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

## CDA-AMC REIMBURSEMENT REVIEW

# Patient and Clinician Group Input

**pasireotide (Signifor LAR)**

(Recordati Rare Diseases Canada Inc.)

**Indication:** Signifor LAR (pasireotide for Injectable Suspension) is indicated for the treatment of adult patients with acromegaly for whom surgery is not an option or has not been curative.

**October 15, 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.

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

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CADTH

# CADTH Reimbursement Review
# Patient Input Template

## Patient Input for CADTH Reimbursement Review of Signifor LAR for Treatmet of Acromegaly

Name of Drug: Signifor LAR (
Indication: Acromegaly
Name of Patient Group: Acromegaly Canada and Canadian Organization for Rare Disorders
Author of Submission: Durhane Wong-Rieger

### 1. About Your Patient Group

Acromegaly Canada: Our mission is to raise awareness of acromegaly and gigantism through education while providing a network of support for patients and their families across Canada. We offer resources to help patients and their support networks understand acromegaly and gigantism, learn what treatments are available, and explore how to best manage symptoms. We connect individuals with acromegaly and gigantism to local support groups, so they can socialize, share experiences, and offer guidance specific to their area's health care systems. We raise awareness about acromegaly and gigantism, seeking more timely diagnosis, better quality of life, more integrated care. and a more nuanced, realistic view of the condition. https://acromegalycanada.ca/

Canadian Organization for Rare Disorders: The Canadian Organization for Rare Disorders (CORD) https://www.raredisorders.ca/ is Canada's national network for organizations representing all those with rare disorders. CORD provides a strong common voice to advocate for health policy and a healthcare system that works for those with rare disorders. CORD works with governments, researchers, clinicians and industry to promote research, diagnosis, treatment and services for all rare disorders in Canada.

### 2. Information Gathering

Recruitment: Participants were recruited through two sources, email and Facebook postings by Acromegaly Canada and Acromegaly Community. The latter is a USA-based support network that also includes Canadian members. They were invited to participate in a survey and/or focus group. The online survey asked persons living with acromegaly and/or caregivers to share their experiences about living with acromegaly, access to treatments (including surgery and medications), and the impact of these on their medical condition and quality of life. Participants were directly recruited. The survey was available from late September to mid-October 2024. In addition, one online focus group was held with six participants, three living in Canada and three living in the USA. An additional Canadian participant had to drop out at the last minute because of unexpected serious GI issues that required her to go to hospital. Three of the participants had experience with Signifor LAR and three did not. Two with Signifor LAR experience lived in the USA and one lived in Ottawa, Canada.

There were 26 responses to the survey, 25 were persons living with acromegaly and one was a patient advocate (support group member). All six focus group participants were living acromegaly and had also responded to the survey.

Among the respondents,14 of 26 (54%) provided a state or province of residence. Among these, 64% were Canadians and 36% identified as living in the USA. The Canadians spanned the country, from Northwest Territories, BC, Alberta, and Manitoba to Ontario and Newfoundland. Similarly, the American respondents were widely dispersed, from Alaska, California, and Louisiana to Florida and New Jersey.

Survey respondents were asked to indicate their age category, presented in ten-year intervals. The majority (71%) were between the ages of 50 and 70 years, with 38% between 50 and 59 years old and 33% between 60 and 69 years old. Only 1 person was over 70 years old and 25% were under age of 50, half under 40 years old.

## 3. Disease Experience

Participants were asked about their experience of living with acromegaly, in the survey through (1) open-ended questions asking respondents to describe the experience of patients and caregivers, and (2) ratings along a five-point predefined matrix of symptoms, anchored by “not at all” or “none” to “very much” or “very severe.” Both survey participants and focus group members were also asked to about symptoms or health conditions related to acromegaly, experience with treatments including surgery, drugs directed at managing symptoms of acromegaly and drugs directed at comorbidities, including high blood pressure, high glucose levels, and mental health challenges.

While the survey sample size is too small to conduct meaningful statistical analyses, the demographic breakdown and patient experience of respondents from Canada and the USA are experience. The key difference is the access to drug therapies, with Americans have more options, including the drug under review, Signifor LAR.

In terms of symptoms, the majority (80%) reported severe or very severe enlarged hands and/or feet. Two-thirds (67%) said they had experienced severe or very severe changes in facial features, such as enlarged jaw, brow, nose, or teeth. About 60% had some or moderate joint pains, arthritis, or carpal tunnel syndrome, with only 25% said they did not have these symptoms. Similarly, 60% had experience moderate or severe enlarged organs (liver, kidney, heart) while 40% had little or no such symptoms. In terms of comorbidities, about 50% had moderate or severe diabetes or insulin resistance, and 50% had little or none of these symptoms. Most suffered from respiratory issues (sleep apnea or airway obstruction) with 46% affected severely or very severely and 30% moderately; only 24% had little or no respiratory issues. In terms of high blood pressure, about one-third said this was severe or very severe (34%); one-third said it was moderate (37%); and the remainder (29%) little or not all. Most suffered from excessive sweating, with 42% severe or very severe, 42% moderate, and the remaining 16% little or not at all. Finally, the majority (84%) also experienced mood disorders, with 38% severe or very severe and 42% moderate.

Overall, participant reported significant impact of acromegaly in all aspects of their lives, including the physiological impact, psychological impact and emotional stress and disruption in work, school, family and social life. All participants reported acromegaly as having an “overwhelming” and “devastating” impact on all aspects of their lives, due, in some respects, to the highly visible and often stigmatizing symptoms and the painful and limiting symptoms in bones and joints, fatigue, and lack of energy.

**Qualitative responses from the focus group and survey participants provide insights on the physical toll of this rare disease on patients and families. Patients related the devastating impact of acromegaly, the deformities, comorbidities, and challenges of treating.**

**Physical impact and Diagnostic Challenge:** Patient after patient described the horror of the enlargement of hands and feet and facial features that were always on display. “*It’s a disease that makes monsters out of people.”* In addition, individuals described the pain in joints, bone pain, headaches, tremendous fatigue, arthritis in hips and knees, and organ damage.

