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

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

delgocitinib (TBC)

(LEO Pharma Inc.)

Indication: For the treatment of moderate to severe chronic hand eczema (CHE), including the relief of pain and pruritus, in adults who have had an inadequate response to, or for whom topical corticosteroids are not advisable.

November 12, 2024

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

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

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

CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: <delgocitinib >
Indication: <eczema >
Name of Patient Group: <Canadian Association of Neonatal Nurses>
Author of Submission: <Amy Wright>

1. About Your Patient Group

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

The Canadian Association of Neonatal Nurses is a national, not-for-profit organization that offers education and networking opportunities to neonatal nurses across the country. More information about our organization can be found at www.neonatalcann.ca

CANN's objectives include, promoting the art and science of neonatal nursing, providing opportunities for neonatal nurses to share knowledge, experiences and ideas with other health care providers both nationally and internationally, we participate in provincial, federal and international health care decision making and policy development regarding the care of newborns and their families, promote knowledge translation for effective and innovative approaches to neonatal nursing practice and changes to health policy. We advocate for neonatal nurses regarding quality of work life issues, and develop neonatal nursing scopes of practices, standards of care guidelines, and benchmarks to maintain nurses' professional competency and accountability. We have developed a national competency exam with the Canadian Nurses Association and provided expertise resulting in the development of national guidelines put forward by the Canadian Pediatric Society. Our social media presence has a global reach with more than 30,000 viewers and our quarterly podcast series have been downloaded more than 5000 times since inception in 2020. Our board of leading experts and leaders in neonatal nursing has relationships with nurses in all provinces and territories across the country, offering a wide scope of knowledge concerning neonatal care practices and the needs of our members.

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.

The data gathered for this submission is the result of a multi-faceted approach reflecting my personal experience and the lived experiences of the Canadian Association of Neonatal Nurses (CANN) executive and general members impacted by chronic hand eczema (CHE).

To surface their unique perspectives living and working with this debilitating condition we undertook qualitative dialogues in October 2024, and gathered anonymous data collected through previous qualitative interviews with nurses living with chronic hand eczema in July 2024.

Most recently we conducted an on-line quantitative survey of our nursing members (targeting those living with chronic hand eczema only) which was administered October 23 to November 10, 2024, and was promoted through CANN's email communication and established membership channels. Twenty-seven nurses living with chronic hand eczema survey respondents replied to the outreach and provided input.

All information was gathered in Canada. Survey respondents resided in all provinces spanning British Columbia to Newfoundland and interviewees in Alberta and Ontario.

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?

Although I am the President of CANN, I also suffer with chronic hand eczema and know firsthand the burden of the disease on my own nursing career and personal life. Additionally, one of our board members also has chronic hand eczema, therefore our board is especially attuned to the struggles of those who suffer with this disease. Our own lived experience motivated our interest in collaborating with the Canadian Association of Critical Care nurses and Leo Pharma to conduct a survey to better understand the experiences of critical care/neonatal nurses who suffer with this disease. Our board, and CANN, seeks to advocate on behalf of our members and those living with CHE to promote better access to treatments and cleaning products in our hospitals that do not aggravate the condition.

Submission informants report chronic hand eczema impacts many aspects of their day-to-day living. Beyond the physical and functional effects of the disease, it hinders social engagements, parenting, job performance and self-esteem. For participating neonatal nurses, it has meant absenteeism and in some cases workplace leaves and redeployment.

The most significant symptoms reported included open wounds with cracked, bleeding skin, deep, throbbing pain, awakening through the night with itch, pain & blood, blisters that are not clearing up during disease flares, intense itching to the point of distraction and swelling that affects their ability to use their hands.

For some chronic hand eczema causes anxiety and worry about when the next flare will occur, it affects their self-esteem and weighs on their mind heavily.

“(CHE) has been life altering, I have deep emotions talking about it, CHE really impacts life.”

“Having others to talk to helps with the isolation, I like to talk to others, so I do not feel like a freak.”

“Flares concern me, flares bring on anxiety.”

“I had to create a lifestyle change; I had to change my habits and behaviors.”

“Working at the hospital, where I had to apply cream, protection and then gloves was so terrible, frequently the blisters were popping, it got very bad with open sores. When at work I would try to get my gloves on it was like acid burning my hands, cherry red palms up to my wrist, it looked like I was burned by acid.”

“My job was the disease trigger, constant friction, repetitive sanitizing and the chemical in the latex gloves.”

“I have had huge financial considerations as I had to go casual at the hospital to allow my hands to heal and therefore did not get WCB. Eventually had to leave my high paying hospital career with great promise for a job in research.”

“I am not doing bedside care anymore; Occupational Health sent me to a Dermatologist…had to leave bedside NICU care with the little babies you are constantly sanitizing up to 100 times in a 12-hour shift…the Dermatologist just seeing my hands said he knew I was a NICU nurse. I had to take a desk job in the hospital to quell a very bad flare.”

“The trial and error of creams, ointments and other therapies causes expense…it changes your life, had to take sick days to heal my hands, impacted my work, parenting, activities and food choices.”

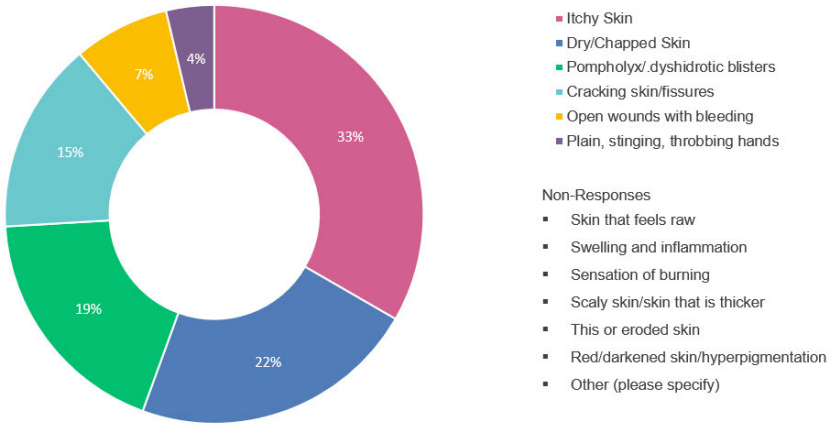
“I could not wash my baby in the tub, too painful, even breastfeeding, had to put on lotion, Vaseline and gloves to breastfeed my baby.”

“It is also embarrassing, parents (of NICU patients) look at it (eczema) and worry about it being contagious, in a hospital, I hide my hands. With those open wounds on my hands I went to Occupational Health, they knew I could not work with open wounds on my hands and would have to leave…it is in their best interest to get me back to work.”

“Trying to take care of my baby with cotton gloves is not an easy way to change diapers.”

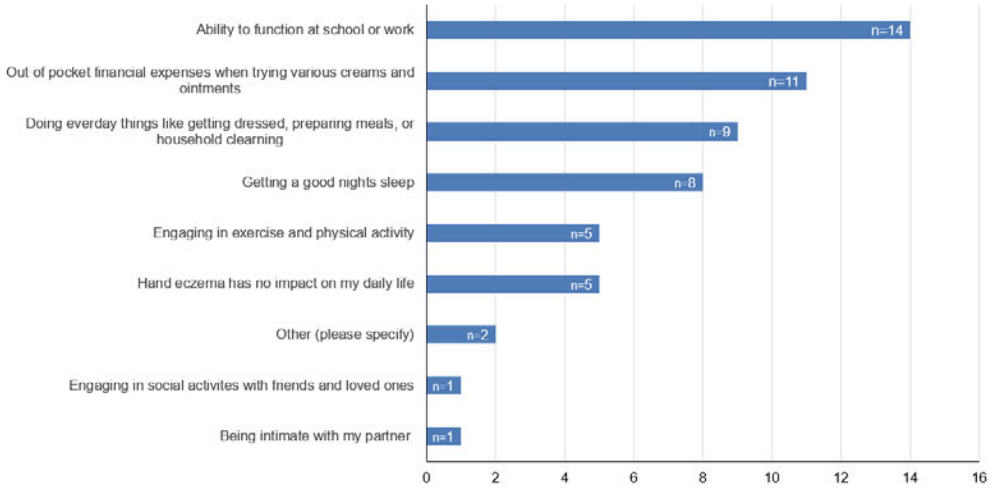
Survey respondents reported itchy skin is the symptom that causes them the greatest burden followed by dry, chapped skin.

Q: Of those symptoms you experience, what symptom causes you the greatest burden and is most important to control? (27 responses)



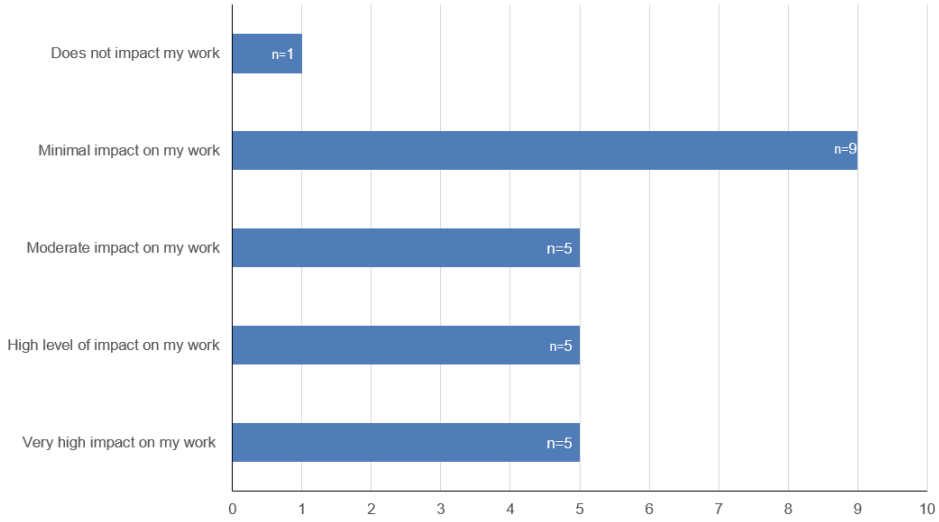
More than half the survey participants reported that chronic hand eczema impacts their ability to function at school or work. More than a third of respondents indicated their condition impacts them doing everyday tasks, such as getting dressed, preparing meals or doing household cleaning and another third stated their sleep is impacted.

