CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

spesolimab (Spevigo)

(Sponsor's Name)

Indication: Spevigo (spesolimab for injection) is indicated for the treatment of generalized pustular psoriasis (GPP), including treatment and prevention of flares, in adults and pediatric patients 12 years of age and older.

June 17, 2024

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

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Patient Group Input

CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: <Spevigo (spesolimab)>
Indication: <Generalized pustular psoriasis>
Name of Patient Group: Canadian Psoriasis Network (CPN) and the Canadian Association of Psoriasis Patients (CAPP) – consolidated as Psoriasis Canada
Author of Submission: Antonella Scali, incumbent CEO, Psoriasis Canada (current Executive Director of CPN)

1. About Your Patient Group

Describe the purpose of your organization. Include a link to your website.

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

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

CPN and CAPP have recently consolidated into Psoriasis Canada, a single, national, psoriatic disease organization (www.psoriasiscanada.ca).

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

This submission is informed by three main sources of information:

1. Findings from a virtual summit focused on generalized pustular psoriasis (GPP) held on November 21, 2023 by CPN in collaboration with CAPP and the Canadian Skin Patient Alliance. Seven participants attended, included two people who had a formal diagnosis of GPP and one who had symptoms that are aligned with GPP but no formal diagnosis. Five out of seven GPP virtual summit participants completed a brief, pre-summit questionnaire with sociodemographic questions. In addition, everyone in attendance shared where in Canada they live. Geographically, three lived in Alberta; two were from Ontario; one was from Quebec; and one lived in Newfoundland and Labrador. Of those who responded to this question, three identified as living in urban centres and two lived in rural areas. Most were European in ethno-cultural background or preferred not to

share this information. One participant identified their ethno-cultural background as being from Southern Africa. Of those that shared their gender, three identified as female and two as male. In terms of those who shared their age range, two were 35-44; one 45-54; and two were 65+.

2. Survey responses from ten people who had indicated interest in attending the GPP virtual summit but were unavailable to attend live.
3. Interviews with four people who live with GPP, including three who have used the drug under review, as well as one caregiver (spouse).
    - All of the people interviewed are from Canada except for one who we connected with through our international colleagues at the International Federation of Psoriasis Associations

Given the rarity of this disease and small numbers of patients undergoing treatment, we have elected to use the generic pronouns "they/their/them" when describing individual stories to minimize identifying information.

It was challenging to reach people with this rare skin condition. Moreover, at the virtual GPP summit, and in the subsequent outreach to people who had expressed interest in the event but could not attend, it was clear that patients living with other forms of psoriasis (e.g., plaque psoriasis, palmoplantar psoriasis) were in attendance and responding to the post-event survey. **For this submission, we are highlighting feedback that is clearly derived from people who live with GPP and will identify when we are referring to GPP patient feedback specifically.**

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

General pustular psoriasis (GPP) is a rare form of psoriasis whereby people experience symptom flares that are often unpredictable and that are characterized by the sudden appearance of widespread, painful, pustules that are noncontagious. Other symptoms may be present during a flare including fever, fatigue, chills, joint pain, headache, and nausea. One participant of the virtual GPP summit described their skin coming off in layers during a flareup of GPP symptoms. Flares are disruptive, frightening, and in some cases, potentially life threatening if not treated quickly.

The severity of flares and symptoms can vary across patients and experiences. Emergency department visits or inpatient care may be required depending on the level of skin impacted and the degree of systemic involvement. More severe involvement can lead to serious complications including heart failure, renal failure, and sepsis. For instance, one participant of the virtual GPP summit that lives with GPP described their experience with the disease as "survival". They were "in the hospital for three days on IV fluids and IV antibiotics." Their first flare was a life-threatening event. The pustules covered seventy percent of their body. They "lost all that skin at once" and had to miss almost a month of work.

Typically, the onset of GPP occurs in working-age years, though it can also occur in infancy and childhood. GPP is clinically different than plaque psoriasis (the most common form of psoriasis), however many people with GPP have a history of plaque psoriasis and the two can occur together.

Living with GPP, even in the absence of active flares, can present challenges like those presented by other forms of psoriasis. For instance, people with these conditions may experience poor self-image, difficulty with intimacy,

disruptions in school and work life, burden on personal finances, experiences of stigma and discrimination, feelings of isolation, and difficulties accessing diagnosis, care, and treatment throughout different times in their lives.