*Said one respondent: “My hands and feet started to grow; my jaw started to protrude, my forehead too. But I had no idea what was happening.”*

Another said: *“"Before diagnoses my face / eyelids were huge/ fat. I was ashamed to face anyone else.After diagnoses (end 2023) a lot of other ‘small’ malfunctions / issues over the past 20 years made sense: a ring that I can’t remove, shoes that don’t fit anymore, thick tongue, larger jaw, quervain, etc. I was grateful to finally get a diagnosis of acromegaly!”*

Another person recounted: “*Acromegaly takes a while to be diagnosed. By the time of my diagnosis, I had sleep apnea, increased blood pressure, my hands were falling asleep while driving and sleeping. I also had joint pain and had arthritis that was progressing quickly and affected my mobility.”*

According to another: *“My life has changed greatly as I have arthritis throughout my body. Both hips have been replaced (before the age of 50 years) and both knees are in very bad shape. In the last year I have developed extremely painful 'arms and shoulders'. This has been a huge problem for me. I use a cane to walk (due to knees). I was swimming laps and doing yoga and now am very limited in what I can do in the pool and on the mat.”*

Even with surgery and treatment, individuals are not back to normal life. *"Acro has changed my body. I am now almost always in pain. My stamina is a fraction of what it used to be, I love to garden, and I have to ask for help for so much of it. I've had over a dozen surgeries all due to acro.”*

**Mental health impact:** Not surprisingly, acromegaly is a condition that exacts an equally devasting psychological and mental health toll.

One respondent said simply, *“Clown size nose, forehead, hands, feet."*

Similarly, another said, “I feel that it is a hard disease to explain to other people, so that they understand."

Another young woman described her feelings: *“I haven’t wanted to do things, I can’t fit in cute clothes and shoes, I get tired easy, I sweat all the time, I always feel bad, I don’t want to take pictures, my joints hurt so I don’t want to do things with my kids, I hurt all the time so I miss work. I don’t want to go anywhere because I am ugly. People comment on my big hands and feet and ask if I am a man or trans.”*

For another, it was the mental toll of the condition, the treatments and the impact on her family: “Physically having to deal with pain and inflammation and body changes. Mentally having to deal with the stress of medical Dr visits and keeping your insurance company on your side and pharmacy sending your meds. My family is always in fear of me getting sick.”

**Family and Social Relationships:** The impact on family and social relationships was a repeated theme, with individuals feeling bad about not being able to take part but often the feeling of guilt because of the impact on the family.

One person’s rather wistful statement spoke volumes: *“Harder on hubby now cause I can't ride Harley now. We use to love doing this together.”*

Others commented on missing out on family activities: “*My family worries about me and hate seeing my like this."*

*"Acromegaly has affected every part of mine and my family’s life.”*

**Work and Financial Impact.** Related to the family and social impact is impact on work and consequently finances.

Said one person, ‘“The joint and back pain combined with the mood issues, brain fog, and the inability to multitask, focus, or concentrate prior to apoplexy and subsequent surgery made me unable to work, and post- surgery, only able to work part-time.”

The fear of not working is related to the impact on finances and in some cases insurance coverage: *“I sometimes worry I will not be able to continue working full-time, but need to so I have health insurance to help cover these very expensive medications.”*

Another respondent spoke to the financial impact on herself and family, ““The financial impact is immeasurable at this point. Now that I am no longer in remission and need to apply for Ontario's Trillium drug program, I am being penalized

due to living with my elderly parents and their income must be included in my application. My whole family's suffering financially because of my acromegaly. “

**Treatment (Surgery) and Medication Impact**: For most, the experience of surgery to correct deformities and/or to remove the tumour(s) was not experienced as a success but only partially resolved the issues..

According to one: *“The joint pain prior to having the adenoma resection, limited my ability to exercise adequately. Die to the lower jaw growth, my bite is grossly out of alignment to the extent that I cannot chew food properly. The only remedy is jaw surgery. With the possibility of the tumour reoccurring, the prospect of another surgery is terrifying.”*

This was experience of surgery and medications of one person: “I had two major surgeries to remove the pituitary tumour but still have residue, which is actively producing IGF. I have monthly injections and have side effects.”

For others, medication has been beneficial if not totally effective or stress-free: "I am on a lot of different medications, for replacement hormones,I have to be vigilant about taking them and also carrying them around with me.”

Another reported the importance of the right medical setting, *“Somnovert & Somatuline seem to have effect and looking forward to (scary) operation. I’m in right hospital with kind endo who has the right knowledge.”*

**Impact of Signifor LAR:** The following was the brief statement from one person who had received the treatment being reviewed:

*“Diagnosed Dec of 2014, started Signifor lar in drug trial January of 2015. Drug trial over in July I think and drug company continued to pay for my injections. Shrunk my tumor beautifully and had removed Feb of 2016. After surgery went into full remission on GH and IGF1 while on Signifor felt funky 2 or 3 days after getting injection and 2 or 3 days before getting injection and developed diabetic traits. Was given medication for this but I was able to control my numbers with strict diet. Signifor lar was a wonderful drug that did what it was suppose to for me. My number did not get down as far as they should but that was because nurses who gave shots for 2 months wasted half the shot. After that I gave up and gave them to myself with difficulty but success***.**

## 4. Experiences With Currently Available Treatments

The responses to this question come from the rating scales.

Among all respondents, 88% had received one or more treatment; 12% reported having received no treatments. Participants were presented with a list of treatments for acromegaly and asked to indicate whether they had received these once, more than once, or not at all, with the option of “not sure” included.

Most frequently experienced treatment was surgery, with 71% receiving surgery once and 18% more than once. In terms of medications, most (88%) had received somatostatin antagonists (SSAs), with 12% saying once and 76% more than once. The second most frequently used category of medications was the dopamine agonists, Cabergoline and Bromocriptine, with 24% receiving it once and almost 30% more than once. Only 47% had never been treated with this category of medicines.

About two-thirds (65%) had never been treated with growth hormone receptor antagonist (Somavert), with 6% reporting access once and 30% reporting more than once.

In terms of medications for comorbidities, the most frequently reported was medication for high blood pressure (59%). Slightly less than one-third had received treatment for diabetes or insulin resistance. And the same percentage had received treatment for mood disorders (depression or anxiety). Only 6% reported receiving treatment for sexual dysfunctions. Among survey respondents none were sure of receiving Signifor (pasireotide) immediate release (one was unsure). And 25% (6) had been treated with Signifor LAR. Among those who had received Signifor LAR, one was Canadian and all the others were from the USA.

## 5. Improved Outcomes

The responses to this question come from the rating scales, open-ended comments, and focus group discussion.

EFFECTIVENESS

Participants were asked to rate the effectiveness of each of the treatments experienced, on a three-point scale from “little or not at all” to “much or very much.” The percentages reported do not necessarily add to 100% because some respondents said they were not sure of the effectiveness of that specific treatment.

In terms of surgery, most (59%) rated this as being “some or moderate” in terms of effectiveness, while 29% said “much or very much” and 12% rating is as ineffective. For more than half (52%) of respondents, SSAs were considered as effective or very effective and only 6% said they had little or no effect; 35% considered the impact as moderate. Among those who had received dopamine agonists, the ratings were not as positive, with only 12% rating them as providing “much or very much” in terms of benefits; 35% rating them as moderate; and 29% considered them as having little or no effectiveness. The ratings for Somavert, among those who had received it, were similar with only 18% rating them as effective and 35% considered them to provide little or no benefit.