Q: How, if at all, does chronic hand eczema impact your day-to-day living? (Please select all that apply) (25 responses)



Further, 58% of participants living with chronic hand eczema reported their condition had a moderate to very high impact on their nursing work and/or career.

Q: To what extent, if at all, does chronic hand eczema impact your nursing work/career? Please indicate the level of impact... (26 responses)



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).

With little advancement in CHE treatment over the past several years, most respondents employ a combination of protecting their skin barrier, identifying, and eliminating triggers with the use of topical corticosteroid creams. During cycles of disease flares and symptom severity most have tried additional high potency steroid ointments prescribed by their Dermatologist or oral steroids such as Prednisolone.

Interview respondents expressed concerns about long-term steroid use and the side effects that result.

“My Dermatologist gave me a steroid which I do not use because of steroid adverse effects, I use Protopic and Vaseline.”

“I was referred to a Dermatologist who gave me more corticosteroid topicals, but they did not work.”

“I decided to take oral steroids and monitor the side effects to remain at work. I later weaned off the oral steroids, took time off work and when I tried to go back to work it (CHE) flared again, ...the Dermatologist said you must change careers, now I am doing research.”

“Ointments are messy, I prefer creams, less mess.”

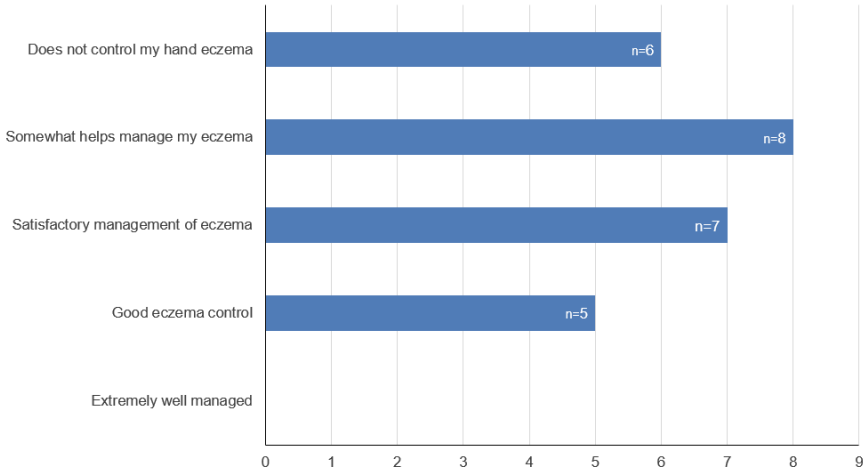
Phototherapy was also mentioned but discontinued because of the time commitment and travel burden to the healthcare centre as well as out of pocket costs incurred.

“Phototherapy I also used, going three or four times a week with little kids, I only lasted a couple of months.”

“Yes, I adhere to my creams well but stopped phototherapy because of cost and time commitment and oral steroids because of side effects.”

Of those surveyed, 52% reported their current hand eczema treatment and management does not control or only somewhat helps manage their hand eczema.

Q: How well does your current hand eczema treatment and management work to control your hand eczema? Please use a scale from 1 to 5. (26 responses)



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?

Most importantly respondents want to decrease severity and frequency of flares, if not eliminate them altogether, they want to stop the intense, burning pain, they experience and control their

disease. Informants desire the ability to function normally, to return to work and decrease the risk of infection from blisters and open wounds. They want to stop night-time waking and itching.

“A way to make it stop quickly, increase the timeliness of treatment in decreasing itch and pain, stop the flare in its tracks and not let it get to the bleeding stage.”

“To avoid flares, reduce my extreme pain, to decrease fear, I am so cautious, chronic hand eczema guides my day, what I can and cannot do…I want to be able to function, be able to pick up a fork and eat or make dinner.”

“To have non-steroidal solutions and upstream prevention by eliminating harmful irritants, environmental, food and chemical so the flares do not happen.”

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.

One respondent participated in the clinical trial.

“To get rid of it, during the clinical trial I got rid of it.”

“My previous creams did not work, my Dermatologist prescribed more potent steroid creams, I went through them all, I do not want to take systemic treatment, as a nurse I understand what the side effects might be. Only thing left was a clinical study, so I am on a clinical trial that is working, I am very grateful, I worry my insurance won’t cover it.”

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.

N/A

8. Anything Else?

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

"More needs to be done for nurses and respiratory therapists, for their retention, need to support nurses' health and safety, we need to address these issues and look after them."

"It is effecting people, hand eczema, it is a problem and not getting enough attention, people suffer silently and would benefit from more support and better treatments with less side effects."

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.

   Tara Addis, of Addis & Associates, supported the completion of this submission. Addis & Associates is a stakeholder and engagement consultancy and supported the engagement of neonatal nurses by way of participating in the design of the survey and conducting interviews with affected nurses. Their involvement was sponsored by Leo Pharma.

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.

   CANN co-created the survey with the Canadian Association of Critical Care nurses, sponsored by Leo Pharma. Leo Pharma oversaw the methodological design and distribution of the survey and Tara Addis analyzed the data.

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
Leo Pharma			√	

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: Amy Wright
Position: President, Canadian Association of Neonatal Nurses
Patient Group: Canadian Association of Neonatal Nurses
Date: November 12, 2024.

CADTH

CADTH Reimbursement Review
Patient Input Template

Name of the Drug and Indication	**Delgocitinib (brand name TBC)** **Manufacturer Requested Reimbursement Criteria:** For the treatment of moderate to severe chronic hand eczema (CHE), including the relief of pain and pruritus, in adults who have had an inadequate response to, or for whom topical corticosteroids are not advisable. **Indications:** For the treatment of moderate to severe chronic hand eczema (CHE), including the relief of pain and pruritus, in adults who have had an inadequate response to, or for whom topical corticosteroids are not advisable.
Name of the Patient Group	Eczema Society of Canada
Author of the Submission	Eczema Society of Canada
Name of the Primary Contact for This Submission	Amanda Cresswell-Melville Executive Director, Eczema Society of Canada
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

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

2. Information Gathering

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

3. Disease Experience

The Impact of Chronic Hand Eczema (CHE)
Chronic hand eczema (CHE) is characterized by extremely itchy, painful, inflamed, dry, scaly patches of skin that can flake, crack, and bleed. This can occur on the palms, fingertips, in the web spaces, and on

the dorsal surface of the hands. CHE profoundly affects everyday living and one's quality of life. It is commonly job-related and can be made worse by frequent hand washing and exposure to chemicals. One method for assessing CHE (that is caused by Allergic Contact Dermatitis – a subset of CHE) is patch testing. However, very few people living with CHE in Canada have access to patch testing or adequate treatment. Many dermatologists do not provide this type of testing.

A person living with CHE can experience physical pain from the time they wake up until they go to bed. Simple activities such as showering, hand washing, cooking, dressing and driving can be challenging and can cause excruciating pain. CHE can impact individuals in certain professions more than others, such as auto mechanics, machinists, florists, estheticians, and hairdressers – and for each of these professions, the hands are the most crucial tool of the job.

We use our hands for almost everything we do. Something as simple as hand washing and dressing can be unbearably painful. Patients report intense pain from any contact with cosmetics, shampoos, and hair care products. Simply getting ready for the day can become an arduous and stressful task. CHE is incredibly itchy, which causes stress and pain and can interrupt daily activities, including sleep.

Many individuals who suffer with CHE are left with limited treatment options, yet also the knowledge that their careers or everyday living are contributing to their condition – frequently washing for a nurse, latex gloves for a dental hygienist, solvents and chemicals for a machinist, and lotions and laundry detergents for a parent. The condition can leave sufferers feeling socially isolated.

Other CHE sufferers have expressed:

- Shame, embarrassment, self-esteem issues
- Living with constant and chronic pain, burning and itching
- Thickening of the skin and swelling of the hands and fingers
- Fearing the use of potent topical steroids as there are safety concerns related to touching their children with such potent medication on their hands
- Experiencing feelings of isolation, depression and similar symptoms – anxiety, frustration, and hopelessness because there is no treatment that works
- Experiencing frequent infection cycles
- Fear of shaking hands with people, or fear that someone will see their hands
- Unable to bathe their children
- Unable to hold their baby or fearing that the rough hands will hurt the baby, or make it uncomfortable for the baby
- Emotionally drained because they do not see a light at the end of the tunnel. They feel that they will have to live with this unrelenting disease for the rest of their lives

Sleep

ESC survey data revealed that loss of sleep and poor sleep quality are reported as significant quality of life impacts due to eczema, especially for those with more severe forms of the disease. Patients interviewed shared that the urge to itch is more pronounced at night, and the ability to sleep can be significantly affected. Pain can also impair sleep and even wake patients if the fissures or open wounds on the hands are disturbed at night.

"Sleep during a flare-up is challenging. On one end, I can sleep throughout the night, but scratch my hands raw in a deep slumber…I will lose sleep because the itchiness keeps me up."

Skin Impacts

Patients also reported skin damage, burning, and lesions that would itch, crack and bleed. Some patients also reported that the skin on their hands became very tender, red, and thick, and patients reported scars or marks on their skin from scratching. Others reported that they experienced deep cracks and blistered skin that would break or split from movements as minor as signing their name. These experiences can be embarrassing and significantly affect patients' confidence, sexual relationships, and intimacy. Episodes of itch can also be difficult for a non-eczema sufferer to appreciate or fully understand. The intensity and drive to scratch the skin is described as overwhelming and uncontrollable.

