Canada's Drug Agency
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CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

Risankizumab (Skyrizi)

AbbVie Corporation

Indication: For the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, loss of response, or were intolerant to conventional therapy, a biologic treatment, or a Janus kinase (JAK) inhibitor.

April 11, 2025

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

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

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Patient Group Input

Patient Input Template

Name of the Drug and Indication	**Risankizumab (Skyrizi®)**
Name of the Patient Group	**Gastrointestinal Society**
Author of the Submission	**Jaymee Maaghop**

1. About Your Patient Group

The GI (Gastrointestinal) Society is committed to improving the lives of people with GI and liver conditions, supporting research, advocating for appropriate patient access to healthcare, and promoting gastrointestinal and liver health.

We are a national charity formed in 2008 on the groundwork of its partner organization, the Canadian Society of Intestinal Research (CSIR), which was founded in Vancouver in 1976. We receive national and international attention, simply because we have earned the respect of both the gastrointestinal medical community and Canadians who battle GI and liver issues daily. Our website, available in English and French, received 9,329,479 pageviews in 2023 and 8,890,977 in 2024.

All our programs and services focus on providing Canadians with trusted, commercial-free, medically-sound information on gut (including obesity) and liver diseases and disorders in both official languages. Our BadGut® lectures, quarterly *Inside Tract*® newsletter, pamphlets, support groups, and educational videos arm Canadians with the information they require to better understand and manage their specific needs. We also work closely with healthcare professionals and governments at all levels toward system-wide improvements in care and treatment.

2. Information Gathering

The information we used to complete this submission was obtained primarily through questionnaires and interviews:

1. One-to-one conversation with a patient who is living with ulcerative colitis and is receiving the medication under review, risankizumab (Skyrizi®).
2. 2025 roundtable with a dozen experts, including gastroenterologists and patients/patient groups across Canada, on revising the pan-Canadian IBD Criteria for Advanced Therapy. The report will be available soon.
3. 2024 survey about the unmet needs of individuals living with IBD, with 514 respondents from Canada, available at https://badgut.org/2024-ibd-survey-results/. We then conducted a follow-up survey focusing on opinions regarding biologics and biosimilars. This survey received 55 respondents.
4. 2023 interviews with seven individuals living with IBD, in both English and French, available on our website at https://badgut.org/ibd-patient-interviews/
5. 2022 survey about the IBD patient journey with 54 Canadian respondents with IBD

6. 2022 focus group with several persons living with IBD so we could map the patient journey and animate it (pictured here), which is available on our website at www.badgut.org/patient-journeys, and we encourage your reviewers to watch these short videos
7. 2020 survey on biosimilars with 145 respondents, most of whom had IBD (some had other inflammatory conditions)
8. 2020 survey completed by 579 respondents regarding the unmet needs of IBD
9. 2018 survey on the unmet need in IBD completed by 432 Canadians with IBD
10. 2015 survey on biologics and biosimilars (then called subsequent entry biologics) completed by 423 Canadians (English: 317 and French: 106) with inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis
11. We also had contact with patients affected by IBD through one-to-one conversations at our BadGut® Lectures, a patient roundtable, recent phone/email/social media interactions with individuals who have IBD, and stories submitted over time from patients.

3. Disease Experience

Ulcerative colitis is an inflammatory bowel disease (IBD) that can arise at any age, commonly occurring in young people. There is an increased risk for those who have a family member with the condition. Currently, Canada has among the highest prevalence and incidence of IBD yet reported in the world, with approximately 270,000 diagnosed individuals. A recent report from Crohn's and Colitis Canada predicts this to increase to 470,000 Canadians living with IBD by 2035.

Diarrhea, pain, rectal bleeding, and loss of bowel control are common recurring symptoms of ulcerative colitis. Inflammation decreases the intestine's absorptive surfaces, triggering watery stools that can lead to fecal urgency and poor control of bowel function. Low red blood cell count (anemia) can result from blood loss due to ulcerations in the intestine and from general malnutrition due to decreased nutrient absorption and the debilitating effects of the disease.

Some patients have extra-intestinal manifestations, including fever, inflammation of the eyes (uveitis) or joints (arthritis), ulcers of the mouth or skin, tender and inflamed nodules on the shins, and numerous other conditions. Anxiety, stress, and mental health are major factors.

Symptoms do not always reflect the level of inflammation, making regular testing essential. It's important for individuals with IBD to continue their medication, even if they feel well.

Ulcerative colitis often has a profound effect on an individual's life – physically, emotionally, and socially, both at home and at school or in the workplace. Symptoms can be relentless, embarrassing, and scary. The severity of the disease can fluctuate, making it necessary to go through routine testing, reassessments, and medication changes. It is particularly difficult for children and young adults, since it often affects a person's sense of self.