GPP virtual summit participants discussed the challenges of daily life, including at work. For some, sun was a trigger so they must be completely covered up, including hands, which prompts questions from people around them such as "why are you dressed like this when it's so hot and it's the middle of summer?" For others, people avoid swimming or wearing clothes that reveal their affected skin because people stare. One participant shared that they must be completely covered at work due to the nature of their work that requires hands-on contact with equipment. For some, they cannot be touched. For others, forming intimate relationships can be difficult. Areas of the body can be so sore that it prevents intimacy with one's partner.
People with GPP also experience unique challenges related to the rarity and potential severity of the condition. Living with a skin disease can already be isolating, but this is further compounded by living with a rare form of disease that is less known and understood. Since rarely seen in clinical practice, GPP often goes undiagnosed or misdiagnosed for years. One virtual summit participant with a diagnosis of GPP described "having to go through layers" to see a dermatologist in the first place – including needing to try different, ineffective treatments with a family physician prior to receiving a referral. Another, who had a timelier diagnosis (under two weeks of their first flare), acknowledges that their doctor had connected with the only local dermatologist who had actually seen GPP cases.

A person's life can be completely disrupted during GPP flares, including missing work, being bed-ridden, and being hospitalized. In some cases, they report depending on their family and caregivers almost entirely during severe flares, even for basic activities of daily living. One person with GPP who we spoke with described GPP as one of the most painful and exhausting experiences of their life, and they have had other health conditions that have required surgery.

The impact of the disease can also be significant between flares. GPP patients report living with the fear and worry of triggering another flare. One virtual summit participant with GPP described how they must diligently manage their physical and mental health between flares because of concern that anything can trigger another flare. They also expressed being acutely aware about how much they depend on their current job because they have health benefits, and their employer understands their situation and needs. They have concerns about changing jobs in the future because their employer may not be as understanding about what it is like to live with a chronic disease and disability.

GPP can also negatively affect relationships. Numerous people expressed frustration with having to repeatedly explain their condition and assuage other people's concerns, such as "is your condition infectious?" As a virtual summit participant with GPP said, "it's a very crazy moment, where you meet somebody, you have to explain every time, I have this, I have this, it's too much craziness." Another shared, "it's a lifetime of explaining."

All of the above challenges can take a significant negative toll on people's mental health.

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

Current approaches to treating GPP are inadequate according to the individuals we spoke with.

One virtual summit participant with GPP described being better able to "catch and manage" oncoming flares, although they are always preoccupied by whether something will trigger a flare-up. They have been historically treated with prednisone and steroid creams, which is troubling because of the risks associated with prednisone. They shared that they were wheelchair-bound after severing all the tendons in their knee, likely due to the need for long-term prednisone.

The international GPP patient we spoke with had their first flare after giving birth (they had a previous history of plaque psoriasis and guttate psoriasis). They used Cyclosporine because they could not afford a biologic. This treatment worked for about a year, but the side effects were problematic. They switched to methotrexate and eventually had another significant flare-up. They were eventually given a biologic (secukinumab) in hospital at no cost to them. They would not have been able to afford their ongoing treatment. This treatment maintained their condition for about a year or two. They were eventually able to join a clinical trial for spesolimab (more information on their experiences with this treatment is described in the next section).

Generally, GPP virtual summit participants described frustration with going through a variety of different treatment options before finding an effective one. Some expressed frustration with having to go through many ineffective treatments in order to qualify for an effective one that was covered by insurance.

Participants also described having to try many different dermatologists to find the right expertise. Many indicated the need to travel to distant urban centres to access dermatologists with relevant expertise. One person with GPP who lives in an urban centre of 80,000 people must travel three hours to see their dermatologist in one larger city and two hours to receive treatment in a different city. Some treatments must be paid for out of pocket, which is an additional treatment access challenge.