"The worst thing about hand eczema is that it is always dry, it's rough, and it can crack, and when it cracks, it hurts, and it also itches a lot."

"My hand eczema often flares at the joints of my fingers and around my wrists. I get embarrassed about my hand eczema in public. It's hard to see my skin swollen, red, and dry."

"My hand eczema started with a terrible burning, and then lesions started to develop that would itch, crack, and bleed, and eventually, the skin on my hands became very thick."

"The eczema flare-ups felt like a constant battle. The band aids on my hands were always a stark reminder of the pain and discomfort I was in."

"The constant itching is unbearable. No medication seemed to bring relief, and I felt trapped in my own skin."

Work Impacts

CHE patients very commonly report that their CHE impacts their ability to work, and often, the work itself causes their CHE. Many patients report having to change careers due to their CHE, such as health care workers, hairdressers, and mechanics being unable to work due to their disease. Patients report that their disease also impacts work, including both productivity and contributions while at work. Many patients report that their hands are swollen, infected and impossible to use. Individuals also report physical pain and embarrassment from the look and feel of their hands.

"Imagine not being able to work due to your CHE, or having to change a job that you love because you can't use your hands?"

"In my profession, I had to deliver many presentations and showcase deliverables, constantly using my hands. It was challenging when all I could think about was people staring at the eczema covering my hands and face. I felt exposed as if my skin condition overshadowed my skills and everything I was capable of."

"The itch from hand eczema can be very painful and distracting. I work at an office job, so I often have to take sick days from work if I'm in too much pain. I try my best to manage my itch triggers. However, the itch is often unpredictable. When I get an itch attack, I take deep breaths and get an ice pack, if possible."

"On my right hand, the eczema swallowed my cuticles. It became yellow. I thought it was getting infected. [CHE] is impossible to deal with."

Social impact

In addition to the physical pain, itch, and burning of CHE, the condition can negatively impact mood, relationships, school, and social interactions. Embarrassment is also reported, as patients find it difficult to hide their hands throughout the day, but there is shame and embarrassment related to how the hands look and feel.

"Going out with hand eczema took a big toll on my confidence. I felt self-conscious every time I saw people staring, wondering what they were thinking. It was hard not to feel like my skin was all anyone could see."

"Hand eczema affects my life every day from the moment I get up to the moment I go to bed. I want to hide my hands because they are so rough and red and dry. I also don't wear any rings on my fingers because I don't want to draw any attention to my hands."

"I'm conscious every time that I shake somebody's hand that that person will notice my hands are rough and dry."

"Once, I was waiting to pay for an item, and the woman at the cash was giving the change back into each person's hands, but when she saw my hands, she just put the change on the counter because she didn't want to touch my hands."

"The hand eczema is one of the worst areas on which one can have an eczema flare – everyone sees your hands, you use them daily, and they are such a sensitive area."

"My battle with hand eczema was very painful and distressing, and what surprised me was how frustrating and stress-inducing it was."

Family Burden

CHE can also cause a burden to family, relationships, and social life. For some patients, CHE means they cannot bathe their children, hold their babies, continue the job they have trained for, or even tie their own shoes. This is an incredible burden for the patient and can negatively impact family and personal relationships.

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

Patients report that social life, fitness, sport, and intimacy are significantly negatively impacted.

"When you cannot participate in activities you love – going to the gym, swimming, etc., hand eczema can have a real negative impact on your mood, self-esteem, and desire to live an active life."

"When my skin is flaring painfully, I often have to cancel plans with friends."

Hygiene

CHE patients also report that their CHE can negatively impact their hygiene, as bathing and hand washing can be excruciatingly painful. Shampoo and hair care are also very challenging, with products stinging and burning, as well as challenges related to gloves. This cycle of poor hygiene is not only

uncomfortable and socially disruptive, but it also perpetuates the cycles of infection and the need for additional options of antibiotics and treatments.

"Hand eczema is challenging due to the numerous touch points you can experience day to day. With numerous handwashing, it can aggravate skin that is trying to heal. I would put on rubber gloves anytime I had to take the garbage out."

"I can't wash my hands properly when my skin is flaring badly. I use fragrance-free cleansers at home and bring a bottle to work to avoid the harsh soaps. Showering can be really painful. Even if my skin is in a better condition, it is still mentally challenging to get into the shower. I've started wearing plastic / nitrile gloves when doing certain activities to protect my hands."

4. Experiences with Currently Available Treatments

Topical corticosteroids (TCS) are the typical treatment for patients with CHE, and potency is typically higher than used in atopic dermatitis on other areas of the body. Some patients require potent or super-potent TCS for some relief. Patients are concerned about the side effects of long-term, chronic use of TCS, and the side effects of this class of medication are well known. TCS are typically prescribed to be used in short bursts under the guidance of a healthcare provider. However, the chronicity of CHE often requires prolonged use of these TCS. Patients have significant concerns about the risks associated with prolonged steroid use.

For many patients with CHE, these current available topical treatments are inadequate, and there remains a significant gap in treatments for these individuals. These patients report that even though they adhere to their prescribed topical treatment plans and follow instructions closely, they feel frustrated when the treatments don't work.

In addition to TCS, alitretinoin is an approved oral retinoid treatment for CHE. For some patients, this may be an effective option, but for others, the limitations include: (1) for some patients, it is not an effective treatment to manage or clear the symptoms of CHE; (2) many patients cannot tolerate the adverse effects including headache, nausea, and potentially devastating hair loss in women; (3) limitations for women of reproductive years as the medication is teratogenic; and (4) costly and time-consuming blood monitoring is required while using alitretinoin. While this medication is helpful for some patients, it is not suitable for all patients, highlighting the need for additional treatment options.

CHE sufferers also cycle through many different medications. Patients report frustration with the trial-and-error process of cycling through currently available treatments. Patients interviewed have tried many therapies with little success. They report having suffered for decades and commonly report having little hope and low expectations when it comes to finding a treatment that will help to control their disease and bring them relief. This significant challenge highlights the need for improved treatments. Patients continue to seek medication and interventions that will improve their skin disease, reduce flares, and improve their quality of life.

Gloves have long been a recommendation for patients with CHE, but they pose their own challenges and can make symptoms and quality of life worse. Irritation from glove materials and additives like powders is a significant challenge, and thick gloves that are often required (e.g., a cotton liner, a protective soft layer, and an outer waterproof layer) can make dexterity challenging.

Given all of the information above, we believe it is clear that there is a need and opportunity to introduce new therapeutic options to patients to treat their CHE.

"Itches a lot" that's a big understatement. My CHE is so bad that I've resorted to wearing gloves 24/7. Doctors so far haven't been helpful."

"Treatments included very potent steroids, which worked only marginally well and which required constant application, and then I had to cover my hands in cotton gloves. That in itself was socially embarrassing and made work difficult. The pain would be exacerbated by daily activities such as self-care, working around the house, and at my job. I am also an artist, and working with clays and sculpture materials became impossible. It's very hard not to be able to do the things you love to do. It also impacted my job, as I work with my hands every day."

"The use of increasingly potent topical corticosteroids doesn't provide long-term relief. A new therapy that works to not only clear the hands by providing prolonged periods of clear skin, would be a game changer."

5. Improved Outcomes

The primary desired outcome is better control of the disease, with a treatment suitable for long-term use, as CHE is a chronic condition. Many patients with CHE report little success managing their CHE with current available therapies and report serious concerns surrounding the long-term use of these medications.

Delgocitinib would offer patients the first on-label topical therapy, with phase three clinical trial data on safety and efficacy to treat CHE. There is currently no topical medication indicated specifically for moderate to severe CHE, and this treatment would give patients an effective topical option. Delgocitinib can offer patients a Health Canada-approved longer-term control option with a favourable safety profile. Safety is important to patients as CHE requires the ongoing use of treatment. The lives of patients can be significantly improved by having access to Delgocitinib.

Patients are seeking relief from the itching, stinging, burning, and pain as well as an improved appearance of their hands. They would like to regain their confidence and self-esteem and once again want to venture out and socialize with others.

6. Experience With Drug Under Review

Experience with this new drug has been very positive. It is reported that Delgocitinib offers patients relief and is well tolerated – without stinging, burning, or a greasy feel on the hands, which can make work and daily functioning difficult. For patients who work with their hands, going to work was a daily challenge or nearly impossible with their previous treatment, and patients report that after using delgocitinib, they can continue or return to work. Overall, patients report being more productive in life, and patients report that their symptoms can completely resolve, which is reported as being life-altering.

7. Companion Diagnostic Test

N/A

8. Anything Else?

CHE patients in Canada have been suffering with significant discomfort and diminished quality of life.

In summary:

1- For patients who have tried other treatments and failed, access to new treatments like delgocitinib is potentially life-changing.

2 - Patients with CHE suffer greatly due to itch, pain, and skin symptoms, including sores, fissures, blisters, crusting, and scaling, as well as thickening of the skin and infections.

3 - Many patients have diligently exhausted all current treatment options, including following topical treatment plans, working closely with their health care professionals, and educating themselves about their condition, but still fail to achieve relief.

4 - Patients need and deserve access to innovative medicines which can give them a chance at controlling their disease and improving their quality of life.

5 - Health care providers need more options to treat their CHE patients, and patients deserve to have innovative treatments and improved quality of life.

"Hand eczema is painful, frustrating, and prevents me from doing the work and activities I love. A chance at a treatment that can help would be life-changing."

"Having a treatment that would work well, allow me to work, and resolve the symptoms could be life-changing."

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? NO.

(2) Did you receive help from outside your patient group to collect or analyze data used in this submission? NO

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

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
LEO Pharma Inc.				X

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

Name: Amanda Creswell-Melville
Position: Executive Director
Patient Group: Eczema Society of Canada
Date: November 11, 2024

Unite.
Educate.
Empower.