In terms of treatments for comorbidities (hypertension, high glucose, and/or sexual dysfunction), about one-quarter of participants reported each of these as effective, although 25% to 40% reported they were not effective.

Participants clearly had very diverse experiences with regard to the various treatments for acromegaly. One of the challenges in sorting out the response to a specific treatment is that patients were put on successive treatments and sometimes more than one treatment at a time. Moreover, recall was a factor given the length of time some had been living with the condition. This is not surprising given that most were directed towards reducing symptoms and, other than surgery, not directly treating the cause of the disease. Following are some of the open-ended comments with respect to all their treatments.

*“Surgery after shrinking tumor was successful, 8 yrs later still no sign of tumor and numbers have been good.”*

*“These medications slowed the progression of my acromegaly symptoms. My feet and hand growth slowed. My carpal tunnel syndrome improved with Cabergoline but after surgery, they didn’t fall asleep while driving or when sleeping. After surgery the edma decreased. The Cabergoline didn’t prevent my tongue from swelling but after surgery it did improve. Also after surgery my blood pressure has improved and I’m not needing to nap during the day due to fatigue.”*

*“They have been helpful, but a lot of damage was already done. I had Acro for more than 20 years before being Dx.”*

*“Personally, bromocriptine has not cured joint pain and anxiety. I still have huge hands and legs despite my hormones being in range.”*

*SIDE EFFECTS*

Participants were asked to rate the side effects experienced with each of the treatments, on a three-point scale from “little or not at all” to “much or very much.” The percentages reported do not necessarily add to 100% because some respondents said they were not sure of the side effects or had not received that specific treatment.

In terms of surgery, the responses were mixed, with one-quarter experience severe or very severe side effects, one-third moderate side effects, and slightly less than one-third reporting no side effects.

The responses to statin were similarly varied but less so, with only 12% reporting severe or very severe side effects, about half (53%) reporting moderate side effects and about one-fourth (24%) said they had no or little side effects.

Side effects with dopamine agonists showed similar pattern of responses, as well as Somavert. Among those received the medication, about one-third had little or no side effects; one-third experiencing moderate side effects, and one-fourth to one-third reporting the side effects were severe or very severe.

In contrast, among those receiving Signifor LAR, 40% reported no or little side effects and 60% said these were moderate; none reported severe side effects.

Comments provided by the respondents illustrate the varied nature of the population and response to treatment. Some also reacted to the treatment schedules, namely frequency of daily or weekly shots, the need to go to hospital for administration, storage, and cost.

*"One made me feel sick and did nothing (cabergoline/bromocriptine). The others would help to bring my IGF-1 down, but not within range, and after a few months it would start to creep up, necessitating an increase in dose."*

*"For the monthly intramuscular injections, it can sometimes be painful either during the injection or in the day or two after it. It also seems to wear off in the week or so leading up to the next dose. Having to schedule the injection can be a hassle, and makes travel difficult."*

*"For the daily subcutaneous injections, they can sometimes be painful, and sometimes I hit a vein and cause a lot of bleeding. I typically have bruises on the four injection areas (lower abdomen and upper thighs)...not from every injection, but they take time to fade, so I end up with a new one before the old ones fade. It's also a hassle to do everyday, and travelling with the medication is a burden. There's also the worry about keeping it at the optimal temperature."*

*"Cabergoline is an oral medication which makes it easier to take. But, it did not reduce my Igf- 1 to a normal range. Even though it decreased my Igf-1 the changes that occurred from acromegaly did not become less until after surgery when my growth hormone finally fell into normal range."*

*"Limitations of treatments are that injectable medications usually need to be refrigerated. Some need a nurse to inject them. For most of these medications, especially injectable, is the cost. Most people would not be able to afford them without assistance. Financial assistance requires notes from doctors or forms to be filled out. The stress of not knowing if the costs will be covered is anxiety provoking. Or, families may pay for it but it means making trade offs.*

*"I had to do 6 shots a day of octreotide. It was not convenient. It was hard to take treatments at work."*

*"They are expensive, administration is a hassle either navigating a nurse to inject you and/or injecting yourself. Painful injection sites. Difficulty getting medications as they need to be refrigerated. Difficulty traveling with needles and medication needing refrigeration."*

## 6. Experience With Drug Under Review

Six participants had experience with Signifor LAR. Among the five reported their city and country of residence, four lived in the USA and one in Canada. All those in the USA had been prescribed the treatment and had coverage through their insurance carrier. The Canadian patient had access through private insurer (husband's policy). Patients were mostly very satisfied with the drug and rated it very positively relative to all other treatments, although one had no experience with any other medication.

All except one of the recipients had had surgery. Among medications received, most (5) had experience with SSAs, two with dopamine agonists, three with Somavert, In terms of treatments other than Signifor, most rated them as ineffective or moderately effective, In terms of side effects to other medications, their responses were similar to those for the entire sample. All rated Signifor LAR as effective or very effective in reducing and/or managing symptoms.

*"Signifor LAR very quickly lowered my IGF-1 to well within the target range, after years of being on other, less-effective mediations and continually having to increase my dose. I am very relieved to finally be on something that works."*

Most reported little or manageable side effects.

*"Diabetic condition controlled with diet and numbers were above normal but not so high that I wanted to take medication since I was only going to be on Signifor lar long enough to shrink tumor. 13 months was all."*

*"I have tolerated Signifor LAR well. I occasionally have a few gastro issues or feel tired the day after my injection, but these are very mild. I know there are concerns re: blood sugar, but I've not experienced these to any significant degree. The benefits for me have far outweighed the side effects/risks."*

*"If the shot is not located perfectly it's very painful and the raised injection sight rubbing on pants or skirts"*

*"I sometimes do get loose stools and slight upset stomach. I tend to not make appts or plans a day or 2 after the shot."*

*"My body seems to have gotten used to it, so it's not to bad."*

*"Little side effects for me such as pain at injection site and GI discomfort for about a day after the injection. In others it can cause hyperglycemia leading to type 2 diabetes."*

## 7. Companion Diagnostic Test

NA

## 8. Anything Else?

When asked to consider the benefits to risks and their recommendations for access, all were highly supportive of Signifor LAR being an option for all patients with acromegaly.

“It is a very effective drug and anyone that needs it should have it available to them. Not 2nd or 3rd choices. We all deserve the best treatment.”

“This is a much more effective medication. Without it, patients will continue to suffer from acromegaly symptoms and the ongoing effects of high IGF-1 will cause future issues. Not having it available will place an additional burden on the patients, their loved ones, and the healthcare system as a whole.”