More than anything, patients have told us that sustained remission/treatment response is more important than relieving any one symptom. As a chronic disease, it is never just one flare that dominates the impact of the disease, but the constant concern that there will be future flares, possibly worse than the last, at unpredictable times, which can disastrously disrupt their lives.

The following quotes are from individuals describing what it feels like during an IBD flare, and what their biggest concern is, in their own words:

- "In my experience, some of the most difficult aspects of IBD, pain aside, are its **unpredictability** and the constant, often **overwhelming fatigue**."
- "**Hopelessness**, for although I have done everything I can humanly do and researched my problem, I can't get any medical professional to listen to me or help or refer me. However, I was **approved for MAID** within 3 months time!!

- "It takes almost a year to determine a **drug isn't working** and then we do a scope, change drugs and the cycle starts all over again… **over and over with no improvements**… **depressing** and making me feel **suicidal**."
- "Your gut aches and burns and there is often blood in the toilet. You lose your appetite and weight, unhealthily! **My biggest concern is I'm going to run out of meds to help!"**
- "It's like I can't control anything, I feel weak and can barely get up. My biggest concern is usually when I see blood and determining **at what point to go to the ER**."
- "The **pain is worse than childbirth**... and I have 3 kids...1 labour without drugs."
- "Worst flu symptoms, fatigue, lethargy, like swallowing glass and chili and then having constipation and diarrhea at the same time. Gut cramps and hunger cramps at the same time. **Want to die. Biggest concern is needing a toilet at all times with zero minutes waiting time**."
- "It feels like my guts are in a vise. **The nausea can be so bad I can't move or even vomit and the diarrhea is so painful I'll be literally screaming in the bathroom**."
- "**It is so exhausting and feels like it will never end**. You start to question if you can still live the life you planned. And no-one gives you a break."
- "**A flare can come out of nowhere and completely disrupt your life.** Pain can sometimes be so bad that it keeps you in bed. **You mostly spend life either asleep or on the toilet**. My biggest concern during a flare is being able to keep up with my responsibilities (work, school, social, etc.)."
- "It feels like your body is betraying you. **You can't plan anything in advance because you don't know how your body will feel on a day-to-day basis**."
- "There's a huge element of **fear and worry** and being faced with **mortality** at such a **young age**."

It's one thing to read a list of common symptoms or data on how IBD affects patients, but it is the individual stories of these patients, as summarized above, which astound us and motivate us to support patients' need for more diversity in effective treatments. In addition, treatments should improve quality of life, not cause more symptoms, pain, frustration, or hardship.

4. Experiences With Currently Available Treatments

The treatment of ulcerative colitis is multi-faceted; it includes managing the symptoms and consequences of the disease along with therapies targeted to reduce the underlying inflammation. Since IBD is a chronic disease and there is no cure, it is vital to have a variety of treatment options available. If untreated, it can lead to irreversible tissue damage, reduced quality of life, permanent disability, and even death.

Unfortunately, Canada has a jurisdictional patchwork of criteria that gastroenterologists must follow when prescribing medications for IBD, including Crohn's disease and ulcerative colitis. The specific government-established criteria involve a tiered approach, which differs from province to province. Typically, a patient starts on one type of treatment and, if there is inadequate response, then switches to another type. It starts with the use of 5-aminosalicylic acid (5-ASAs), followed by corticosteroids, immunomodulators, and advanced targeted therapies, such as originator biologics, biosimilars, Janus kinase (JAK) inhibitors, and sphingosine-1-phosphate (S1P) inhibitors. The exception to this approach is Quebec, which we describe below.

5-ASA helps to settle acute inflammation and, for some patients, keeps the inflammation inactive when taken on a long-term basis (maintenance). However, this type of medication can have side effects such as headaches, loss of appetite, and nausea. It is also ineffective for patients living with moderate to severe ulcerative colitis.

To reduce inflammation in moderate to severe cases, corticosteroids can help but they are not well-tolerated and can have potentially serious side effects, so they are best for short-term treatment only and are not for maintenance of remission. For topical relief in the colon, corticosteroids are available in rectal formulations. These are inconvenient therapies that make it difficult for patients to keep a normal routine. Also, if a patient has significant diarrhea, then the rectal medications may be difficult to hold in place for sufficient time to be effective.

Immunosuppressive agents reduce dependence on steroids and can help patients who have steroid-resistant disease, but it could take up to six months or more of therapy to see results. Recent studies have shown that they are not as beneficial as biologics when used on their own, are less effective in healing the mucosa, and can increase the risk of some infections. Yet, many individuals living with ulcerative colitis have received, and continue to receive, off-label prescriptions for thiopurines, such as azathioprine (Imuran®) and mercaptopurine (Purinethol®). Health Canada has not approved these medications for IBD, and the Canadian Association of Gastroenterology has cautioned on their use.[1] Unfortunately, many provincial governments require their use before patients can receive coverage for advanced, targeted therapies.