November 5th, 2024

Reimbursement Reviews
Canada's Drug Agency
865 Carling Ave., Suite 600
Ottawa, ON
K1S 5S8

Dear Members of the Canadian Drug Expert Committee,

I am writing today to provide the Canadian Skin Patient Alliance's support to the patient submission developed and submitted by the Eczema Society of Canada for Delgocitinib on behalf of chronic hand eczema patients in Canada.

The Canadian Skin Patient Alliance (CSPA) is a national registered charity that improves the health and well-being of people across Canada affected by skin, hair and nail conditions. Founded in 2007, CSPA supports this mission through collaboration, advocacy and education initiatives for the skin patient community. As there are thousands of different skin conditions – and more than 1,000 rare skin diseases – CSPA helps bridge the gaps among the public, patients and their loved ones, healthcare professionals, and researchers. To further support our patient communities, we work with our Affiliate Members, a formal network of over 30 Canadian patient organizations and the Eczema Society of Canada is one of these important organizations.

The Eczema Society of Canada completed a thorough survey of patients in order to populate their submission. Given the limited resources for all of us, the Canadian Skin Patient Alliance agreed to not duplicate efforts but instead to write this letter of support for their submission.

Thank you very much for your attention to this letter of support.

Sincerely,

Dana Gies
Executive Director
Canadian Skin Patient Alliance

G303-851 Industrial Ave
Ottawa, Ontario K1G 4L3
[redacted]
www.canadianskin.ca

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: SR0875-000
Generic Drug Name (Brand Name): Delgocitinib
Indication: Chronic hand Eczema (chronic hand dermatitis)
Name of Clinician Group: Atlantic Dermatology Group
Author of Submission: Dr. Irina Turchin

1. About Your Clinician Group

Atlantic Dermatology Group is a group of dermatology-certified specialists practicing medical dermatology with vast experience managing various skin conditions including chronic hand dermatitis. Several members are engaged in clinical research and have extensive experience in managing chronic hand dermatitis. Some of the group members were involved in the DELTA clinical trials and have first-hand experience with delgocitinib cream.

2. Information Gathering

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

3. Current Treatments and Treatment Goals

Chronic hand dermatitis (CHD) is common form of dermatitis affecting 10-15% of adult population. It is more prevalent in young women and in individuals with history of atopy. The term CHD is interchangeable with chronic hand eczema (CHE).

CHD is an inflammatory skin disease that has a profound impact on the quality of life of the affected individuals. It is a debilitating condition that can significantly impair patients' daily activities (washing hair, getting dressed, wiping after toilet use) and work productivity. CHD is associated with increased rate of infections and morbidity associated with antibiotic use.

CHD can have profound occupational impacts. Patients with poorly controlled moderate to severe CHD may require to go on disability or change occupations if unable to perform work duties. Populations at high risk include health care workers, construction workers, mechanics, and hair dressers.

CHD is a clinical diagnosis. The disease severity is often classified as clear, almost clear, mild, moderate or severe. All patients with CHD benefit from the use of emollients and irritant avoidance. Patch testing may be considered if allergic contact dermatitis is suspected.

Mild CHD is most often managed with the use of topical corticosteroids (TCS) for acute flares. TCS use is often episodic for flare management. Topical calcineurin inhibitors (TCIs) and topical phosphodiesterase 4 inhibitors (TPD4I) can be beneficial for some patients as a maintenance therapy and are utilized off label.

All recent clinical guidelines recommend short-term use of TCS as the first-line treatment for moderate to severe CHD. For more severe disease, TCS with increasing potency can be utilized. However, long-term use of TCS is not recommended due to the risk of skin atrophy and the common occurrence of TCS-related adverse events. Adverse events associated with TCS use in patients with CHD include skin atrophy, skin infections, pain, burning, fissures, reduced hand dexterity, and bleeding. Majority of patients with chronic hand dermatitis in clinical practice express a preference for non-steroidal topical treatment. Chronic TCS use is also associated with tachyphylaxis.

It is estimated that approximately 2-4% of patients with severe CHD are refractory to TCS. Data from the RWEAL study indicate that a significant proportion of patients with moderate to severe CHD who received treatment with TCS within the past year did not achieve adequate control with high to ultra-high potency TCS.

TCIs and TPD4I are also used off label for the management of CHD but their use is limited by inadequate efficacy and poor tolerability due to burning, irritation, stinging particularly in patients with moderate to severe disease.

Phototherapy and systemic treatments have also been utilized for the management of moderate to severe CHD. Unfortunately, the use of phototherapy is limited by efficacy and poor access.

The safety and efficacy of once daily oral alitretinoin in patients with severe CHD unresponsive to potent topical corticosteroids have been evaluated in two randomized, double-blind, placebo-controlled phase 3 studies. The pivotal trial included approximately 85% of patients with hyperkeratotic CHD, and post-hoc analyses suggested that oral alitretinoin might be more effective in this subtype compared to vesicular CHD subtypes. In the hyperkeratotic CHD subgroup, a higher proportion of patients achieved clear or almost clear skin with oral alitretinoin compared to placebo, while response rates were similar in the pompholyx (vesicular) patient population. The treatment course of oral alitretinoin typically lasts for 12 to 24 weeks with the option for further treatment courses in case of relapse. Based on clinical experience some patients require ongoing therapy to maintain treatment response. Discontinuation of treatment is recommended if there is an inadequate response after the initial 12 weeks of continuous therapy. Retreatment can be effective for patients who initially respond well but subsequently experience a relapse. Oral alitretinoin can also be used in combination with topical corticosteroids to enhance effects and manage the initial flare of CHE.

Systemic steroids (prednisone) and methotrexate are utilized off label for patients with severe CHD. Systemic steroids are limited to short term use for acute flares with the goal to transition to a safe long term effective treatment. Methotrexate is used off label for moderate to severe disease but is limited by adverse events of hematologic and hepatic toxicities.

Alitretinoin and methotrexate are contraindicated for women trying to conceive or pregnant limiting their use in women of childbearing potential.

Dupilumab, interleukin-4 (IL-4) and interleukin-13 (IL-13) inhibitor and JAK inhibitors such as upadacitinib and abrocitinib modulate the immune responses, reduce inflammation, and improve symptoms in immune-mediated conditions such as atopic dermatitis. Dupilumab and JAK inhibitors have been shown to control signs and symptoms of CHD in case reports and small case series. Neither dupilumab or JAK inhibitors are approved for CHD and their use is limited.

CHD treatment goals would include effective and safe topical and/or systemic therapies that would control signs and symptoms of CHD and allow for patients to have normal lives. CHD can be associated with significant occupational impacts that may require change in occupation or for young adults to select an occupation that allows them to avoid use of their hands. This may impact mental health and may lead to life course impairment.

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.

While the current treatment options provide some relief, there are unmet needs in the management of CHD.

There is a need for safe and effective therapies that would control signs and symptoms of CHD, normalize QoL and reduce or abolish occupational impacts.

Due to the limited body surface area of hands, ideal treatment would be a topical preparation that can be used to control flares and used as a long-term maintenance therapy if needed. The ideal treatment would be effective for various morphologic CHD subtypes (hyperkeratotic, dyshidrotic, etc) and would be safe for use in patients of all ages.

Unfortunately, current topical and systemic therapies are limited by either efficacy or long-term safety, or both.

5. Place in Therapy

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

Delgocitinib is a first-in-class, topical, pan-JAK inhibitor that targets all four members of the JAK family of enzymes, including JAK1, JAK2, JAK3, and TYK2. Delgocitinib inhibits the intracellular signaling pathways associated with cytokine receptor chains. These pathways play a crucial role in regulating a wide range of physiological and pathological processes, including inflammatory responses that occur in chronic hand dermatitis.
Upon cytokine-receptor interaction, JAKs are activated and subsequently phosphorylate and activate signal transducers and activators of transcription (STATs). Activated STATs trigger the expression of cytokine-responsive genes, leading to specific biological responses in target cells. By inhibiting JAK activity, delgocitinib effectively prevents the phosphorylation and activation of STATs, thus blocking the signaling of multiple pro-inflammatory cytokines including IL-2, IL-4, IL-6, IL-13, IL-21, IL-23. This leads to downregulation of immune and inflammatory responses involved in the underlying immune dysregulation and reducing inflammation in CHD.

DELTA 1 and DELTA 2, were multicentre, double-blind, placebo-controlled trials investigating delgocitinib cream (twice daily 20 mg/g) in adult patients with moderate to severe chronic hand dermatitis. These studies included a total of 960 patients from ten countries including Canada. Across both trials, the primary endpoint was met with significantly more delgocitinib- treated patients having a 0 or 1 score starting from week 4. At week 16, 64 (20%) patients in DELTA 1 and 91 (29%) in DELTA 2 delgocitinib groups had a clear or almost clear result as compared with 16 (10%) and 11 (7%), respectively, in cream vehicle groups (both trials p≤0·0055). The proportion of patients with 75% and 90% improvements in the Hand Eczema Severity Index (HECSI) score at week 16 was greater in the delgocitinib group (HECSI-75: 160 [49·2%] in DELTA 1 and 155 [49·5%] in DELTA 2 delgocitinib-treated patients *vs* 38 [23·5%] in DELTA 1 and 29 [18·2%] in DELTA 2 patients in the cream vehicle groups; HECSI-90: 96 [29·5%] in DELTA 1 and 97 [31·0%] in DELTA 2 delgocitinib-treated patients *vs* 20 [12·3%] and 14 [8·8%] patients in the cream vehicle groups. Dermatology Life Quality Index was also improved in delgocitinib-treated patients versus cream vehicle across both studies. Importantly, both studies demonstrated that there were no adverse events of special interest that were seen with the use of oral JAK inhibitors.

