical corticosteroids and antihistamines provide limited relief, many patients experience persistent symptoms or become refractory to these options. Systemic treatments, including immunosuppressants and neuromodulators, are often prescribed off-label due to the absence of approved targeted therapies, but they carry risks of adverse effects and offer variable to limited efficacy. Dupilumab is the only biologic approved in Canada for PN, but its accessibility is limited as it is not publicly reimbursed. This creates significant gaps in effective care, particularly for patients with moderate-severe disease burden requiring systemic therapy.

Unmet needs in PN treatment include therapies that provide rapid and sustained relief from severe itch, improve skin lesions and ultimately address the psychosocial impacts of the disease, such as sleep disturbances and mental health issues. Current treatments are often poorly tolerated or inconvenient, leading to reduced patient adherence. Additionally, existing therapies do not target the underlying neuroimmune mechanisms driving PN, highlighting the need for innovative biologics like nemolizumab, which has shown promising efficacy and safety in clinical trials by targeting the IL-31 pathway.

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 fit into the current treatment paradigm for prurigo nodularis (PN) as a targeted, second- or third-line option following failure or insufficient response to topical therapies and phototherapy, where accessible and available. Positioned after first-line treatments like corticosteroids and narrowband UVB phototherapy, nemolizumab would address the substantial unmet needs of patients with moderate to severe PN who remain symptomatic or refractory. By targeting the IL-31 receptor α, a key pathway in the itch-scratch cycle and neuroimmune dysregulation of PN, nemolizumab provides a mechanism-focused approach, distinct from symptom-based treatments. Its use would offer an effective and better-tolerated alternative to systemic immunosuppressants or off-label options, providing rapid and sustained relief of itch, promoting lesion healing, and improving quality of life. Nemolizumab's subcutaneous administration and well-documented efficacy and safety in clinical trials make it a promising addition to the therapeutic arsenal, particularly for patients requiring advanced systemic management of PN.

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?

Nemolizumab would be most suitable for patients with moderate to severe prurigo nodularis (PN) who have failed to achieve adequate relief from topical therapies and phototherapy, or for those who cannot access or tolerate these first-line treatments. This includes patients with persistent and intense pruritus, widespread nodular lesions, or significant impairment in quality of life due to sleep disturbances, pain, or psychological comorbidities such as anxiety and depression. The drug is particularly well-suited for patients whose disease is driven by the neuroimmune dysregulation of the IL-31 signaling pathway, given nemolizumab's mechanism of action in blocking the IL-31 receptor α.

Conversely, nemolizumab would not be suitable for patients with contraindications, such as a known hypersensitivity to the drug or its components, or those with milder disease that responds well to first-line treatments like topical steroids. Additionally, it may not be ideal for individuals with conditions that significantly compromise immune function unless the benefits outweigh the risks.

Patients most likely to respond to nemolizumab include those with active, ongoing pruritus and well-defined PN characterized by inflammatory and neuroimmune dysregulation. Identifying these patients involves clinician assessment of the intensity and persistence of itch, the extent of nodular lesions, and the impact on daily functioning and quality of life. Laboratory tests or diagnostic tools may not be required beyond clinical examination, although histopathological confirmation of PN could help in ambiguous cases.

Diagnosis of PN can present challenges, as the condition is often underdiagnosed or misdiagnosed as other pruritic dermatoses. This underdiagnosis may delay appropriate interventions, particularly in cases where atypical presentations or overlap with other conditions complicate the clinical picture. Clinician education and awareness are key to improving diagnostic accuracy and ensuring that patients most in need of intervention are identified and treated effectively.

Patients best suited for nemolizumab therapy can be identified through thorough clinical evaluation, focusing on the severity and chronicity of pruritus, the extent of nodular lesions, and the failure of prior therapies.

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, the primary outcomes to determine a patient's response to treatment for prurigo nodularis (PN) center on the patient's experience of itch relief, reduction of lesions and overall patient satisfaction. A meaningful response is typically characterized by the patient reporting a significant reduction in itch, which directly improves their quality of life. This outcome is often assessed using patient-reported measures such as a numeric rating scale (NRS) for itch, where a reduction of at least 4 points is considered significant, as well as subjective feedback on daily comfort and sleep quality. Achieving sustained itch relief allows patients to return to daily activities, improve sleep, and reduce the psychosocial burden of PN.