Biologics treat IBD when older medications fail to relieve symptoms. There are a variety of mechanisms through which they work. Patients also find the patient support programs associated with biologics to be significantly beneficial to their treatment plan and disease journey.

There are new classes of medications that target inflammation. These are Janus kinase (JAK) inhibitors and sphingosine-1-phosphate (S1P) inhibitors. JAK inhibitors typically work faster than biologics, pose no risk for immunogenicity, and are easy and convenient to take since they are in pill form. These include a pan-JAK-inhibitor, tofacitinib (Xeljanz®), and a selective JAK-inhibitor, upadacitinib (Rinvoq®). There are two S1P inhibitors available currently: etrasimod (Velsipity™) and ozanimod (Zeposia®).

To support patients in navigating the various kinds of medications available for inflammatory bowel disease, we created the IBD Medication Guide, available at https://badgut.org/ibd-medication/search/. It provides lay information on how the medications work, use in specific groups, such as children, pregnant/breastfeeding women, and older individuals, and links to the product monographs.

Patients with IBD still have a lot of difficulty obtaining remission or adequate symptom relief. In our 2020 survey, 33% of respondents did not believe that their IBD was well-controlled by their current medications. In our 2024 survey, this number was 29%, compared with 38% who find it well-controlled and 33% who were unsure. When asked how concerned they were about running out of treatment options, 82% were at least somewhat concerned. Patients are still suffering, and each person living with IBD has a different experience. This is why it is so important that those living with IBD have access to varied effective treatments.

Despite advancements in care and evidence, provincial government algorithms still follow a one-size fits all approach within each jurisdiction that is not recommended by gastroenterologists. These outdated protocols are not meeting the healthcare needs of those who are living with IBD. They also are not based on clinical practice guidelines, which have evolved. The STRIDE-II recommendations call for personalized treatment with mucosal endoscopic healing with clinical remission as the ultimate long-term treatment target.[2] Also, the 2020 American Gastroenterological Association Institute Clinical Guidelines recommend initiating advanced therapies for patients with moderate to severe ulcerative colitis and advise against using thiopurines for inducing remission in this population.[3]

The exception is Quebec, where INESSS released recommendations that removed the requirement of trialing conventional therapy before patients living with IBD can receive coverage of biologic therapies (i.e.,

adalimumab, infliximab, and vedolizumab). These are evidence-based best practices recognized around the world, and we encourage CDA to follow this approach.

5. Improved Outcomes

Patients affected by ulcerative colitis need access to medications that work. Inadequate access to medication results in preventable patient suffering (e.g., continual, debilitating disease symptoms; secondary illnesses such as depression and anxiety disorders; and loss of family/social interactions). It also leads to unnecessary usage of healthcare resources (e.g., hospital stays, surgeries, diagnostic procedures, other medications) and a ripple effect of financial burden on the government and taxpayers (e.g., through inability to work, long-term disability claims, biologic-related debt, and even bankruptcy).

When the patient receives the right medication at the right time and for the right duration – as determined between physician and patient – these individuals can live full, rewarding lives as productive, valuable citizens who participate in the workforce and community. However, since patients are unique, they respond differently to various medications, and in some cases stop responding to medications after using them for some time, so it is important to have a variety of options available.

6. Experience With Drug Under Review

We know that biologics and biosimilars have revolutionized care for patients living with IBD. For many, they are effective, **life-changing therapies**, and they can heal the mucosa.

We interviewed one patient who is living with ulcerative colitis and is taking risankizumab (Skyrizi®). She was diagnosed with ulcerative colitis in January 2020, right at the start of the COVID pandemic. Her gastroenterologist prescribed Pentasa® and Salofalk® suppositories. When she was first diagnosed, she lost a significant amount of weight and had severe inflammation near her rectum.

Managing day-to-day life became a constant challenge. She had to plan everything around the possibility of finding a public washroom, and often times it just felt easier to stay home. She even carried extra clothes with her, in case of an accident. Ulcerative colitis had drastically changed her life.

For 18 months, the suppositories provided some relief, but the flare-ups kept coming back, and she was often in tears, feeling frustrated and helpless. She cried to her gastroenterologist for solutions, who then suggested she try Skyrizi®, which led her to apply for a clinical trial. She was accepted and started the trial in March 2022. After just two to three weeks, she began to notice a significant improvement.

Once her gastroenterologist felt her disease was stabilizing, he decided to cut her dose in half and switch to injections instead of infusions. Unfortunately, her body reacted poorly to the change, and she had another flare-up. In December 2022, she had a rescue dose and the dose was doubled. Since then, she's been on the same dose (360mg) and has felt great. It's been two years now, and she hasn't looked back.