In addition, DELTA FORCE trial, a 24-week head-to-head trial comparing delgocitinib cream with oral alitretinoin in patients with severe CHD demonstrated consistently greater reduction in HECSI scores, itch, pain and DLQI reduction in patients treated with delgocitinib cream compared with oral alitretinoin. Treatment with delgocitinb was well tolerated with more treatment discontinuation seen in the alitretinoin treatment arm.

These studies underscore the high efficacy and favourable safety profile of delgocitinib cream in patients with moderate to severe CHD.

In clinical practice, delgocitinib could be used as a first line or second line treatment for adult patients with moderate to severe CHD for whom topical corticosteroids are inadequate or inappropriate. In clinical trials, this was defined as failure to achieve and maintain a low disease activity despite treatment, with potent to very potent TCS. This group supports delgocitinib cream treatment prior to the use of systemic therapy unless contraindicated.

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?

Delgocitinib would be considered as a treatment for patients with moderate to severe CHD of any morphological subtype who have failed prior treatment with potent topical corticosteroids or for whom topical steroids are not inadvisable or contraindicated.

As supported by the clinical trial data, delgocitinib cream is superior to oral alitretinoin in patients with severe CHD and this group would recommend delgocitinib cream prior to the introduction of systemic therapy.

CHD is a clinical diagnosis. Careful history and physical examination are required to establish correct diagnosis and rule out the possibilities of allergic contact and irritant contact dermatitis. This group would recommend that patients with moderate to severe CHD are evaluated by a dermatology specialist to establish diagnosis, rule out CHD mimickers (psoriasis, mycosis fungoides, irritant dermatitis) and initiate comprehensive management plan.

DELTA trials included patients with various CHD subtypes. Superior responses in one particular CHD subtype vs other were not reported.

DELTA FORCE trial had demonstrated clear benefit of delgocitinib cream over oral alitretinoin in patients with severe CHD.

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?

Most HCPs would categorize CHD as clear, almost clear, mild, moderate or severe. Physician global assessment (PGA) is currently used in clinical trials and can be readily adopted for routine clinical use. It is a validated tool where score is selected using the descriptors that best describe the overall appearance of the lesions at a given time point. It is not necessary that all characteristics under Morphological Description be present. The score 0 corresponds to “clear”skin, the score 4 corresponds to “severe” disease.

The Hand Eczema Severity Index (HECSI) is a tool utilized in clinical trials to assess the severity of various clinical signs of hand eczema. These signs include erythema, infiltration/papulation, vesicles, fissures, scaling, and edema. The extent of the lesions in five hand regions (fingertips, fingers [excluding fingertips], palm of hands, back of hands, and wrists) is also evaluated using standard scales. The HECSI score ranges from 0 (indicating the lowest possible score) to 360 (indicating the highest possible score). HECSI-75 and HECSI-90 are used to denote at least 75% or 90% improvement in the HECSI score from the baseline, respectively. A clinically significant improvement is defined as a ≥ 75% improvement in the HECSI score. This scoring is not utilized in clinical practice. It is time consuming and lacks clinical meaning in regards to disease severity outside of clinical trials.

Clinically meaningful improvement would be to improve and/or control signs and symptoms of disease which would be determined by a physician and patient together. Ideally, patients with moderate to severe disease should achieve an improvement which would correspond to a “mild” on PGA scale. However, some patients may be satisfied with significant reduction in pain, pruritus or fissures even if their disease remains moderate.

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

Patients with moderate to severe CHD treated with delgocitinib should be reassessed at around 16 weeks after initiating the treatment and then once yearly if the treatment is beneficial. It is important to mention that upon adequate improvement the treatment with delgocitinib cream can be used on as needed basis rather than continuously.

Treatment with delgocitinib should be discontinued if there has been lack of response after 16 week of therapy or if the patient reports intolerance to treatment, or at any time if the treatment benefit is lost.

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]?

This group feels that patients with moderate to severe CHD should be evaluated by a dermatology specialist to rule out CHD mimickers and to initiate delgocitinib cream prescription. Once adequate improvement is achieved, follow up treatment and prescriptions can be maintained by a non-dermatology health care providers.

6. Additional Information

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7. Conflict of Interest Declarations

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

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

   Not applicable

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.

   Not applicable

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: Irina Turchin
Position: Dermatologist, Fredericton, NB
Date: 11-Nov-2024

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

Table 1: Conflict of Interest Declaration for Clinician 1

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

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

Declaration for Clinician 2

Name: Dr. Tracey Brown-Maher
Position: Dermatologist, St. John's, NFLD
Date: 11-Nov-2024

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

Table 2: Conflict of Interest Declaration for Clinician 2

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

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

Declaration for Clinician 3

Name: Martin Leblanc
Position: Dermatologist, Moncton, NB
Date: 11-Nov-2024

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

Table 3: Conflict of Interest Declaration for Clinician 3

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

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

Declaration for Clinician 4

Name: Kerri Purdy
Position: Dermatologist, Halifax, NS
Date: 11-Nov-2024

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

Table 4: Conflict of Interest Declaration for Clinician 4

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

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

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: SR0875-000
Generic Drug Name (Brand Name): Delgocitinib (TBC)
Indication: Chronic hand eczema (CHE)
Name of Clinician Group: 1. Canadian Dermatology Association (CDA) Pharmacy and Therapeutics Advisory Board

Additional supporting groups:

- 2. Saskatchewan Dermatology Association
- 3. Canadian dermatologists with an interest in CHE

1. About Your Clinician Group

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

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

2. Information Gathering

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

3. Current Treatments and Treatment Goals

Chronic hand eczema (CHE) is a chronic, inflammatory skin condition that can range in levels of severity and burden. Especially when moderate to severe, CHE is a challenging condition to effectively treat and presents with inflammation, pain, itching (pruritus), fissuring/cracking, dryness, vesicles (blisters) and functional disability affecting the hands and wrists. Many different subtypes exist; irritant contact dermatitis, vesicular hand eczema, allergic contact dermatitis, atopic hand eczema and hyperkeratotic eczema. Frequently, patients present with signs and symptoms spanning multiple subtypes in clinical practice and real-world studies (Fargnoli et al., 2024).

Beyond the physical, CHE can significantly influence patients' quality of life (including work and social interactions), mental health, and occupational abilities which is more magnified in severe disease. Although the condition can present at any age, it is particularly seen in adults, with a notable impact on working-age patients (Diepgen & Mahler, 2002). CHE can lead to a substantial reduction in quality of life, comparable to that of chronic diseases such as diabetes or heart disease (Bae et al., 2021). The physical symptoms can also lead to psychological distress, including anxiety and depression, further exacerbating the impact of the condition (Zhou et al., 2018).

International prospective observational studies have estimated the prevalence of CHE in Canada to be up to 6%, and more commonly seen in females (Apfelbacher et al., 2024), with higher rates observed among certain occupations (López et al., 2020).

Professions with frequent exposure to irritants and allergens, such as healthcare, cleaning, and hairdressing, report particularly higher incidence rates, and this also reflects our experience in real-life practice. Studies have indicated that CHE often presents in adults, with a peak onset in working-age individuals, emphasizing the condition's potential economic and social implications by substantially impacting the adult patient's quality of life and physical ability to work and contribute to society (Koch et al., 2021). The occupational consequences of CHE are particularly concerning. Patients may need to take time off work due to flare-ups or may even be forced to change careers altogether. Studies indicate that individuals with CHE are more likely to experience unemployment or reduced work capacity (Larsen et al., 2020). The financial burden associated with lost productivity, medical expenses, and treatment can be substantial, creating a cycle of stress and worsening health. When more severe in nature, these effects are magnified.

CHE treatment ladders in Canadian guidelines (Lynde et al., 2010) firstly include non-prescription and lifestyle factors such as trigger avoidance, hypoallergenic skin care, and moisturizing which is recommended for all. If CHE is not controlled, prescription topical therapy is considered in which topical steroids are most commonly employed as first-line therapy since the 1950s, in which potency can be adjusted based on severity. In Canada, the currently available two classes of topical prescription treatments commonly used for CHE include: 1. Topical corticosteroids (TCS), and 2. Topical calcineurin inhibitors (TCIs). In clinical experience, higher-potency topical steroids are often used for flares and moderate to severe cases as there is limited effectiveness seen with TCIs. Should these fail, phototherapy or alitretinoin would be next-line, but these have their own challenges. Not all are able to access phototherapy, especially in rural, remote or underserviced areas, often has limited effectiveness, and is time burdensome. Alitretinoin has very limited access coverage, especially for public plan patients and requires ongoing lab monitoring, is teratogenic, and has numerous potential side effects associated with systemic retinoids. Alitretinoin is recommended for severe CHE patients who failed topical steroids, however, given the lack of treatment options available, it would be generally preferable to have another first-line topical agent instead of having to initiate a systemic treatment. For the vast majority of patients, alitretinoin is not an option.

Off-label systemic immunosuppressants and biologics conventionally used in moderate to severe disease can be considered third-line in guidelines, however, given that CHE is isolated to the hands/wrists, a more cost-effective treatment with a preferable safety profile in the form of a topical administration would be welcome instead of having minimal options other than escalating systemic treatment with side effect profiles for such a localized area of involvement. Use off-label broad immunosuppressants (eg. methotrexate, cyclosporine, oral steroids) are associated with a range of systemic side effects, some potentially severe such as cytopenias, hepatotoxicity, hypertension, renal damage, infection and malignancy and often aren't recommended for long-term use (eg. Cyclosporine). These therapies require consistent and regular safety monitoring (eg. clinical follow-up, recurrent labwork, baseline and ongoing chest X-rays, others like TB or quantiferon tests). Monitoring for and managing side effects of traditional systemic immunosuppressants can be challenging for patients without family physicians, already limited specialists (dermatologists) who are managing such medical cases, or those who have lack of lab or healthcare facility access in underserviced, rural and remote areas of Canada to appropriately conduct safety monitoring. A recent review (Borg et al., 2024) had found that approximately one quarter of CHE patients had received biologic therapy, indicating unmet needs in simpler, effective, and cost-effective therapies in the form of topicals for this localized and isolated area of special site involvement and impact.