“It has really helped manage good number with little negative interaction “

“Signifor has helped me in ways that Sandostatin and Somatuline did not. My numbers are better and I feel better.”

“I think Canadian patients should have that option.”

## Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

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

   No

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

   Acromegaly Community in the USA helped to recruit and distribute the survey and to recruit for participants for the focus group.

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 For Acromegaly Canada

**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 |
|---|---|---|---|---|
| <Pizer and Acromegaly Canada – Conferences: 2022, 2023, 2024 | | | | x |
| Novartis and Acromegaly Canada -Acromegaly Canada Conference: 2022, 2023 | | | x | |

| | | | | |
|---|---|---|---|---|
| Ispen and Acromegaly Canada- Acromegaly Canada Conference: 2022, 2023, 2024 | | | | x |
| Crjnetics and Acromegaly Canada- Acromegaly Canada Conference: 2022, 2023, 2024 | | | x | |
| Recordati and Acromegaly Canada – Acromegaly Canada Conference: 2022,2023. | | | x | |
| Chiesi and Acromegaly Canada – Acromegaly Canada Conference: 2024 | | x | | |
| Pfizer and Acromegaly Canada – Acrhomegaly Web Platform | | | x | |
| Ispen and Acromegaly Canada – Acrhomegaly Web Paltform | | x | | |
| Pfizer and Deanna Badiuk – Patient Engagement Sessions: 2022, 2023 | 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: <Deanna BadiukEnter Name and details below>**
**Position: President**
**Patient Group: Acromegaly Canada**
**Date**: October 11th 2024

## Table 1: Financial Disclosures For Canadian Organization for Rare Disorders

| Company | $0 to 5,000 | $5,001 to 10,000 | $10,001 to 50,000 | In Excess of $50,000 |
|---|---|---|---|---|
| Pfizer Canda | | | x | |
| Ipsen Canada | | | X | |

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

**Name: Durhane Wong-Rieger**
**Position: President & CEO**
**Patient Group:Canadian Organization for Rare Disorders**
**Date**:15 October 2024

CADTH

# CADTH Reimbursement Review

## Clinician Group Input

CADTH Project Number: < SR0859-000>
Generic Drug Name (Brand Name): Pasireotide (SIGNIFOR LAR)
Indication: For the treatment of patients with acromegaly
Name of Clinician Group: Canadian Society for Endocrinology and Metabolism
Author of Submission: Dr. Constance Chik, MD, PhD, FRCPC

### 1. About Your Clinician Group

The Canadian Society of Endocrinology and Metabolism (CSEM) is a professional organization bringing together academic and community-based endocrinologists and researchers engaged in providing health care, education and research within the broad domain of endocrinology. The CSEM is a national advocate for excellence in endocrinology research, education, and patient care, and its mandate is to advance the discipline of endocrinology and metabolism in Canada. Website: https://www.endo-metab.ca/

We are responding to this call for clinician input as medical experts in support of pasireotide for the treatment of patients with acromegaly when surgery is not an option or has not been curative, and have had a suboptimal response to first generation somatostatin analogs (SSAs). As lead, I will present this information on behalf of the group. I am a Professor Emeritus of Medicine, Division of Endocrinology and Metabolism, University of Alberta. I have a clinical practice with a focus in pituitary disorders and have ongoing research in neuroendocrinology. I was a founding member the Alberta Pituitary Patient Society, a patient support group.

The group of clinicians being represented includes several leading experts specialized in the treatment of patients with acromegaly from across Canada.

### 2. Information Gathering

An initial draft was first developed based on a discussion with a handful of the membership. The broader membership group were asked to review the initial draft of the clinician input response. That collective input was then shared amongst the group members and a final document was developed based on the clinician group's collective input. Any disagreements or regional specific issues were maintained in the document to provide CADTH/CDA-AMC with a full sense of how this treatment is anticipated to impact clinical practice across the provinces that are being represented by the clinician group.

### 3. Current Treatments and Treatment Goals

Acromegaly is a rare, life-long endocrine disease characterized by excessive growth hormone (GH) secretion.[1,2] This overproduction of GH leads to an induction of insulin-like growth factor-1 (IGF-1) production, that then is linked to inhibition of apoptosis and stimulation of cell proliferation.[3] In the vast majority of cases, this excessive production of GH

is linked to a benign tumor of the pituitary gland (i.e., pituitary neuroendocrine tumor, also known as pituitary adenoma).[2-5]

Having chronic high levels of GH and IGF-1, as well as the presence of the pituitary tumor itself, lead to structural and functional abnormalities as well the development of secondary systemic illnesses and significant comorbidities including metabolic, endocrine, cardiovascular, respiratory and neoplastic complications. [3-5] A plethora of data is available that have demonstrated mortality is increased in patients with acromegaly compared to the general population.[6-19]. The life expectancy of sub-optimally managed patients with acromegaly has been reported to be reduced by nearly 10 years compared to the general population.[20] The primary causes of death in patients with acromegaly are cardiovascular diseases and cancer.[9,21,22]

Clinical consensus states that normalization of both GH and IGF-1 serum levels is the primary goal of acromegaly treatment.[23] Additional therapeutic aims include control of the growth and size of the pituitary tumor as well as prevention and management of acromegaly-associated symptoms and comorbidities.[23]

The available treatments recommended for patients with acromegaly include surgery (tumor resection), medical pharmacotherapy, and radiotherapy.[23]

Surgery - Tumor resection by surgery is the recommended first-line treatment approach for patients with acromegaly.[23] It is reported that 54% to 80% of patients diagnosed with acromegaly receive surgery as primary treatment, indicating that a substantial proportion of acromegaly patients are either ineligible for or not willing to undergo surgery.[10,24-26]