Her treatment now involves two injections on each side of her abdomen every eight weeks, for a total of four injections. Initially, the thought of self-injecting was intimidating, but now, it's just part of her routine.

"Now it's much better. My social life is good again, even my diet, I find I can eat anything. I have my life back."

Thanks to the treatment, she's been able to travel with ease. In 2024, she went to Thailand for four weeks

with her siblings, and she didn't have any issues at all. Then, in early January 2025, she traveled to Cancun, enjoying her vacation without the stress of carrying syringes. She asked her nurse if she could take her injections early, who told her that she can take her injections seven days ahead of her due date, which meant no worries for her while on vacation.

Her injections are every 8 weeks, and she's noticed that by about week 6 she can feel that she needs the medication again. She has underlying eczema and by week seven, her eczema flares up.

Looking to the future, she hopes for a treatment that still works every eight weeks but with fewer injections as four times feels like a bit much for her. However, this is really the only point she raised because this medication has been a blessing for her life. She's still on Pentasa® as a backup, but since starting Skyrizi®, her colonoscopy results have been normal.

We know that patients want more options, with a variety of administration methods and dosages to meet their unique needs. In our 2024 survey on IBD, 30% of respondents indicated that they have no preferred route of administration, 41% prefer a daily oral medication, and monthly injections were less preferred. When we followed up with respondents who have, or currently take, a biologic medication, 58% said they prefer to self-inject and 18% said that it doesn't matter. This data illustrates that patients have varied preferences for medication administration, influenced by a range of factors. What's crucial is that they have public coverage for a variety of treatment options that cater to their individual needs, without the requirement to trial conventional therapies before accessing targeted treatments.

7. Companion Diagnostic Test

n/a

8. Anything Else?

n/a

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the 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. CDA-AMC may contact your group with further questions, as needed.

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

No.

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

No.

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

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
AbbVie				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: Jaymee Maaghop
Position: Health Policy and Outreach Manager
Patient Group: Gastrointestinal Society
Date: 2025-04-09

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1 Marshall JK *et al.* Canadian Association of Gastroenterology position statement regarding the use of thiopurines for the treatment of inflammatory bowel disease. *Can J Gastroenterol Hepatol.* 2014;28(7):371-372. https://www.cag-acg.org/_Library/clinical_cpgs_position_papers/thiopurine_position_cjg_aug14_2014.pdf

2 Turner D *et al.* STRIDE-II: An Update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): Determining Therapeutic Goals for Treat-to-Target strategies in IBD. *Gastroenterology.* 2021 Apr;160(5):1570-1583. Epub 2021 Feb 19. https://doi.org/10.1053/j.gastro.2020.12.031

3 Feuerstein JD *et al.* AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. *Gastroenterology*. 2020;158(5):1450-1461. https://doi.org/10.1053/j.gastro.2020.01.006.

CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: Skyrizi (Risankizumab)
Indication: Ulcerative Colitis
Name of Patient Group: Crohn's and Colitis Canada
Author of Submission: Patrick Tohill

1. About Your Patient Group

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

Crohn's and Colitis Canada website (https://crohnsandcolitis.ca/)

Crohn's and Colitis Canada is the only national health charity focused on finding the cures for Crohn's disease and ulcerative colitis, the two main forms of inflammatory bowel disease (UC), and improving the lives of everyone affected by these diseases.

Crohn's and Colitis Canada is one of the top health charity funders of Crohn's and colitis research in the world, investing over $150 million in research since our founding in 1974. The organization also delivers on its promise through patient programs, advocacy and awareness. We help improve the quality of lives today by:

- Sharing accurate and reliable information on treatments, research and issues related to life with Crohn's and colitis through website, print materials, webinars and live events;
- Increasing public washroom access through the GoHere program;
- Raising awareness about these Canadian diseases with bilingual public communication;
- Providing a peer support program to newly diagnosed people; and
- Advocating on behalf of the patients and caregivers on priority concerns and needs.

Crohn's and Colitis Canada is comprised of approximately 65,000 supporters including volunteers, donors or individuals interested in engaging with the organization. There is no paid membership. Crohn's and Colitis Canada is governed by a national volunteer Board of Directors. The organization has a network of volunteer-led Chapters in 24 communities across the country, offering information, events, fundraising opportunities and encouragement. There are thousands of volunteers from coast-to-coast supporting Crohn's and Colitis Canada's mission.

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.

Information summarized in this submission was compiled from a variety of sources, including Crohn's and Colitis Canada's report *2023 Impact of Inflammatory Bowel Disease in Canada*, a 2022 unmet needs survey (includes responses from 1706

Canadian patients, including 354 with moderate to severe ulcerative colitis) as well as interviews with patients who have had experience with Skyrizi.

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?