General important goals of CHE therapy include maximizing efficacy and safety benefit, as well as efficiency and ease of treatment for the patient and physician. This includes treating signs and symptoms (eg. short and long-term management, addressing inflammation and itch), improving quality of life and mental health status associated with the condition (eg. sleep quality, anxiety, depression), keeping ability to function or restore to a 'normalized life' (eg. reduce presenteeism/absenteeism from work, school), preventing occupational dysfunction or need to switch occupations, and reducing adverse events and serious adverse events. Aside from topicals, some goals of therapy may be difficult to address in those who face barriers to care (such as northern and remote populations). Many goals of therapy can be assessed using the patient history and physical exam, supplemented by ongoing follow-up. It is worth noting that severe hand involvement is very impactful and thus 'special' site of consideration for new treatments.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

There is a strong need for new topical prescription therapy options for CHE; currently there is a lack of Health Canada approved treatment options. Over-the-counter moisturizers, emollients, hypoallergenic products, and other adaptations such as

trigger avoidances represent first-line lifestyle therapies. However, when first-line prescription treatment is required, currently, in Canada we have only two easily available prescription topical categories under the public system, which both represent broad (eg. non-targeted) mechanisms of topically local immunosuppression. 1. Topical corticosteroids (TCS) - Various classes that have restrictions based on potencies, body site, formulation (delivery vehicle), and duration of use; 2. Topical calcineurin inhibitors (TCIs; Topical tacrolimus 0.03% or 0.1% ointment, pimecrolimus 1% cream). Generally, these topical options are used for those who have mild-to-moderate disease that failed non-prescription therapy, with limited effectiveness in more severe forms of disease. In practice, patients often find themselves in 'frustrated cycling' of limited options for topical prescription therapies with overall low satisfaction of disease control.

Other than topical prescription treatment failures, some require treatment discontinuation due to intolerance/side effects. Particularly, use of TCS has restricted use of applications to sensitive areas/areas of thin skin. Especially when escalated to higher strengths, TCS can come with increased risk of both local side effects, such as atrophy, striae, slowed wound healing, aggravation of secondary infection, steroid-induced acne, rosacea, perioral dermatitis, and pigmentary changes, tachyphylaxis, amongst others, and systemic side effects in more extreme cases such as those associated with Cushing syndrome. Common adverse events seen with TCIs, such as stinging, burning and irritation reported by some users can prohibit compliance and effective use for those with AD. Many patients report not being able to tolerate the greasiness of steroid and topical tacrolimus ointments (eg. stains clothes), which may decrease compliance (eg. there is a need for better tolerated AD cream-based formulations). While topical corticosteroids can provide temporary relief, the risk of skin thinning and tachyphylaxis is significant (Kasper et al., 2019).

For concerns regarding escalating to systemic therapy, including broad systemic immunosuppression, please see the section above. First-line topical therapy, if optimized, represents an overall more convenient, safer and easier option if it can control the disease. Bloodwork or other ongoing safety monitoring such as TB tests or imaging is not required with topicals. With poorly controlled rates of CHE being seen and currently limited topical prescription options, an effective new topical therapy can potentially prevent the patient from requiring initiating and monitoring systemic therapy in the first place and is strongly needed. This can alleviate burdens off the patient, health system, and prescribing/monitoring clinicians.

5. Place in Therapy

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

The proposed indication for delgocitinib is for treatment of moderate to severe CHE in adults who have had an inadequate response to, or where topical corticosteroids are not advisable. This also reflects the DELTA 1,2 trials where adult patients had failed TCS. As CHE is a chronic disease, delgocitinib cream could be used in the short term, or on an as-needed basis, reflecting trial use. Patients apply delgocitinib twice daily for 16 weeks in these trials and move into the open-label extension trial DELTA 3, where they apply delgocitinib as needed moving forward to manage flares.

Delgocitinib, topically, under review is expected to cause a shift in the current treatment paradigm through representing a new and unique class for a new targeted topical prescription therapy as a topical JAK inhibitor that is intended and studied for CHE. Topical corticosteroids (TCS) which have a broadly immunosuppressive mechanism have been the first-line mainstay of treatment since the 1950s. TCIs, often also prescribed, are also broadly immunosuppressive by mechanism and literature and clinical experience has demonstrated many rates of these failures or intolerances.

The study population in the pivotal randomized control trials (DELTA 1 and DELTA 2) is for use as a second line treatment option for moderate to severe CHE in adult patients refractory to topical corticosteroids. In the open-label extension DELTA3, delgocitinib was effectively continued on a prn (as-needed) basis. In DELTA-Force, compared to alitretinoin as a systemic medication, delgocitinib was more efficacious across clinician (eg. HECSI – Hand Eczema Severity Index) and patient-reported outcomes with a more preferable safety profile (including less adverse events and discontinuations). This study emphasizes that a topical measure (delgocitinib) would be preferred second line treatment for CHE, as the alternative would be systemic therapy. Topical options offer benefits over systemic therapies with regards to preferably safety profiles, and lack of requirement for ongoing lab monitoring. Reassuringly, delgocitinib is shown to have minimal systemic absorption.

The Phase III pivotal trials, DELTA 1&2, assessed efficacy and safety of twice daily topical applications of delgobitinib vs. placebo (vehicle) in adults with moderate to severe CHE. Canada was also included in these studies. Primary endpoints include IGA-CHE success at week 16 (IGA 0 - clear or 1 - almost clear). By week 16, IGA-CHE treatment success was seen at approximately 20-

30% of patients which was significant over placebo. It is worth noting that in real-life clinical practice, even those who did not meet primary endpoints, but showed clinical improvement (eg. IGA2/mild disease), continued trials of therapy would be extended to assess for further response. Adverse events were similar in both groups, with no concerning signals for thromboses, MACE or infections. Longer-term open label extension studies from DELTA3 contains information for a continuing 36 weeks. Of those who completed week 16 treatment periods, participants continued on a PRN (as-needed) basis with twice daily delgocitinib (n=801). Those with IGA 2 on more (eg. mild disease and above) continued delgocitinib until meeting the primary endpoints of clear (IGA 0) or almost clear (IGA 1). Here, primary and secondary endpoints included adverse events, clinician-reported outcomes (IGA-CHE (0/1) and 75% or 90% improvement in HECSI (Hand Eczema Severity Index), and patient-reported outcomes (itch/pain). Significant rates of IGA-CHE 0/1, HECI75, HECI90, and 4-point reduction in itch/pain were maintained, and for those on placebo (vehicle), response rates continued improvement from baseline. No concerning signals for safety events were raised with regards to MACE, thromboses, or infections.

From a cost-benefit perspective, it is worth distinguishing that delgocitinib is on-label for use on the hands and wrists which is a localized and limited body surface area. As a result, we do not expect prescriptions to be in high volumes/high body surface area. The hands are generally considered a 'special site' in the sense that active disease (eg. moderate to severe CHE), despite the low body surface area involvement, is incredibly impactful.

In the current traditional therapeutic stepwise approach, if traditional systemic immunosuppression or targeted biologic or oral JAK1 inhibitor therapy is the next step for failed severe CHE cases, one potential benefit to having Delgociintib as a new targeted topical treatment option is that it may spare patients and provide a safer and easier option from requiring systemic or biologic therapies. Patients and clinicians also generally value treatments that have low impact on daily life activities. Another benefit to delgocitinib as a topical measure is that it can reduce time burdens, multi-tiered regimens and improve adherence, and reduce visits to primary care physicians, dermatologists, and reduce flares.

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?

The proposed indication for delgocitinib is for treatment of moderate to severe CHE in adults who have had an inadequate response to, or where topical corticosteroids (TCS) are not advisable. It would be used in patients with moderate to severe forms of CHE which have failed TCS. A trial of 16 weeks would be to assess response. See section 5.1 for further information on which patients would most likely respond or benefit from treatment.

No specific diagnostic tools or companion diagnostic tests are required for delgocitnib cream; the diagnosis of CHE is clinical (eg. meeting currently accepted standards of diagnostic criteria supported by history and clinical exam). Misdiagnosis and under-diagnosis in CHE would be considered uncommon for those that can recognize this condition, but there are some rare forms of skin conditions that may mimic disease morphologies. However, this is often ruled out through history, clinical exam and morphology, and skin biopsy/histology or other appropriate tests should concerns for alternate diagnoses arise. Currently, there is no bedside test or biomarker tests that are used in CHE, but certain assessments such as patch testing, or occupational assessments may be indicated in those who may have contributing factors. Treatment responses currently are identified from information gathered from patient history and physical exam, and clinician and patient-reported outcomes. In this case, although HECSI is not standardly applied in clinical practice, it may be required to renew the medication and could be adopted into practice. However, it may prove time-consuming and an extra burden on clinicians; an overall assessment of clinically meaningful response would be preferred.

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?

Please see 5.2 above. Overall, clinically meaningful responses improve disease severity including improved short and long-term signs and symptoms of CHE. For CHE, clinical practice uses a combination of information gathered from patient history and exam, physician-reported clinical scoring systems (eg. CHE-IGA) and patient reported outcomes. In particular, improvement in clinical disease severity including improved signs and symptoms and pruritus/pain measures, and functional and quality of life impact. See section 5.2 for further information. 'Special sites' such as hands carry higher patient impact. Many of these scoring systems represent some used in clinical trials as primary and secondary outcomes, but in real life practice due to time limitations only some are used and mostly in context of moderate-to-severe disease/those requiring systemic therapy.