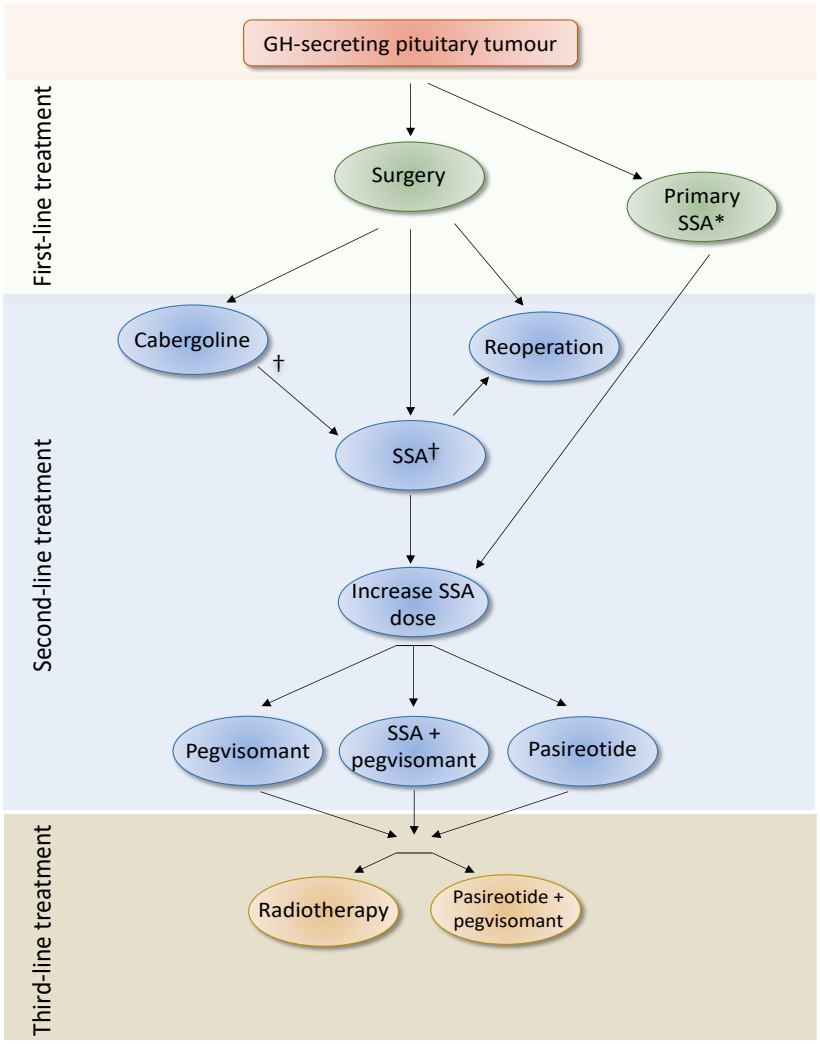
Medical Therapy - Medical therapy is recommended for the long-term treatment of acromegaly following inadequate response to surgery or in cases where surgery is not an appropriate treatment option.[23,27] First-generation SSAs, octreotide and lanreotide, are the mainstay of 1$^{st}$-line medical management. Both octreotide and lanreotide are SSAs that reduce levels of GH and IGF-1 by inhibiting GH, glucagon and insulin.[23,28-31] Both are widely funded and have been the cornerstone of acromegaly pharmacotherapy for the past 15 years. However, not all patients respond to treatment with first-generation SSAs. Specifically, patients presenting with sparsely granulated tumors tend to have a lower probability of achieving biochemical response with first-generation SSAs.[32]

Pegvisomant is a second-line medical therapy for patients with acromegaly who are uncontrolled on first-generation SSAs, but has limited funding across Canada.[33] Pegvisomant is a GH receptor antagonist that binds to GH receptors, thereby preventing interaction of receptors with natural GH.[34,35] This leads to inhibition of GH signaling and results in decreased serum concentrations of IGF-1.[34,35]

Radiotherapy - Radiotherapy is reserved only for patients that have declined, failed or are unfit for surgical and/or medical treatments.

A summary of the recommended treatment algorithm for patients with acromegaly is provided below.[23]

Figure 1. Algorithm for the management of acromegaly




* Only if curative surgery is not an option

†Combination SSA and cabergoline may also be considered in patients with co-prolactin-secreting tumors or in patients with mildly to moderately elevated IGF-I levels.

SSA = somatostatin analog

**Source**: Adapted from Giustina et al. 2020[23]

**Alt Text :** Treatment algorithm for patients with acromegaly. Illustrates which medical therapies would be considered by line of therapy.

## 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.

Biochemical control (normalization of both GH and IGF-1 levels), is the primary treatment objective for patients with acromegaly.[23] However, a significant proportion of patients are not achieving control with current therapeutic options. A proportion of acromegaly patients are either ineligible for or not willing to undergo surgery.[10,24-26] It is well reported that over 40% of patients treated with first-generation SSAs do not achieve full biochemical control.[36-38] Pegvisomant has limited funding, thus, many patients across Canada will not have access to therapy. Moreover, pegvisomant is a GH receptor antagonist and is therefore effective at controlling IGF-1 but not GH.[34,35] Evidence suggests normalization of IGF-1 alone may not be sufficient to reduce the mortality, humanistic and economic burden associated with acromegaly, highlighting the importance of both GH and IGF-1 control in acromegaly treatment.[39-42] In terms of tumor volume, pegvisomant has not demonstrated to be able effectively impact tumor volume. In addition, pegvisomant is administered daily by subcutaneous self-injections, which can lead to injection site reactions, adherence issues and suboptimal treatment effectiveness.[34,35,43,44] Lastly, radiotherapy which carries important safety risks, impairs quality of life (QoL), is associated with greater pain and discomfort and more severe anxiety and depression.[23,41,45,46]

Therefore, there is an unmet need for alternative treatment options that provide full biochemical control, reduce tumor volume and disease symptoms and improve QoL in patients who are uncontrolled on first-generation SSAs, while also providing for a reduction in treatment burden.

## 5. Place in Therapy

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

Pasireotide is a second generation, injectable SSA. Like the natural peptide hormones somatostatin-14 and somatostatin-28 [also known as somatotropin release inhibiting factor (SRIF)], pasireotide exerts its pharmacological activity via binding to somatostatin receptors (SSTRs). As a second generation SSA, pasireotide has been demonstrated to be more efficacious than continued SSA in patients with acromegaly inadequately controlled on maximum doses of octreotide LAR or lanreotide ATG.[47] Pasireotide has demonstrated both significant improvements in biochemical control as well as a meaningful reduction in tumor volume.[47] These improvements were maintained for over 5 years after initial treatment.[48] Pasireotide also has demonstrated the ability to improve patients' QoL.[49] As a result, pasireotide is expected to provide a treatment option in the setting post-first generation SSA that can improve both the signs and symptoms of acromegaly.

As per the current treatment algorithm, (Figure 1) pasireotide is expected to be used when surgery and medical management with first generation SSA fails to provide biochemical control. The only other available treatment options in this setting are either continued use of sub-optimal 1st generation SSAs or pegvisomant, which is not funded in all provinces, does not control GH levels and is not effective at preventing tumor growth, while also requiring daily SC

administration. Off-label use of combination SSA and cabergoline may also be considered in patients with co-prolactin-secreting tumors or in patients with mildly to moderately elevated IGF-I levels.

It is anticipated that pasireotide would not be used in combination with ineffective 1st generation SSA or pegvisomant, but instead be used in replacement of ineffective 1st generation SSA (in jurisdiction that do not fund pegvisomant) or in replacement of pegvisomant for patients that do have access to funding.