Ulcerative colitis (UC) is a form of inflammatory bowel disease (IBD) that inflames the lining of the gastrointestinal tract, disrupting the body's ability to digest food, absorb nutrition and eliminate waste in a healthy manner. Typically, the disease affects the colon (large intestine) including the rectum and anus and only invades (inflames) the inner lining of bowel tissue. It almost always starts at the rectum, extending upwards in a continuous manner through the colon. UC can be controlled with medication and in severe cases can even be treated through the surgical removal of the entire large intestine.

The results from the patient survey provide a window into how moderate to severe ulcerative colitis (UC) patients live and manage their symptoms. 78% of the respondents were female, 21% male and 1% non-binary. The vast majority of patients (73%) who participated in our 2022 survey assessed the severity of their IBD as being moderate (56%) to severe (17%).

The most common symptoms experienced by patients included fatigue (experienced by 100% of IBD patients surveyed), abdominal pain/cramps (99%), other types of pain (98%), constipation (97%), gas (95%), bloating (79%), urgency to use the bathroom (78%), diarrhea (73%), nausea and vomiting (39%), diminished appetite/weight loss (38%) and rectal bleeding (34%).

When asked what UC related complications they are experiencing currently or within the past year, most frequently reported were mental health and stress (65%), followed by joint inflammation & arthritis (51%), anal fissures and hemorrhoids (40%), anemia (33%), and skin conditions and malnutrition and weight loss both at ~ 30%. Other complications include strictures, adhesions (scar tissue), bowel obstruction, eye inflammation, perianal or anal fistulas and abscesses, internal (or intra-abdominal) fistulas or abscesses, stricture, ankylosing spondylitis (arthritis of the spine), liver conditions, and cancer. 13% of the respondents were currently experiencing at least one complication of UC.

Thinking back to when they were first diagnosed, patients noted that they hid aspects of their diagnosis from friends, coworkers and classmates. There is a general misunderstanding of what UC is, which could impact how patients navigate social situations. Nine-in-ten agree that most people don't know what UC is. This is further compounded by the fact that almost two thirds (63%) of patients agree that their family and friends don't understand what they are going through. In spite of their medications, two thirds of the patients continue to experience at least one symptom of UC, the most frequent of which are bloating and urgent and frequent need to use the washroom. **Over half (56%) believed that different treatment options could make them feel better.** At least half of patients felt they could not be open about their UC, felt isolated due to their UC, and believe that their UC has had a negative impact on their romantic relationships with their spouse or partner.

A significant proportion of patients have adjusted their lifestyle and expectations. 72% agreed that they have changed the expectations they had of themselves or that they are always adapting their lifestyle to account for their UC. Two in five patients reported that they changed their travel plans and one in five changed their career aspirations.

Ulcerative colitis affects every aspect of a person's life from family, friends and work activities. Due to unpredictable urgency of bowel movements, accidents are not uncommon, especially when patients are experiencing flares. Patients often hide their disease from work colleagues, friends (35%) and even relatives because of the perceived stigma of the condition being a "poop"

disease. Unable to predict when their next flare will occur and how to control their flare, isolation, stress and anxiety are constant companions to the patient's disease journey.

At least half of patients felt they could not be open about their UC, felt isolated due to their UC, and believe that their UC has had a negative impact on their romantic relationships with their spouse or partner.

One patient we interviewed described what her life was like before her diagnosis:

[B]efore I was diagnosed, I was running to the washroom, I had accidents. It got to the point that I was pre-planning trips to the malls. I had scoped out every washroom in the malls or in restaurants, and my symptoms got worse and worse. I had no quality of life. And it got to the point where it was just easier to stay at home than to go out and be embarrassed and always carrying an extra change of clothes with me. And then once I was diagnosed and put on meds, I responded quickly and there was relief.

For this patient, the most important symptom to control is "bowel urgency". Relates the patient:

I had to stay home. My world got so small. And no quality of life. It was easier to stay at home because the bathroom is nearby and he anxiety of going out and wondering if I could get to a washroom in time… I was working at the time and I had a change of clothes with me at all times. [M]y coworkers… understood the urgency. If we were on a Teams meeting… you know, this was during COVID, so I worked from home… if I had a meeting with my supervisor… we would be going over, you know, work issues and then all of a sudden, I would have to say, I gotta go. I would close my laptop and she knew. She was very supportive. [W] hen we did return to the office, luckily, there was a washroom very, very close to my desk.

Other issues of importance noted by the patient were "cramping and "loss of appetite".

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).

Disease management is incredibly important to ensuring patients can live a life of normalcy. In our 2022 survey, most patients reported having used a combination of medications to manage their UC, with systemic steroids (79%), sulfasalazine & 5Aminosalicylates (76%) and biologics (57%) being most common among those with ulcerative colitis, followed by immunomodulators (45%), antibiotics (42%), and non-systemic steroids (38%).