In addition, participants experience challenges working with their physicians. One has a family physician that will not refer the individual to a dermatologist, thinking instead that they can manage the condition. Another expressed that their dermatologist is not willing to consider any other treatment options, despite the seriously harmful side effects of the treatment being used. They did note, however, that their doctor has indicated that they would seek spesolimab treatment for this person's next flare. Others had to self-advocate for a diagnosis, including through online research to bring to their family physician and through researching multiple specialists and travelling for multiple opinions before finding an effective practitioner and treatment protocol.

One person who has lived with their psoriatic condition in different countries and in multiple Canadian jurisdictions described the frustration that their medical history and information never followed them to each new jurisdiction. This would lead to less effective treatment and care in each new place.

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

When asked what would be most helpful to them in terms of treatment, the GPP patients we spoke with had several insights.

One person who accessed spesolimab through a clinical trial described the long process they experienced to access a medication that worked for them. They stated, “I hope that everyone else in the GPP community can have access to medicines like this…I hope governments a can help GPP community to have this medicine.”

Another person said that it is frustrating when a treatment that can prevent problems in the long run is not covered. They point out that each individual expense is not as important as the cumulative costs of untreated or poorly treated GPP.

Based on our interviews, other insights that we gleaned about what would be most beneficial to GPP patients as an outcome of treatment include:

- Treatment that reduces symptoms to the extent that people can work and live with minimal disruption for as long as possible and with few side effects;
- Treatment that manages flares and that helps reduce the frequency and severity of flares, as well as the symptoms/impacts between flares;
- Timely care and treatment. Ideally, we would like to see every person have access to appropriate care and treatment close to them and to reduce barriers related to geography. From our interviews, however, people are willing to travel to appointments and see dermatologists in locations outside of where they live in order to address their disease;
- People are worried about their next flare. A treatment that can help them feel more in control of their disease could help to reduce some of this ongoing distress.

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways? If applicable, please provide the sequencing of therapies that patients would have used prior to and after in relation to the new drug under review. Please also include a summary statement of the key values that are important to patients and caregivers with respect to the drug under review.

The following are summaries of three people we spoke with who have used spesolimab for GPP:

1. This individual lives in the Philippines and was diagnosed with psoriasis in 2003. It started with guttate and progressed into plaque. In 2014, after giving birth, they had a GPP flare. Their spouse, who participated in the interview, recount’s the experience from their perspective: "I was so scared when she was perspiring pus from neck to legs…doctors were rushing to put a line in her heart and get fluids in her…she was about to go into shock. I was so worried -– our son was just 4 months old…NO crying because he needs you…” The spouse feared how they would take care of a young baby alone, fearing that that the patient could die.

The memory of this struggle, and the risk to the patient's life, changed their perspective on having another child. They do not want to risk going through that again and the patient would not want to stop their current treatment to try getting pregnant again. They fear the outcomes of stopping the medication – an even worse flare, or even death.

To treat the first flare, this person used cyclosporine because they could not afford a biologic. This treatment worked for about a year, but the side effects were problematic. They switched to methotrexate and eventually had another significant flare-up. They were eventually given a biologic (secukinumab) in hospital at no cost to them. However, they were only given the initial dosing and could not afford subsequent treatments as they did not have health insurance. Their condition was maintained for about a year or two.

They joined a clinical trial for spesolimab in 2021. The first year was blinded but they began to see improvements. Three years into the trial, their skin is much clearer. They had one flare during the trial at which time they were given the maximum IV dose that managed the flare. They are happy with the medication and describe spesolimab as "a blessing for me". The patient is very fearful of what will happen to them when the trial ends and they can no longer have access to this medication that has changed their life.

Prior to spesolimab, this person's experience with GPP was very difficult. When their symptoms flared, they could not get out of bed due to excruciating pain. Between flares, the disease affected the way they dress (long sleeves only) and made them photosensitive. They expressed feeling emotional about challenges with parenting and not being able to breast feed their child due to medications.

The most helpful supports to this individual have been their spouse and their family, though GPP has been difficult for them too. Their spouse describes watching them suffer and knowing they can't do anything about it except offer support and comforting words. These social resources helped the patient overcome the "pain and shame" of living with GPP. Having a doctor that was able to identify GPP quickly and who checks on them regularly is also integral. They also identified the patient group that they're affiliated with as a "second family". Before they found this community resource, they felt alone and "wondering if there were others [like them]".