### 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?

Sub-groups

The treatment under review would be considered: 1) for whom surgery is not an option or has not been curative, and 2) who are inadequately controlled on treatment with another SSA. The available evidence has demonstrated that pasireotide is more efficacious than continued SSA in patients with acromegaly inadequately controlled on maximum doses of octreotide or lanreotide. Pasireotide provides improved biochemical control (GH and IGF-1), improved tumor control, and improved QoL, while also reducing treatment burden relative to daily SC injections of pegvisomant.

There are no specific patient sub-groups of interest. All patients with a sub-optimal response to a first generation SSA are expected to be candidates for pasireotide, with the exception of patients who have uncontrolled diabetes. As per the pasireotide product monograph, pasireotide is contraindicated in patients "with uncontrolled diabetes (≥8% HbA1c while receiving anti-diabetic therapy)".[50] For patients with uncontrolled hyperglycemia, treatment with pasireotide will be deferred until there is acceptable glycemic control.

Diagnosis

There are no perceived issues with diagnosing the condition. The Endocrine Society (2014) and Pituitary Society (2021) have published globally accepted guidelines on the diagnostic criteria for acromegaly in clinical practice, recommending[27,51]:

- Typical acromegaly symptoms (acral and facial features)
- More than one acromegaly-associated condition, such as carpal tunnel syndrome, debilitating arthritis, hyperhidrosis, hypertension, sleep apnea syndrome, type 2 diabetes mellitus
- A pituitary mass

- Measurement of IGF-1 using a well-validated assay with age- and sex-specific reference ranges.
- Measurement of GH after an oral glucose tolerance test (OGTT) to confirm acromegaly diagnosis in patients with elevated or ambiguous serum IGF-1 levels
- Magnetic resonance imagining (MRI), or computed tomography when MRI is not available or contraindicated, to visualise tumor size, appearance and parasellar extent in patients with a biochemically confirmed acromegaly diagnosis
- Visual field testing in patients with tumors in close proximity to the optic chiasm

Based on the established set of criteria, there is little concern with misdiagnosis in clinical practice.

### 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?

The primary treatment objective for patients with acromegaly is biochemical control (i.e., normalization of both GH and IGF-1 levels).[23] Additional treatment goals include prevention and management of symptoms and comorbidities, and tumor growth control and size reduction.[23] Patients who do not achieve biochemical control experience a greater frequency of symptoms ($p<0.001$) and comorbidities ($p<0.05$) compared to biochemically controlled patients.[24] The definition of biochemical control in acromegaly has evolved, reflecting the more sensitive assays available and better understanding of the pathophysiology of the disease. The American Association of Clinical Endocrinologists guidelines published in 2011 originally recommended a cut-off level of random GH <2 µg/L and age normalised IGF-1 <ULN as the threshold for remission.[52] However, updated and stricter criteria (random GH <1 µg/L and age normalised IGF-1 <ULN) have since been recommended by the Pituitary Society, the Acromegaly Consensus Group and the Endocrine Society.[23,27,51]

A meta-analysis of studies published between 1965 and 2008 reporting on the mortality of patients with acromegaly found that insufficient biochemical control was associated with an increased risk of mortality.[53]

Tumor growth control, tumor size reduction and prevention and control of acromegaly-associated symptoms and comorbidities may also be used to assess treatment effectiveness alongside biochemical control.[23] While there is no consensus threshold for clinically meaningful change in tumor volume, clinical studies generally define significant tumor shrinkage as a 10% to 25% reduction in tumor volume or diameter.[54]

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

Patients should continue to receive treatment until they fail to achieve a clinical benefit from therapy or are unable to tolerate treatment. If patients discontinue treatment due to uncontrolled hyperglycemia, despite appropriate medical management, fasting plasma glucose and hemoglobin A1c should be monitored. Patients on anti-diabetic therapy may require more frequent blood glucose monitoring and anti-diabetic drug therapy dose adjustment to mitigate the risk of hypoglycemia.[50]

### 5.5 What settings are appropriate for treatment with Pasireotide (SIGNIFOR LAR)? Is a specialist required to diagnose, treat, and monitor patients who might receive Pasireotide (SIGNIFOR LAR)?

Patients are anticipated to be treated in the community, via a multidisciplinary team with experience in the treatment of patients with acromegaly, including an experienced endocrinologist who will monitor for any adverse events in particular hyperglycemia.

Given medical treatment regimens are already available, there is no anticipated change in treatment settings, however, a highly effective treatment may reduce treatment burden associated with additional specialist visits, and/or monitoring requirements attributed to less effective therapies.

## 6. Additional Information

Dr. Connie Chik – case example

A 29-year-old woman with acromegaly diagnosed 3 years earlier. She had increased headaches, increased perspirations, increased skin tags and an increase in her shoes size from 10.5 to 12. Acromegaly was confirmed based on an elevated IGF-1 to three times the upper reference range and hemoglobin A1c was normal. MRI showed a 2.4 cm macroadenoma. She underwent transsphenoidal resection of the adenoma and pathology showed a sparsely granulated somatotroph adenoma. With persistent elevation of IGF-1 at twice normal after surgery, she had trials of 1st generation SSA and dopamine agonists and there was no improvement of her IGF-1. MRI showed no lesion amenable to addition surgery. She then was placed on pegvisomant and at a dose of 15 mg daily, IGF-1 was near normal; however the patient had to stop treatment because of profound fatigue. IGF-1 was not controlled on a combination of SSA and cabergoline. Given her limited treatment options, she will benefit from a trial of pasireotide LAR if the medication is covered.

Dr. Juan Rivera – Case example

A 41-year-old man was referred to endocrinologist by his dermatologist because of progressive deepening of his voice along with an increase in shoe size from 12 to 13. His dermatologist had been removing multiple skin tags and 2 dermoid cysts over 8 years. The diagnosis of acromegaly was confirmed based on classical clinical features and a IGF-1 at 3.5 times the upper reference range (URR). He had 2 5mm adenomas on MRI of the pituitary gland and underwent transsphenoidal surgery with pathology confirming a pit-1 tumor. Unfortunately, his disease remains active despite the absence of visible residual pituitary lesion (IGF-1 now 2.5-3X URR). Treatment with octreotide at maximum dose for 2 years, alone and in combination with cabergoline, failed to normalize his IGF-1 which was at best 1.7-2X URR, and was associated with severe fatigue and other acromegaly symptoms. He was switched to pegvisomant which, at maximum dose of 30mg daily, brought his IGF-1 down to ~ 1.5X URR. However, he remains symptomatic with diaphoresis and fatigue. Given his limited treatment options at this point, he will benefit from a trial of Pasireotide LAR if the medication is covered.