One patient interviewed for this submission relates her experience prior to being put on the study drug:

I was on Pentasa and Salofalk suppositories, I'm thinking for two years. I responded well…but eighteen months after the initial prescription, I started having flare ups… My GI then suggested that I join the clinical research group. I jumped at it… then, because I was having flare ups, I was put on steroids, on Prednisone.

Importantly, the severity of their IBD plays an important role in deciding which medications are being used. Those who described their condition as moderate to severe were more likely to have used almost all medications asked except immunomodulators, which is more commonly used by patients who have a severe state.

More than one in five are currently taking steroids (30% within last year). Roughly one third of the UC patients have also tried medical cannabis, anti-anxiety medications, and antidepressants to manage their symptoms

Steroid use is also an important aspect in symptom management and patients aren't particularly supportive of this treatment option. Almost all patients surveyed agree that they only take systemic steroids if absolutely necessary (93%) with four in five in agreement that they wish they could eliminate systemic steroids from the list of medications they use.

This is true as well of the patient we interviewed:

I did not like Prednisone at all. The first time I was on it for three or four months. I didn't like how it made me feel. I didn't like being on it. I was on it again when I started Skyrizi. About six more weeks. I do not like taking them.

Half of respondents say that systemic steroids is/was a burden in their UC management. This is particularly true among those with moderate to severe forms of UC, and among women. Those under the age of 55 are more likely to agree that they have had side effects from systemic steroids. Those with a severe state of UC indicate that they have also experienced side effects from systemic steroid use (90%).

Among those who are using steroids 84% have been on systemic steroids for less than 12 months; with 42% less than three months; and 13% of the respondents having been on steroids for over a year. Two thirds of the respondents feel that systemic steroids are a burden to their UC treatment, with 71% indicating that they have experienced side effects of the steroids.

Among patients who say managing medication use is important, having enough of their treatment options, understanding side effects, and minimizing steroid use were most important. Women are more likely than men to find it important to ensure they have enough treatment options, understand the side effects of long-term use, and minimize the use of steroids.

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?

Patients seek any treatments that can mitigate these symptoms to protect a patient's ability to work productively, attend school and social events, and even basic daily necessities like leaving the house to run errands or have the energy to maintain a household or raise children. Quality of life could be greatly improved in UC patients if their flares are brought into remission. Based on our survey results, the majority of patients with moderate to severe UC continue to experience symptoms with current treatment options.

The UC patient interviewed for this submission related that going into the clinical trial, she was "hoping for any relief" and mainly looking for her "symptoms to go away" and for improved "quality of life". While the drug has met all these expectations as well as others. She's been pleased, for example, with being able to self-inject at home and that because of the time between doses she's even been able to travel without having to bring her medication. The one thing she noted she feels could be improved in future was the size of doses, noting that each of her doses requires four separate injections. While she's gotten used to the needles, she said that if there's one thing that she could change, it would be the ability to deliver the medication she needs in a single injection.

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.

According to the patient we interviewed for this submission:

As of March 2022, I was accepted by abbvie, for the clinical trial... [and] started infusions... in July [2023]... I had flare ups because the dose was cut in half. So in... the fall of 2023, I was put on a full dose... that's where I've been ever since. I can't say enough about Skyrizi. I have quality of life again.

The main benefits experienced by the patient since getting on Skyrizi include alleviation of her "bowel urgency and cramping", with "no side effects", which has led to her "feeling better". "Once I was getting the infusions," explained the patient, "there was relief. My quality of life improved and I could tell. From the first infusions, it was about four to six weeks that I started feeling better... started eating a full diet again". Adds the patient:

I'm not symptom free, but [they're] mild symptoms and bearable. And I can go through them with ease.

This patient and others we've interviewed on previous occasions have all ascribed similar key values to Skyrizi, chiefly: near immediate alleviation of symptoms; no side effects, ease of administration; painless; convenience of being able to self-inject.

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.

Skyrizi has no companion diagnostic. Access to other diagnostics were covered for patients participating in the clinical trial. There were no out-of-pocket costs. All travel was local.

8. Anything Else?

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

Patients and clinicians need a range of options so that the right treatment can be prescribed to the right patient at the right time. While there are other treatments that alleviate UC symptoms, research and the experience of patients we interviewed bears out that Skyrizi provides near immediate relief of symptoms with few to no side effects. Add to this that the drug is a self-injectable and has an eight-week dosing schedule, far longer than other self-injectable advanced therapies currently in market, attributes that deliver huge improvements in terms of improved quality of life.

Appendix: Patient Group Conflict of Interest Declaration

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

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.

   The first survey was conducted in collaboration with Leger who performed the initial analysis of 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.