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A trial period for assessment of delgocitinib response would be 16 weeks. A clinically meaningful response can widely vary, from more stringent definitions as in Phase 3 RCTs (eg. CHE-IGA 0,1), to those more relatively interpreted in practice; even a partial response (eg. Improving to a level of IGA 2 which represents mild disease as opposed to IGA3-4 which is moderate to severe) in therapy can be very meaningful for patients and clinicians if they are able to gain back function or have improved quality of life. Often, partial responses can be further improved to clear or almost clear (IGA 0,1) or at least much more manageable disease characterized by normalization of life by extending the duration of therapy or adding combination therapy. The global context of patient response relative to their individual situation, including support from clinician and patient reported outcomes, is ultimately what determines a clinically meaningful response in real-life practice.

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

General reasons for discontinuation include poor efficacy or inadequate response, recurrent flares, worsening, or nonresponse of disease despite an adequate therapeutic trial, or intolerance/side effects requiring discontinuation.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

Given that this is a topical therapy for CHE, this should be able to be appropriately prescribed by physicians including both generalists and specialists who know about, diagnose and manage CHE.

6. Additional Information

It is important to note that dermatology is likely the medical specialty with the most off-label therapies. Topical therapies, when practical, feasible, and recommended by guidelines, are the preferred first-line therapies. Currently, our first-line therapy consists of topical steroids since the 1950s. It is imperative we provide clinician input due to the lack of new innovations and availability for dermatologic conditions. Delgocitinib represents a new topical prescription therapy option with a novel mechanism, ideally more targeted, and well tolerated, that is relatively safe and effective and may reduce escalation to systemic therapy is needed by both clinicians and patients. Despite the rise in targeted advanced therapies for severe inflammatory skin disease, we continue to emphasize needs for the most simple and easiest to employ measure in real-life practice – topical prescription therapies with a favorable safety and efficacy profile.

Addressing the unmet needs of patients with CHE requires systemic changes within healthcare policies. Advocacy for better access to advanced treatments, including topical therapies, is essential to ensure that all patients can benefit from the latest innovations in care.

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

Chronic hand eczema poses a significant clinical challenge with profound effects on patients' lives. While there are treatment options available, considerable unmet needs remain in terms of accurate diagnosis, effective treatment strategies, and psychosocial support. By improving the management of CHE, we can enhance the quality of life for those affected and reduce the broader socioeconomic impact of this condition.

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7. Conflict of Interest Declarations

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

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

   No, this submission was completed by dermatologist clinicians.

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.

   Yes, with regards to collecting information, Leo's medical sciences had sent us some academic articles on delgocitinib to reference. However, the information was synthesized by our clinician group.

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

Declaration for Clinician 1

Name: Rachel Asiniwasis MD MSHS FRCPC FAAD [1,2]
Position: 1. Member, CDA Pharmacy and Therapeutics Advisory Board 2. President, Saskatchewan Dermatology Association
Date: <30-10-2024>

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

Table 1: Conflict of Interest Declaration for Clinician 1

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

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

Declaration for Clinician 2

Name: Cathryn Sibbald [1]
Position: Dermatologist, Staff Physician -the Hospital for Sick Children, Assistant professor - University of Toronto, Member – CDA Pharmacy and Therapeutics Advisory Board
Date: 05-11-2024

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

Table 2: Conflict of Interest Declaration for Clinician 2

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

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

Declaration for Clinician 3

Name: Yuka Asai [1]
Position: Dermatologist; Associate Professor, Chair, Division of Dermatology, Department of Medicine, Queen's University; Member – CDA Pharmacy and Therapeutics Advisory Board
Date: 06-11-2024

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

Table 3: Conflict of Interest Declaration for Clinician 3

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

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

Declaration for Clinician 4

Name: Brittany Waller [2]
Position: Dermatologist - Origins Dermatology; Assistant Professor - University of Saskatchewan
Date: 06-11-2024

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

Table 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
LEO Pharmaceuticals	X			
Add company name				
Add or remove rows as required				

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

Declaration for Clinician 5

Name: Reetesh Bose [3]
Position: Dermatologist, Lecturer University of Ottawa
Date: 06-11-2024

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

Table 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
Add company name				
Add company name				
Add or remove rows as required				

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

Declaration for Clinician 6

Name: Kirsten Walker [2]
Position: Dermatologist -Walker Dermatology, Assistant Professor, Chair, Division of Dermatology, Department of Medicine, University of Saskatchewan
Date: 07-11-2024

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

Table 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**
Leo Pharmaceuticals	X			
Add company name				
Add or remove rows as required				

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

Declaration for Clinician 7

Name: Marlene Dytoc [3]
Position: Dermatologist, Clinical Professor, University of Alberta
Date: 08/11/2024

☒ **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 7

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

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

Declaration for Clinician 8

Name: Dr. Alim R. Devani [3]
Position: Dermatologist
Date: 10-11-2024

☒ **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 8

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

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

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: SR0875-000
Generic Drug Name (Brand Name): delgocitinib
Indication: For the treatment of moderate to severe chronic hand eczema (CHE), including the relief of pain and pruritus, in adults who have had an inadequate response to, or for whom topical corticosteroids are not advisable.
Name of Clinician Group: Dermatology Association of Ontario (DAO)
Author of Submission: Dr. David N. Adam

1. About Your Clinician Group

The DAO provides broad representation for Ontario dermatologists. The DAO membership consists of community dermatologists as well as national and internationally recognized experts in the treatment of chronic hand eczema (CHE).

2. Information Gathering

Information gathered for this submission is based on published literature, clinical trial experience, and clinical practice experience from the members of DAO.

3. Current Treatments and Treatment Goals

CHE is an inflammatory skin disease affecting the hands and wrists of patients and is especially prevalent in patients whose occupations result in prolonged skin exposure to water, irritants, or trauma. The loss of functionality in the hands and the visible signs of CHE lead to a detrimental effect on a patient's social and psychological well-being. The current treatment approach in Ontario is well reflected in Canadian and European CHE management guidelines.[1,2,3]

First and foremost, all patients, regardless of severity, are educated on prevention and avoidance strategies which could include wearing gloves to provide skin protection and/or avoiding triggers which can be identified through patch testing or reviewing the patient's history. All patients should frequently apply emollients throughout the day to improve the skin barrier function which may help to prevent itching and reduce flares.

When prevention strategies and emollients fail to control CHE, topical corticosteroids represent the mainstay of first-line pharmacotherapy for the management of CHE. The potency of the corticosteroid may vary depending on the severity of the disease - where moderate to severe disease typically requires the use of high or ultra-high potency topical corticosteroids. Topical calcineurin inhibitors like tacrolimus are sometimes used in mild cases of CHE when a steroid sparing therapy is required due to adverse events related to steroid use (such as excessive thinning of the skin). For moderate and severe forms of CHE, topical calcineurin inhibitors are not effective treatment alternatives for high and ultra-high potency topical corticosteroids.

If patients remain uncontrolled despite the use of high/ultra-high potency topical corticosteroids, second-line treatment options include phototherapy or alitretinoin. Phototherapy is effective in treating moderate and severe CHE however access to phototherapy is inconsistent across Ontario and requires patients to make frequent visits to treatment sites. Alitretinoin is more accessible and is listed by the Ontario Drug Benefit program and covered by most insurance companies. While the indication for alitretinoin is formally limited to severe CHE, in practice, a patient who is refractory to high or ultra-high potency topical corticosteroids will be treated the same whether they register a "moderate" or "severe" score of PGA 3 or 4, respectively. Given the waxing and waning nature of CHE

it is not unusual for an individual patient's PGA to land between 3 to 4 on any given day, thus the distinction between moderate and severe is not relevant. What is more important is recognizing that these moderate/severe patients are experiencing uncontrolled CHE despite high and ultra-high potency corticosteroids and require new treatment interventions. Alitretinoin is not suitable for all patients however given the associated contraindications (for example, pregnancy and breastfeeding) and requires lab monitoring.

If phototherapy and alitretinoin are not suitable, accessible, or fail to control the condition, several off-label systemic options are typically considered, including traditional immunosuppressants (for example, methotrexate and cyclosporine), biologics (particularly ones used in atopic dermatitis such as dupilumab), and oral JAK inhibitors (for example, upadacitinib). Selection of treatment depends on several factors including accessibility/cost (for example, coverage criteria may make a biologic therapy inaccessible, or co-pay cost to the patient may be a barrier), safety considerations (black box warnings and contraindications across the oral systemic therapies), and expected effectiveness (where traditional immunosuppressants are not as effective in managing CHE compared to biologics or oral JAK inhibitors).

The most important treatment goals in managing CHE center around the patient being able to feel that they can function "normally" again and improving the appearance of their hands as refractory cases of CHE often disfigure the hands causing significant distress to patients. Improvement in appearance of the hands is directly related to improved function as the signs of CHE are linked to the challenges patients often express (for example, the hands being cracked, bleeding, and swollen make it difficult for the patient to grab/hold things and causes pain).

References:

1. https://journals.sagepub.com/doi/abs/10.2310/7750.2010.09094?journalCode=cmsa
2. https://pubmed.ncbi.nlm.nih.gov/34971008/
3. https://onlinelibrary.wiley.com/doi/10.1111/ddg.15179

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.

Managing moderate/severe CHE patients is challenging given that few therapies have been developed for CHE in the past decade. As well, currently available treatments have limitations that do not address the needs for patients.

While high or ultra-high potent topical corticosteroids are the mainstay of first-line treatment, not all patients respond and some will be unable to tolerate the effects of prolonged use (namely, skin thinning, further compromising the skin barrier).

For second-line treatments, phototherapy as we alluded to above, is not widely accessible across Ontario. And where it may be available, the frequency of treatment visits required may make it impossible for some patients to commit to (may require at least 3 visits every week for several months). Alitretinoin, as we also alluded to above, has several safety considerations that limit its use across CHE patients – specifically in females due to contraindications in pregnancy and breastfeeding.[1] The overall tolerability and suitability of alitretinoin is also broadly limited by additional contraindications (in patients with hepatic/renal insufficiency) and the need to conduct regular lab monitoring (which could include blood glucose, lipids, thyroid function etc.).