Dr. Ali Imran – Case example

A 34-year-old male was admitted under cardiology for congestive heart failure and was identified as having clinical features of acromegaly. Subsequent investigations confirmed autonomous GH producing pituitary adenoma measuring 1.6 cm pituitary tumor with partial cavernous extension that was successfully removed during trans-sphenoidal surgery with no obvious residual tumor. Initial post-surgery IGF-1 was within normal range but 12 months later IGF-1 started rising with abnormal OGTT. Based on the initial pathology, patient was given Lanreotide q 4 weekly which he was unable to tolerate so the dose was decreased and Cabergoline therapy was added without any biochemical improvement. He was then switched over to Pegvisomant which led to rising liver enzymes causing to stop the medication. There was no surgical or radiation therapy target and given the patients normal glucose, he would benefit from Pasireotide.

Dr. Heather Lochnan - Case Example

A 42-year-old male followed for acromegaly, has had numerous complications, mostly orthopedic and suffers from chronic pain as well as dealing with infertility and pan-hypopituitarism after having multiple surgeries for residual/recurrent GH secreting adenoma. He has been unable to achieve control of his IGF-1 with levels consistently elevated despite high dose octreotide, pegvisomant, and cabergoline. Coverage and access to these medications is an ongoing challenge, accessed via Trillium and compassionate use in Ontario. Clearly would benefit from access to and likely longterm treatment with pasireotide.

Dr. Jessica MacKenzie-Feder - Case Examples A and B:

Case A:

52 M presented with diplopia and headache found to have 4.3 cm pituitary mass and IGF-1 959 ug/L (65-200). After transsphenoidal surgery, pathology was consistent with sparsely granulated somatotroph adenoma. Postoperative IGF-1 remained elevated and he started octreotide LAR but IGF-1 remained 2-3.5X upper limit of normal. Addition of cabergoline was ineffective. When it became available, pegvisomant replaced his previous therapy but he experienced an adverse event with significant liver enzyme elevation and it was permanently discontinued. He then completed stereotactic radiotherapy. Because his IGF-1 was persistently elevated, while waiting for radiotherapy to take effect, he started pasireotide LAR 40 mg monthly through exceptional funding through the provincial cancer agency. His IGF-1 fell quickly from 510 to 332 and further to 270 ug/L (55-190) after dose titration to 60 mg monthly. For the first time his IGF-1 was less than 1.5X upper limit of normal. He has benefitted symptomatically with less swelling, sweating and fatigue, allowing him to continue to pursue his career as a firefighter. The rapidity of GH/IGF-1 lowering after the change to pasireotide LAR supports the effectiveness of this medication (vs effect of radiotherapy over this time course).

Case B:

31 M presented in 1991 with headache, confusion, hydrocephalus requiring urgent craniotomy for resection of pituitary macroadenoma. He underwent second craniotomy and then radiotherapy. Tumor pathology confirmed aggressive growth hormone-producing pituitary tumor. Over three decades, his IGF-1 remained elevated accompanied by symptoms of sweating, joint pain, fatigue, weight gain, skin tags, obstructive sleep apnea despite treatment with octreotide LAR at the highest dose. Dopamine agonist therapy was added and, when it became available, pegvisomant was added. Although his IGF-1 initially normalized after addition of pegvisomant, he lost biochemical control after 1 year despite excellent compliance. IGF-1 again rose to 411 ug/L (ULN 190). He started pasireotide LAR 40 mg and quickly his IGF-1 fell to 148 ug/L (ULN190) with rapid improvement of symptoms including improved exercise tolerance, weight loss, and reduced swelling. Biochemical control has now lasted two years and pegvisomant is being carefully reduced with the aim of discontinuing it as he has had excellent response to the starting dose of pasireotide LAR.

For Case A and B: Both of these patients have been able to continue their medication through funding from the BC Cancer Agency; however, no new patients are able to access coverage through this mechanism. There is a need for other sources of funding at this time.

Dr. Fabienne Langlois Case Example

A 24 yo male presented in 2020 with a 4,0cm pituitary adenoma with optic chiasm compression and bitemporal hemianopsia. He reported symptoms of headaches, diffuse pain in the joints and lumbar spine, carpal tunnel syndrome and increased perspiration. He underwent a first partial debulking surgery in November 2020. Initial IGF-1 was 857 ug/L (ULN 255) and 622 post operatively. He was initiated on Octreotide LAR with dose uptitration up to 40mg q 4 weeks and combination with cabergoline over the following months and IGF-1 persisted elevated at 392 (ULN 245) with refractory pain and functional limitations. He underwent a second surgery in Oct 2021 with persistently elevated IGF-1 3 months post operatively. Pasireotide 40mg was initiated in February 2022 with rapid relieve in joint and lumbar pain and decreased in headaches. The IGF-1 levels were persistently normalized and decreased progressively up to 161ug/L (ULN 245) in February 2024, he is now doing well and went back to work. The suprasellar and right cavernous sinus residual tumors are also progressively decreasing from 10x22x19 to 6x19x10mm and from 12x14x9mm to 9x12x5mm between Feb 2022 and July 2023.

Dr. Michelle Johnson Case Example

56-year-old woman who had surgery for acromegaly in 2013. Surgery was very helpful, but she has some residual tumor that is in location where complete resection not possible. Therefore, she has been managed on 1$^{st}$ generation SSA. However, despite maximum dose of Lanreotide, tried in combination with Cabergoline, IGF-1 remains 1.5-2.0 times above upper limit of normal range.

She has fatigue, headache, joint pain, all affecting QOL. We have tried adding Pegvisomant but failed to normalize IGF-1. Furthermore, she is experiencing medication fatigue and finding it difficult to continue with daily Pegvisomant injections. She is an ideal candidate for Pasireotide, allowing her to switch from three medications to one with a simple regime of once per month injection. Pasireotide's simple regime and ability to normalize IGF-1 will improve her QOL.

## 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.

   <The initial draft was completed in collaboration with a medical writer, Colin Vincente, Pivina Consulting Inc.>

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.