This patient is not currently working and although they want to (and could use the income) they fear entering the workforce again. They are worried about having a flare due to stress or missing work because of absences related to their illness that could cause them to lose their job. GPP also affects their physical mobility and confidence (e.g., movements like bending their knee would cause their skin to tear) – "am I going to be physically able to do the job?" This diagnosis has completely disrupted their aspirational career path.

2. This Patient is 44 and lives in central Canada. At the age of 14 they had a small circular patch on their chest. Their family doctor said it was pityriasis rosea and that it would be gone in 6 weeks. Instead of getting better, it kept getting worse and around the age of 17 they saw another doctor who referred them to a dermatologist who diagnosed pustular psoriasis. They were put on Soriatane (acitretin) which helped somewhat but as time went on, their skin got worse, and they started to experience flares.

Stress seems to be their only trigger and they have been bed ridden for over a month with a flare. They experienced extreme pain and discomfort and has even experienced "peeled skin off my eyelids". They shared, "I just did my best to get through everything and stay as low stress as I could."

After their dermatologist retired, they were referred to new dermatologist in 2020 who started them on a biologic (ustekinumab) which has helped them remain relatively well. Stress remained a trigger though and after a family member was diagnosed with colon cancer, they experienced another immediate flare.

In order to stay well, they stay away from anyone who is sick. Their flares often start with a sore throat that triggers hives, which then blister, and peel and they are usually "knocked out" for 3-5 days.

Over the course of their 24-year career they estimate that they missed approximately 2 years of working time and the other time, "I have worked in pain, itchy or uncomfortable …I just got used to working and managing it myself, lots of oatmeal baths and creams and then when the pain gets unbearable, I take medication for the pain."

In October of 2023 they were offered the opportunity to take spesolimab via iv infusion. They jumped at the opportunity to try something that might help. Prior to the infusion, they had blisters on their lower legs, ankles and feet. "Literally 30 hours later the blisters on my ankles were gone…it worked that fast."

Their second IV dose was delayed due to timing issues getting the medication and the patient had a full flare, with "pustules everywhere", head to toe covered except for their face. For the first 8-9 days of the flare, they were unable to sleep due to the extreme pain and discomfort. "I dozed for 30-45 minutes at a time, but I couldn't lie down or get comfortable. Any movement would cause pain and then I would wake up". They also couldn't eat. They missed 3 weeks of work due to this flare. They then received his second infusion in May and is now completely clear. "I get up every morning and do a full skin check to see if any blisters have formed. This drug works, that's it!"

Not having access to this medication would be unfortunate. "Everyone with this condition should have access to this medication…it just works…more than 1000% and it continues to work every day." This person says they are happy to have a doctor who is informed and stays up to date on treatments and brought spesolimab to their treatment regime. "I hit the lottery!"

This person feels fortunate that their insurance plan is as they have not had to pay for treatment out of pocket over the years. Without insurance it would be a challenge.

3. This person lives in a Canadian city of under 80,000 people. They described having "massive attacks" of GPP with full body (90%) coverage and the agony of these periods – difficulty moving, hard to sleep, described pain as "shards of glass" on their skin. The only relief they would get is through baths to try to sooth the itch.

   This person described having plaque psoriasis throughout their life and having their first GPP flare in 2020 (during COVID) during which they were hospitalized.

They said that the doctors in the hospital said it was “regular” psoriasis. They went on to describe the challenges they had getting a proper diagnosis and treatment. They had multiple flares following this initial one, each about three months apart. They described an “agonizing” process of multiple visits to their GP before getting a referral to a specialist after 4-5 months. They described being given a “bunch of needles” with some minimal results that provided about a week or so of relief. When asked if they knew what the treatments were, they said they think it was cortisone shots and steroid creams, with one being a bit “lighter” for his face. They described having biopsies that were inconclusive and described being made to feel like it was “just” psoriasis and that “everyone has it”.

They described that their face was affected around the eyes and nose, and that all the skin around the joints of their body was impacted. They lost significant weight during the “attacks”, they think because their body was working so hard.

While undergoing all of this, they described being barely able to function during the day and being off work for 6-8 weeks for stress leave. They reflected, “I work in an office, imagine if I worked in the field, or did physical labour.”