   Crohn's and Colitis Canada receives grants, sponsorships and scholarship funding from pharmaceutical companies involved in the treatment of Crohn's disease and ulcerative colitis. These funds are used to run patient education events, community programs, research and medical conferences, educational brochures, kid's camps, post-secondary scholarships as well as outreach and advocacy activities on behalf of Canadians living with Crohn's and colitis. The pharmaceutical companies do not influence the design nor the contents of Crohn's and Colitis Canada programs, which they support. The vast majority of Crohn's and Colitis Canada's funding comes from individual donors contributing to fundraising events such as the Gutsy Walk. Crohn's and Colitis Canada is participating in this review as part of our advocacy for Canadians living with inflammatory bowel disease and does not endorse or recommend the use of specific products or treatment or attribute of any product. No sponsor was involved in developing the content of this submission.

Table 1: Financial Disclosures

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

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Abbvie 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: Patrick Tohill
Position: Director, Advocacy and Government Affairs
Patient Group: Crohn's and Colitis Canada
Date: 21 March 2025

Clinician Group Input

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: SR0890-000
Generic Drug Name (SKYRIZI): risankizumab
Indication: For the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, loss of response, or were intolerant to conventional therapy, a biologic treatment, or a Janus kinase (JAK) inhibitor.
Name of Clinician Group: Canadian IBD Physicians Group
Author of Submission: Dr. Christopher Ma, MD, MPH, FRCPC
Associate Professor, Departments of Medicine and Community Health Sciences
University of Calgary Inflammatory Bowel Disease Unit

1. About Your Clinician Group

This clinician input is being submitted by the Canadian Inflammatory Bowel Disease (IBD) Physicians Group: we are a group of over 30 Canadian gastroenterologists with specific interest and expertise in IBD, and with broad representation from across Canada. Collectively, the group has over 250 cumulative years of experience in caring for patients with ulcerative colitis (UC) and has published over 1800 peer-reviewed manuscripts in the IBD field, including Canadian and international guidelines for the management of UC and leadership within the Crohn's & Colitis Canada IBD Impact Report. We are responding to this call for clinician input as medical experts in support of risankizumab (Skyrizi®) for the treatment of adult patients with moderately to severely active UC. Collectively, we feel that this is a critically important treatment option and hope that our input can help elevate the standard of care for patients with UC in Canada.

The lead of this submission is Dr. Christopher Ma. Dr. Ma is part of the University of Calgary IBD Unit, which comprises a group of 9 gastroenterologists who are national and international experts in IBD and have comprehensive expertise from clinical trials, epidemiology, diagnostics, young adult (pediatric to adult transition), and women's health. The unit is one of the top three units in the world with respect to patient volume and research output. The group follows over 8000 patients from across Canada with a mission to further the care of those that suffer with UC and Crohn's disease through excellence in patient care, research, and patient and health-care provider education.

Website:
https://cumming.ucalgary.ca/departments/medicine/divisionssections/gastroenterology/clinical/inflammatory-bowel-disease-group

2. Information Gathering

On March 7, 2025, the Canadian IBD Physicians Group met by videoconference to discuss the current UC treatment landscape and unmet needs. This meeting included individual presentations on currently available therapies, recent therapeutic developments in the UC space, and a critical appraisal of the efficacy and safety data from the risankizumab phase 3 UC development program. Small group workshops were then conducted to gather group feedback, opinions, and reflections on the existing landscape, and potential for risankizumab to fill patient- and system needs in the short- and long-term. An initial draft was developed based on these discussions. The group was asked to review the draft of the clinician input response, including members who were not able to attend on March 7, 2025, and provide any additional feedback or clarifications. This iterative input was then shared, and a final document was developed based on the clinician group's collective input. We have highlighted in this document areas of discussion and regional specific issues across Canada to provide CDA-AMC with a full sense of how risankizumab is anticipated to impact clinical practice across different provinces, different practice settings, and different patient populations and priorities that are being represented by the clinician group.

3. Current Treatments and Treatment Goals

Treatment of Ulcerative Colitis in the Canadian Landscape

Ulcerative colitis (UC) is a chronic, idiopathic, immune-mediated inflammatory bowel disease that affects over 165,000 Canadians.[1] Concerningly, Canada has amongst the highest rates of UC globally, and the prevalence is projected to continue increasing, driven by rising rates of diagnosis among children and young adults. While the natural history of UC is characterized by a relapsing and remitting course, the **impact of this disease on patients is debilitating**.[2] Active UC is characterized by diarrhea (loose, watery, frequent bowel movements), rectal bleeding, abdominal pain and cramping, urgency, loss of bowel control or fecal incontinence, and tenesmus (an uncomfortable sensation that there is a need to have a bowel movement despite not being able to pass one).[3] These symptoms drive significant impairments in quality of life (QoL), lead to impaired work productivity and absenteeism, and can have profound psychological impacts that persist even after acute inflammation is controlled. Moreover, increasing severity of UC translates into a higher burden of disease due to frequent flares, serious comorbidities, high rates of hospitalization, and surgery. While colectomy may be a life-saving measure, it is invasive, costly, and complications occur in approximately one-third of patients; the greatest risk of death in patients with UC is within 30 days following gastrointestinal surgery.[4] In a meta-analysis of population-based cohorts, approximately 13% of patients with UC require surgery within 10 years of diagnosis, most commonly due to disease refractory to currently available medical treatment options.[5]