   < The information used in this submission was collected and analyzed in collaboration with a medical writer, Colin Vincente, Pivina Consulting Inc >

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:** <Constance Chik>
**Position:** <Physician, University of Alberta Hospital>
**Date:** <04-09-2024>

☒ **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** |
| Pfizer Canada | | | | X |

| | | | | |
|---|---|---|---|---|
| Recordati Rare Diseases Canada | | | x | |
| Ipsen Canada | x | | | |
| Novo Nordisk Canada | x | | | |
| Canada's Drug Agency | | | x | |

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

## Declaration for Clinician 2

Name: <Ally Prebtani>
Position: <Physician, McMaster University>
Date: <05-09-2024>

☒ 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**

| | Check appropriate dollar range* | | | |
|---|---|---|---|---|
| **Company** | **$0 to $5,000** | **$5,001 to $10,000** | **$10,001 to $50,000** | **In excess of $50,000** |
| Ipsen | | x | | |
| Novo Nordisk | x | | | |
| Recordati | x | | | |
| Eli Lilly | x | | | |

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

## Declaration for Clinician 3

Name: Juan Rivera, MD
Position: Associate Professor, McGill University Health Center
Date: 06-09-2024

☒ 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**

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

| | | | | |
|---|---|---|---|---|
| Ipsen Canada | x | | | |

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

## Declaration for Clinician 4

Name: Brandon Galm
Position: Clinical Assistant Professor, University of British Columbia
Date: Sep 8 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**

| | Check appropriate dollar range* | | | |
|---|---|---|---|---|
| **Company** | **$0 to $5,000** | **$5,001 to $10,000** | **$10,001 to $50,000** | **In excess of $50,000** |
| Abbott | | | x | |
| Amgen | x | | | |
| Boehringer Ingelheim | x | | | |
| Dexcom | x | | | |
| Novo Nordisk | x | | | |
| Pfizer | x | | | |

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

## Declaration for Clinician 5

Name: <André Lacroix, MD, CAHS>
Position: <Professor of medicine, Endocrine Division, Université de Montréal>
Date: <08-09-2024>

☒ 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** |
| Pfizer Canada | | | x | |

| | | | | |
|---|---|---|---|---|
| Recordati Rare Disease, Canada | | | | x |

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

## Declaration for Clinician 6

Name: <S. Ali Imran >
Position: <Professor of Medicine, Endocrinology, Dalhousie University >
Date: <09-09-2024 >

☒ 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 6: 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** |
| Ipsen | X | | | |
| Ricordati | X | | | |

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

## Declaration for Clinician 7

Name: <Heather Lochnan MD >
Position: <Professor of Medicine , Head Division of Endocrinology and Metabolism, The Ottawa Hospital >
Date: <09/09 /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 7: 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** |
| Ipsen | X | | | |
| Viatris | X | | | |
| Pfizer | | | x | |

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

## Declaration for Clinician 8

Name: <Kirstie Lithgow MD >
Position: <Assistant Clinical Professor, Endocrinology and Metabolism, Cumming School of Medicine University of Calgary >
Date: <09/09 /2024

**Table 8: Conflict of Interest Declaration for Clinician 8**

| | Check appropriate dollar range* | | | |
|---|---|---|---|---|
| **Company** | **$0 to $5,000** | **$5,001 to $10,000** | **$10,001 to $50,000** | **In excess of $50,000** |
| Novo Nordisk | x | | | |

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

## Declaration for Clinician 9

Name: <Jessica MacKenzie-Feder MDCM >
Position: <Assistant Clinical Professor, Endocrinology and Metabolism, University of British Columbia>
Date: <09/10 /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 9: Conflict of Interest Declaration for Clinician 9**

| | Check appropriate dollar range* | | | |
|---|---|---|---|---|
| **Company** | **$0 to $5,000** | **$5,001 to $10,000** | **$10,001 to $50,000** | **In excess of $50,000** |
| Pfizer Canada | x | | | |
| Recordati Rare Disease, Canada | x | | | |

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

## Declaration for Clinician 10

Name: < Fabienne Langlois, MD >
Position: <Associate Professor, Endocrinology and Metabolism, University of Sherbrooke >
Date: < 09/12/2024 >

☒ 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 10: Conflict of Interest Declaration for Clinician 10**

| | Check appropriate dollar range* | | | |
|---|---|---|---|---|
| **Company** | **$0 to $5,000** | **$5,001 to $10,000** | **$10,001 to $50,000** | **In excess of $50,000** |
| Ipsen Canada | x | | | |
| Recordati Rare Disease, Canada | x | | | |
| NovoNordisk USA | x | | | |

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

## Declaration for Clinician 11

Name: < Ghislaine Houde MD >
Position: < Professor of medicine, Endocrinology and Metabolism, University of Sherbrooke >
Date: < 09/16/2024 >

☒ 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 11: Conflict of Interest Declaration for Clinician 11**

| | Check appropriate dollar range* | | | |
|---|---|---|---|---|
| **Company** | **$0 to $5,000** | **$5,001 to $10,000** | **$10,001 to $50,000** | **In excess of $50,000** |
| No conflicts of interest | | | | |

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

## Declaration for Clinician 12

**Name:** Michelle Johnson
**Position:** Clinical Associate Professor, University of British Columbia
**Date:** Sept 16, 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 12: Conflict of Interest Declaration for Clinician 12**

| | Check appropriate dollar range* | | | |
|---|---|---|---|---|
| **Company** | **$0 to $5,000** | **$5,001 to $10,000** | **$10,001 to $50,000** | **In excess of $50,000** |
| Pfizer Canada | X | | | |
| Recordati Canada | X | | | |
| Ipsen Canada | X | | | |
| Novo Nordisk Canada | X | | | |

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

## Declaration for Clinician 13

Name: < Jonathan Poirier MD >
Position: < Associated Professor of medicine, Endocrine Division, Université de Montréal >
Date: < 09/16/2024 >

☒ 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 13: Conflict of Interest Declaration for Clinician 13**

| | Check appropriate dollar range* | | | |
|---|---|---|---|---|
| **Company** | **$0 to $5,000** | **$5,001 to $10,000** | **$10,001 to $50,000** | **In excess of $50,000** |
| No conflicts of interest | | | | |

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

## Declaration for Clinician 14

Name: < Matthieu St-Jean MD >
Position: < Professor of medicine, Endocrinology and Metabolism, University of Sherbrooke >
Date: < 09/16/2024 >

☒ 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 14: Conflict of Interest Declaration for Clinician 14**

| | Check appropriate dollar range* | | | |
|---|---|---|---|---|
| **Company** | **$0 to $5,000** | **$5,001 to $10,000** | **$10,001 to $50,000** | **In excess of $50,000** |
| Recordati rare Disease | x | | | |
| GSK | | | x | |
| HRA | x | | | |

## Declaration for Clinician 15

Name: < Marie-Eve Domingue MD MSc >
Position: < Clinical Professor of Medicine, Endocrine Division, Medecine Department, Université Laval >
Date: < 09/17/2024 >

☒ 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 15: Conflict of Interest Declaration for Clinician 15**

| | Check appropriate dollar range* | | | |
|---|---|---|---|---|
| **Company** | **$0 to $5,000** | **$5,001 to $10,000** | **$10,001 to $50,000** | **In excess of $50,000** |
| No conflicts of interest | | | | |

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

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