They were finally referred to a local dermatologist but experienced ongoing challenges with getting adequate care and treatment to get their disease under control. Last year, their GP eventually made a referral to a dermatologist in a larger city. Their experience with this second dermatologist was life changing. The second dermatologist was able to recognize, diagnosis, and treat GPP. This dermatologist provided a topical prescription and informed the patient to call the clinic when they start to get another “attack”. Two months later, they started to experience a flare and they made an appointment with the dermatologist for treatment.

With the first infusion of spesolimab, they got “some results”. After two weeks, they did one more treatment and after 3 weeks, they started to get clear. Right now, they are “still really good”, several months later.

This person described that it is “kind of stressful” to take a new treatment for a rare condition. After the first infusion, they described being “exhausted” with all of the stress and had to go home and sleep, but for the second one, they were more comfortable and were able to go about their day.

They also said that the stress was “definitely worth it.” They experienced “zero side effects”. They said that not only have they not had a flare since their treatment, but even between flares, it “was never this good without the treatment.”

They described that before the treatment, between “attacks”, their lifestyle was tremendously affected both physically and mentally. Beyond “the public looking at you” they described being physically overwhelmed by their disease, not being able to sleep or move well. They described that they had a lot of skin involvement at their joints and that it was hard to move.

They also described the direct impacts of the disease on work. They were preparing for work trip related to a client project that they had been assigned to. A few days before they were due to travel, they got called into the office by their manager who advised that they were no longer going to be sent on this job. They recalled

being told that they are “in no condition to be working on this site” and to “go try to work this out with your doctor.”

Since spesolimab treatment, they describe sleeping better, being able to move and to actually go for walks and exercise – “this affects your life, it’s a life changer”. They reflected that “a restful person makes a more productive person” and that when a person is rested, they are “not grumpy…you’re happy, you’re moving.” They also shared that it was very hard on their spouse to live with this disease, and this has eased the burden on their spouse as well.

They described that a maintenance dose may be appropriate for them because it is difficult to determine when an “attack” is going to occur and how long to wait, or how severe the symptoms are, before going for treatment again. They reflected that, “it’s obviously preventing something because I haven’t had anything since.” They shared that spring is the worst time of the year for them and March has been typically a harder month. The worry this person experiences about having another “attack” is palpable and the appreciation they have for a diagnosis and supportive care and appropriate treatment is clear.

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

<Enter Response Here>

8. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

We are grateful to the GPP patients who shared their time, input, stories, and care into helping us craft this submission. From their experiences, and from others who we have heard from in Canada and in the global community, the following points are clear:

- Current diagnosis, care, and treatment for GPP is inadequate. Patients who experience GPP flares are grateful for a treatment that treats flares and that could reduce the severity and impact of flares.

- Like other forms of psoriasis, GPP can affect every impact of a person's life, including self-image, personal relationships, and school/work. In every interview, we heard of the significant impact that GPP has had on a person's work life, including in some case, the trajectory of their careers.
- People with GPP who we speak to are driven to help others with this disease because they know how isolating and all-encompassing it can be. They know how important it is to have access to knowledgeable, timely care and to appropriate, effective, affordable treatment and how devastating it is to experience this disease in the absence of these resources.

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.

   One person with GPP reviewed this submission to ensure that it captured the general experiences of the disease well.

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

   N/A

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

Table 1: Financial Disclosures

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

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
AbbVie		X		
Arcutis			x	
Bausch Health		X		
BI Canada			X	
BMS			X	
Janssen			X	
Sun Pharma			X	

Pfizer			X	
Takeda Global			X	
UCB			X	

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

Name: Helen Crawford
Position: Program Manager
Patient Group: Canadian Association of Psoriasis Patients
Date: June 12, 2024

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
AbbVie			X	X
Arcutis			X	
Bausch Health			X	
BI Canada			X	
BMS			X	
Janssen			X	
Amgen			X	
Pfizer			X	
UCB			X	

Name: Antonella Scali
Position: Executive Director
Patient Group: Canadian Psoriasis Network
Date: June 17, 2024

Clinician Group Input

CADTH Project Number: SR0844-000

Generic Drug Name (Brand Name): spesolimab

Indication: generalized pustular psoriasis (GPP). Spevigo (spesolimab for injection) is indicated for the treatment of generalized pustular psoriasis (GPP), including treatment and prevention of flares, in adults and pediatric patients 12 years of age and older.