Additionally, lesional count as measured through a physician or investigator global assessment (IGA) similar to the descriptive measure in trials could be used to assess response. The IGA for PN employs a **5-point scale**, ranging from 0 to 4, with each score reflecting a defined level of disease severity:

- **0 (Clear)**: No visible or palpable nodules present.
- **1 (Almost Clear)**: Minimal residual disease, with very few small nodules.
- **2 (Mild)**: Noticeable presence of nodules, but fewer and less severe compared to moderate cases.
- **3 (Moderate)**: Significant number of nodules present, with moderate size and extent.
- **4 (Severe)**: Numerous, widespread nodules, typically larger and more inflamed.

The IGA is a practical and widely used measure in both clinical trials and practice to determine treatment efficacy. A successful treatment could be a reduction of at least two points from baseline.

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).

Discontinuing treatment with nemolizumab for (PN) should be considered when patients experience ongoing significant itch or show minimal improvement after an adequate trial period, typically 16 to 24 weeks. Incomplete or no response, as evidenced by a lack of meaningful pruritus reduction on a NRS or persistent nodular lesions assessed by the IGA, suggests the treatment is not meeting its intended goals. Additionally, disease progression, such as worsening lesions, increased body surface area involvement, or the development of complications like skin infections, may indicate the need to reassess treatment.

Treatment should also be discontinued if significant adverse events occur, such as severe hypersensitivity reactions, injection site reactions, or long-term safety concerns like recurrent infections. Patient-reported dissatisfaction due to inadequate relief, burdensome administration, or diminished quality of life despite treatment should also guide decision-making. In cases where additional therapies are required to manage refractory disease, such as systemic immunosuppressants or other biologics, nemolizumab may no longer be the optimal choice. Ultimately, the decision to discontinue treatment should be personalized, balancing the risks and benefits while prioritizing patient outcomes and satisfaction.

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 can be administered by the patient at home and prescribed in various clinical settings, including community clinics, hospital outpatient departments, and specialty dermatology or allergist clinics. The diagnosis, treatment initiation, and monitoring of patients receiving nemolizumab require the involvement of a specialist.

Relevant specialties include dermatologists, who are most commonly involved in managing PN, as well as potentially allergists or immunologists in cases where PN overlaps with other atopic or immune-mediated conditions. The specialist's role is critical to ensure accurate diagnosis, assess treatment suitability, monitor for adverse events, and adjust therapy based on response and patient needs. While nemolizumab's administration can occur in any clinic type, its use necessitates the expertise and oversight of specialists familiar with PN and its complex management.

6. Additional Information

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

None

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: Secretary, Dermatology Association of Ontario; Dermatologist; Assistant Professor, University of Toronto
Date: 15-Jan-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
Galderma			X	
Sanofi			X	
Amgen		X		
Incyte			X	

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

Declaration for Clinician 2

Name: Melinda Gooderham
Position: Vice President, Dermatology Association of Ontario, Dermatologist
Date: 16 Jan 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

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

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

Declaration for Clinician 3

Name: Kim A Papp
Position: Treasurer, Dermatology Association of Ontario, Dermatologist, Professor of Dermatology, University of Toronto
Date: 16 Jan 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
Amgen				X
Galderma			X	
Incyte				X
Sanofi			X	

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

Declaration for Clinician 4

Name: David Adam
Position: President, Dermatology Association of Ontario, Dermatologist
Date: <DD-MM-YYYY>

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

Table 4: Conflict of Interest Declaration for Clinician 4

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

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

Declaration for Clinician 5

Name: Geeta Yadav
Position: Founder, Medical Director FACET Dermatology; Clinical Adjunct, University of Toronto
Date: 16 Jan 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

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

Galderma			X	
Sanofi			X	
Add or remove rows as required				

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

Declaration for Clinician 6

Name: Fiona Lovegrove
Position: Dermatologist
Date: 16 Jan 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 6

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

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

Declaration for Clinician 7

Name: Jeff Cowger
Position: Dermatologist
Date: 16 Jan 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

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

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