With regards to third-line treatments, the tolerability of oral treatments such as methotrexate/cyclosporine/oral JAK inhibitors limit its broad use by CHE patients. Blackbox warnings, contraindications, and required lab monitoring are potential factors that make these therapies unsuitable for some patients. For example, Health Canada has advised prescribers to consider the risk/benefit ratio of initiating an oral JAK inhibitor in patients who are current or past smokers, have cardiovascular or malignancy risk factors, or who are at risk of thrombosis.[1] For biologic therapies like dupilumab, as we alluded to above, accessibility can be challenging due to coverage criteria. As well, across all these therapies, there is a lack of RCT evidence demonstrating they are efficacious options for all subtypes of CHE (save for dupilumab and oral JAK inhibitors which have evidence for their use in patients who have atopic CHE only).[2,3,4]

There is a need to expand the therapeutic arsenal for CHE and include therapies that are safe, effective, and accessible, for long term control of CHE.

References:

1. https://recalls-rappels.canada.ca/en/alert-recall/canadian-labelling-all-jak-inhibitors-include-risks-serious-heart-related-problems
2. https://pubmed.ncbi.nlm.nih.gov/37184290/
3. https://www.nejm.org/doi/full/10.1056/NEJMoa2019380
4. https://www.jaad.org/article/S0190-9622(24)00146-4/fulltext

5. Place in Therapy

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

Topical delgocitinib would be utilized as a 2nd line treatment for moderate/severe CHE patients (i.e., PGA 3 to 4) who were refractory to/could not tolerate/contraindicated to topical corticosteroids, consistent to the indication noted on the CDA webpage. This is also aligned to the clinical trials where patients were required to be previously treated with topical steroids, or unable to tolerate it. Delgocitinib would be used in combination with emollients and avoidance strategies (if applicable). As delgocitinib is a topical pan-JAK inhibitor directly targeting the underlying mechanisms behind CHE, complementing it with emollients to restore skin barrier function and avoidance strategies is a sensible treatment escalation strategy should first-line steroids fail to control the disease. Given the topical nature of delgocitinib, it also benefits from having minimal systemic absorption and likely results in its acceptable safety and tolerability profile observed in its phase 3 trials (In DELTA 1 and 2, delgocitinib appears to have similar safety/tolerability to vehicle and the overall picture does not change in DELTA 3 long-term extension trial).[1,2,3]

Delgocitinib is expected to shift the current treatment paradigm where it would be a recommended 2nd line therapy over existing treatments like phototherapy and alitretinoin. Ease of access and treatment administration over phototherapy means delgocitinib would be well within reach for all CHE patients. And compared to alitretinoin, results from the recently published phase 3 DELTA FORCE head-to-head trial demonstrate that delgocitinib was superior in efficacy and safety compared to alitretinoin over 24 weeks in adult patients with severe CHE who were previously treated with topical corticosteroids.[4] It is expected that delgocitinib will not require lab monitoring nor have the contraindications that currently apply to alitretinoin (pregnancy, breastfeeding, renal/hepatic insufficiency etc.). While DELTA FORCE was conducted in severe CHE patients, as discussed above, the distinction between moderate and severe is often not relevant given the waxing/waning characteristics of CHE. The results of the trial therefore likely also apply to moderate CHE patients who, as we alluded to above, would currently be treated with alitretinoin. Thus, it is expected that patients who are refractory/intolerant to first-line steroids would be preferentially treated with delgocitinib as a 2nd line therapy, where phototherapy (which is difficult to access, if at all possible) and alitretinoin (which is less efficacious with poorer safety and tolerability profile), would be looked at for 3rd line therapy. Other oral systemics (methotrexate, oral JAK inhibitors) and biologics would be relegated to 4th line therapy (after phototherapy and alitretinoin).

Consistent with the clinical trials, it is expected that delgocitinib would be applied twice daily to affected areas of the hands and wrists and patients could be advised to adopt an as needed application after they achieve a clinically meaningful response – akin to how patients transitioned from DELTA 1 and 2 into DELTA 3.[1,2]

References:

1. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(24)01027-4/abstract
2. https://academic.oup.com/bjd/article-abstract/191/Supplement_2/ljae266.034/7728665?redirectedFrom=fulltext
3. https://event.fourwaves.com/cda2024/abstracts/292ef2b4-530f-48e3-9f81-5ed3ffd7495f
4. https://www.businesswire.com/news/home/20240925520539/en/LEO-Pharma-Presents-Late-Breaking-Anzupgo%C2%AE-delgocitinib-Cream-Presentation-at-EADV-2024-Highlighting-Results-of-Head-to-Head-DELTA-FORCE-Trial-in-Chronic-Hand-Eczema-CHE

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?

Delgocitinib is best suited for adults with moderate to severe CHE who have had an inadequate response to, or for whom topical corticosteroids are not advisable. This is aligned with where most cases of CHE are observed – adults of working age – and where the greatest need lies given the gaps in treatments that exist today (discussed in the preceding sections). While scales exist to measures the severity of CHE (PGA, HECSI), as discussed in preceding sections, the distinction between moderate and severe CHE is often not relevant given the waxing/waning characteristics of CHE. Practically, if a patient fails to respond to high or ultra-high potency topical corticosteroids and is suffering from uncontrolled moderate/severe CHE (e.g., PGA 3 to 4) that is impacting their ability to function, they are a moderate/severe patient that requires treatment escalation to a 2nd line therapy where delgocitinib would be better suited over the current options, phototherapy and alitretinoin.

Delgocitinib would be least suited for patients with mild CHE (e.g., PGA 2) where topical corticosteroids have not yet been utilized or where it is being adequately managed by emollients/avoidance strategies/topical corticosteroids.

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?

In clinical practice, outcome measures are not strictly defined as they are in clinical trials. Most clinicians will use an informal physician global assessment (PGA, which is interchangeable with the investigator global assessment IGA) which ranks severity on a 5-point scale of clear (0), almost clear (1), mild (2), moderate (3), and severe (4). The closest equivalent outcome studied in the delgocitinib trials is the investigator global assessment of CHE (IGA-CHE) scale, which is a more stringent assessment tool in that it defines “almost clear” as patients only having residual erythema and no other findings. This does not align with clinical practice as if a patient has barely perceptible papulation or edema this is still “almost clear” by clinicians in a general practice setting whereas in the trial this patient would be defined as “mild”.[1,2] With that in mind, considering that in practice, patients attaining a PGA of 1 is clinically meaningful, we expect that translating this to IGA-CHE suggests that patients achieving IGA-CHE 2 could be considered clinically meaningful as it could describe a similar disease state as PGA 1.

Another outcome measure used in the trials is the hand eczema severity Index (HECSI). The HECSI is purely a research tool and is not used in clinical practice and is completely unfamiliar to community dermatologists.

Assessment of treatment response often varies among clinicians and depends on clinical practice wait times, availability of follow up in primary care and patient-specific factors. Many clinicians reassess treatment response in 3-6 months and then every 3-6 months or on an as needed basis. In general, patients with high disease severity, significant QoL impairment, and/or are at heightened risk for adverse events, are reassessed more frequently. An initial assessment of response to delgocitinib at 3-6 months would be reasonable.

References:

1. https://link.springer.com/article/10.1007/s00403-024-02818-3

2. https://www.eczemacouncil.org/assets/docs/Validated-Investigator-Global-Assessment-Scale_vIGA-AD_2017.pdf

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

Reasons to consider discontinuing delgocitinib would be lack of response to treatment or disease progression despite therapy (as discussed above, an initial assessment between 3-6 months would be reasonable), and/or intolerable adverse events or allergies.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

Given the route of administration and safety and tolerability profile of delgocitinib, it would be appropriate to utilize delgocitinib in any setting be it community, hospital, or specialty clinic. We do not feel that a specialist is required to diagnose treat or monitor patient who might receive topical delgocitinib for all the same reasons.

6. Additional Information

The clinician input submitted by our organization includes feedback from delgocitinib clinical trial investigators who have first-hand experience with this topical formulation and have observed the life-changing impact delgocitinib has had on patients. CHE patients in these trials are eagerly awaiting the arrival of delgocitinib as it would be the first new safe and effective therapy developed for CHE in the past decade.

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: Dr. David N. Adam
Position: President, Dermatology Association of Ontario, Dermatologist
Date: <27-10-2024>

☒ **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

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

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

Declaration for Clinician 2

Name: Dr. Mark Lomaga
Position: Dermatologist
Date: <27-10-2024>

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

Table 2: Conflict of Interest Declaration for Clinician 2

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

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

Declaration for Clinician 3

Name: Dr. Jennifer Lipson
Position: Dermatologist
Date: <27-10-2024>

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

Table 3: Conflict of Interest Declaration for Clinician 3

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

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

Declaration for Clinician 4

Name: Dr. Carrie Lynde

Position: Dermatologist
Date: <27-10-2024>

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

Table 4: Conflict of Interest Declaration for Clinician 4

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

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

Declaration for Clinician 5

Name: Dr. Maxwell Sauder
Position: Secretary , Dermatology Association of Ontario, Dermatologist
Date: <29-10-2024>

☒ 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 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
Leo		x		

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

Declaration for Clinician 6

Name: Dr. Carly Kirshen
Position: Dermatologist
Date: <03-11-2024>

☒ 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 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
Leo	x			

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

Declaration for Clinician 7

Name: Dr. Sameh Hanna
Position: Dermatologist
Date: <03-11-2024>

☒ 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 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
Leo	x			

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

Declaration for Clinician 8

Name: Dr. Charles Lynde
Position: Dermatologist
Date: <04-11-2024>

☒ 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 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
Leo			x	

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

Declaration for Clinician 9

Name: Dr. Lyne Giroux
Position: Dermatologist

Date: <05-11-2024>

☒ 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 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**
Leo	x			

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