Name of Clinician Group: Origins Dermatology Centre

Author of Submission: Rachel Asiniwasis MD MSHS FRCPC FAAD

1. About Your Clinician Group

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

Origins Dermatology Centre services urban, rural, and Indigenous populations in an underserviced area with a focus on medical and general dermatology

We are submitting single-center input as currently there are no active working clinician groups for this rare disease of generalized pustular psoriasis (GPP), which is considered a separate entity from the more common chronic plaque psoriasis. GPP carries a unique and burdensome clinical/morbidity/mortality, inflammatory and genetic profile. There are currently no FDA-approved treatments for GPP.

2. Information Gathering

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

Literature resources, clinical experience, input from our experienced nurses. List of references can be found under additional information.

3. Current Treatments and Treatment Goals and 4. Treatment Gaps (unmet needs)

GPP is an auto-inflammatory, neutrophilic and cutaneous pustular disease, associated with acute flares of systemic symptoms and chronic residual disease/recurrences. It is potentially life-threatening, associated with systemic involvement and sepsis in which flares often require in-hospital management.

With regards to literature and clinician experience, GPP patients frequent not only outpatient clinics, but also the hospital, Emergency Department and other healthcare services (eg. labs, imaging for safety monitoring of systemic treatment). Canada is a large landmass; this burden of disease is even more magnified in rural and remote communities with challenges in managing flares including seeking timely care to specialists and hospitals/emergency departments, and arranging and monitoring off-label systemic therapy for those who lack healthcare service access. Similar to chronic plaque psoriasis, underlying chronic inflammatory systemic comorbidities have been associated with GPP, including cardiovascular disease, arthritis and diabetes.

GPP is characterized by acute flares and chronic recurrent disease which frequently runs a relapsing and challenging course. Flares can be difficult to predict and control. Therefore, for this chronic systemic inflammatory disease, both acute life-threatning systemic flare control and long-term maintenance including suppression of flares and treatment of residual disease is needed. In literature (including the GPP Psoriasis Registry dermatologist surveys by Strober et al. (2021) and clinical practice, many patients demonstrate

poor control of both acute flares and experience impactful chronic disease activity post flares. High rates of recurrence as well as persistent disease have been demonstrated in the literature (Kharawala et al., 2020). During acute flares, inflammatory pustules, diffuse erythema (if erythrodermic, patient can have secondary systemic impacts such as high output cardiac failure, electrolyte metabolic and thermoregulatory disturbance), skin pain, pruritus, and secondary infection may occur as some examples. Systemic impacts including during flares can include fever, malaise, cardiac, lung, joint and renal involvement among others. Patients frequently present to emergency or require hospitalization for flares. Per patient, cost to the healthcare system are higher than with those with chronic plaque psoriasis, with demonstrated high rates of hospitalization, outpatient and emergency department visits (Noe et al., 2022, Strober et al. 2020) requiring higher-level monitoring beyond outpatient, and initiating and managing potentially numerous systemic treatments.

Compared to chronic plaque psoriasis, which has several FDA-approved indications, GPP has not only a different inflammatory pathway (eg. with IL36 being a key, central cytokine mediator), but also carries high morbidity, mortality and healthcare utilization costs representing unmet needs. There are no approved therapies or current guidelines for treatment of GPP. Current off-label systemic treatments (systemic immunosuppressants and biologic therapy) for plaque psoriasis have proven inadequate in controlling both chronic and acute forms of GPP. Numerous treatments have been tried in a ‘shotgun’ approach and appear to be ‘all over the map’ including a variety of topical prescription steroids and steroid-free agents, systemic steroids, DMARDs (eg. Methotrexate, Cyclosporine) and other oral systemic agents, biologic agents, and phototherapy (Noe et al., 2022). However, these therapies have proven inadequate in the literature and in real-life which reflects a lack of standard of care and limitations in current off-label treatment options available. For one example, a real-world survey by dermatologists treating GPP by Strober et al. (2021) demonstrated that there are high rates of relapse with current off-label therapies, and treatments are slow to control flares. Most patients will relapse within one year of treatment. Furthermore, use of broad oral systemic immunosuppressants often used for this condition come with side effects such as cytopenias, liver and renal toxicity and increased risk of infection amongst others (eg. Methotrexate, Cyclosporine) which limits both their short- and long-term use in this disease.

There is a need for approved, studied, safe and effective targeted options for patients with GPP. As there are no guidelines or studied, approved treatments for GPP until spesolimab, there is an unmet need for novel and targeted therapies. GPP is considered a different clinical entity with unique cytokine-inflammatory profiles (eg. heavier skewing towards IL36 pathways) compared to chronic plaque psoriasis, whereas unique genetic mutations may be involved (eg. IL36 pathway). From a clinican’s standpoint, upon reviewing the Effisayil 1 and 2- trial data, spesolimab would be considered first-line for this condition to address the unmet needs of resolving flares and preventing them.

The goals of treatment in GPP would include fast control of acute flares, controlling signs and symptoms (eg. fever, malaise, pain, itch, swelling, pustules), and controlling and preventing systemic worsening or collapse as a part of the disease process. Long-term goals would include encouraging sustained responses, preventing flares, improving quality of life impact and an advantageous safety profile. From a clinican’s standpoint, upon reviewing the Effisayil 1 and 2- trial data, Spesolimab meets these unmet needs and would be considered first-line for this condition to resolve flares and prevent them. It is demonstrated to work quickly, with high efficacy, and preferable safety benefit compared to placebo.

5. Place in Therapy

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

This would be a first-line therapy for those diagnosed with GPP for reasoning above, including a lack of effective available on-label treatments. Those experiencing active disease, flares, systemic symptoms, and hospitalization would be most in need of intervention. In the trials, with a GPPGA total score of 3 or above and a pustulation score of at least 2 would be considered eligible. GPPGA is a clinical diagnosis with a limited differential diagnosis, although may be complimented by histology (skin biopsies). In the studies, patients both with IL36R mutations and those without are both likely to respond.

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?

Improved clinician reported and patient reported outcomes as outlined in the Effisayil-1 and 2 data (eg. GPPGA and subscores). In particular, the goals of treatment in GPP would include fast control of acute flares, controlling signs and symptoms (eg. pain, itch, swelling, pustules), and controlling and preventing systemic worsening or collapse as a part of the disease process (eg. cardiac, renal, arthritis, sepsis). Long-term goals would include encouraging sustained responses including preventing flares/keeping patients out of the hospital, through disease control, improving quality of life impact and an advantageous safety profile.

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

Clinical response over time, disease progression, adjunctive therapy may be considered in non-responders who continue to have more severe stages of disease.

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]?

Hospital and IV infusion clinics. Dermatology, Internal Medicine, and Emergency medicine to name some all likely could prescribe and monitor effectively once the diagnosis is confirmed.

6. Additional Information

We thank CADTH for considering unmet needs with the ultimate goal of improving care and reducing morbidity and mortality amongst patients with this rare condition, GPP.

References:

Kharawala, S., Golembesky, A. K., Bohn, R. L., & Esser, D. (2020). The clinical, humanistic, and economic burden of generalized pustular psoriasis: a structured review. *Expert review of clinical immunology*, *16*(3), 239–252. https://doi.org/10.1080/1744666X.2019.1708193

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Strober B, Kotowsky N, Medeiros R, Foster N, Janak J, Valdecantos W, Flack M, Golembesky A, Lebwohl M. Patient-reported outcomes from a large, North American-based cohort highlight a greater disease burden for generalized pustular psoarisis versus plaque psoriasis: Real-world Evidence from the Corrona Psoriasis Registry. AAD April 23-25, 2021 poster presentation.

7. Conflict of Interest Declarations

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

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

N/A. Publicly available references and clinician experience were used.

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.

   Collecting information – I used information from publicly references provided from a previous advisory board, some of it was in-summary.

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

Declaration for Clinician 1

Name: Rachel N. Asiniwasis MD MSHS FRCPC FAAD

Position: Dermatologist and Founder, Origins Dermatology Centre

Date: June 14, 2024

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

Table 1: Conflict of Interest Declaration for Clinician 1 relevant to GPP

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Boehringer-Ingleheim		X (advisory boards)		
Add or remove rows as required				

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