In addition, UC has a significant financial impact on patients. The “2023 Impact of Inflammatory Bowel Disease in Canada” study reported that both indirect (includes unemployment, presenteeism and absenteeism) and out-of-pocket costs (i.e., medical management not funded through public healthcare of private plans) of IBD in Canada are estimated at more than $2 billion (valued as 2003 Canadian dollars).[6]

The most recent Canadian recommendations for the management of UC continues to be the 2015 Toronto Consensus clinical practice guidelines for the medical management of non-hospitalized UC.[7] However, the group acknowledged that in the decade since the publication of these recommendations, the treatment landscape for UC has dramatically changed. This has been characterized by the development of new biologics and small molecule drugs, as well as better diagnostic tools and more intensive monitoring strategies, which have increased the complexity of UC management. More recent guidelines, such as those from the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD)[8,9] and the European Crohn’s and Colitis Organization (ECCO)[10] reflect updated recommendations for treatment goals, treatment sequencing, and treatment administration. While these are not Canadian-specific guidelines, these international recommendations are applied in day-to-day Canadian practice and Canadian gastroenterologists have contributed substantively to the development of these guidelines, which represent the most updated approaches to managing moderately to severely active UC.[7,8]

Broadly, patients with UC may experience mild, moderate or severe disease activity that can impact patients’ overall QoL. Uncontrolled inflammation in UC leads to progressive bowel damage that can result in mucosal fibrosis, functional bowel issues, stricture formation, and critically, a significantly increased long-term risk of colorectal cancer.[11] Patients with mildly-to-moderately active or moderately-to-severely active UC are primarily treated with pharmacologic therapy.[12] In patients with mildly active UC, ECCO recommends using 5-aminosalicylates (5-ASA) (both systemic and topical) to induce and maintain remission, and this is consistent with the 2015 Canadian guidelines and current practice.[7] While 5-ASA therapies are safe and cost effective in milder disease, they are generally not effective for patients with more severe disease activity.[13] Notably, up to 1 in 4 patients with UC will develop acute severe UC (ASUC) that requires hospitalization; this specific phenotype will not be discussed here because this patient population is beyond the scope of this submission and requires different management considerations. However, it should be noted that almost all patients with ASUC who initially respond to corticosteroids will fail conventional therapy with azathioprine within the first year of treatment[14], and these patients will also require outpatient advanced treatments to maintain remission.

For moderately-to-severely active UC, initial induction of remission with systemic corticosteroids such as prednisone is recommended.[7] Budesonide (specifically, budesonide multi matrix system [MMX]) may also be used in inducing remission.[15] However, the clinician group highlighted that **corticosteroid therapy cannot be used for maintenance of remission**, given substantial concerns with respect to long-term safety and the burden of excessive corticosteroid exposure experienced by patients with UC.[16,17]

Therefore, in alignment with other clinical practice guidelines, the clinician group strongly endorsed induction of remission with advanced targeted agents in patients with moderately-to-severely active UC. These advanced targeted agents include anti-tumour necrosis factor (TNF) agents (infliximab [Remicade® or

biosimilars], adalimumab [Humira® or biosimilars], and golimumab [Simponi®]), the $\alpha_4\beta_7$ integrin inhibitor vedolizumab (Entyvio®), the Janus kinase (JAK) inhibitors tofacitinib (Xeljanz®), and upadacitinib (Rinvoq®), the interleukin (IL)-12/23 inhibitor ustekinumab (Stelara®), sphingosine-1-phosphate receptor (S1PR) modulators ozanimod (Zeposia®) or etrasimod (Velsipity®), or the IL23p19 inhibitor mirikizumab (Omvoh®).[7]

Historically, advanced therapies were indicated in patients who were intolerant or had an inadequate response to conventional therapies (e.g., 5-ASA, corticosteroids, and immunomodulators such as thiopurines/azathioprine or methotrexate). However, it should be noted that patients with moderate-to-severe UC may not respond to 5-ASA therapy, corticosteroids cannot be used in isolation to manage UC given the risk of adverse events, and **immunomodulators are not recommended** for induction of remission in UC as several trials have now demonstrated that they are not any more effective than placebo.[18]

In alignment with the Toronto Consensus clinical practice guideline, the American Gastroenterological Association (AGA) published clinical practice guidelines for the management of moderate-to-severe UC that focus on advanced targeted agents to induce and maintain remission.[19] The AGA recommends that in adult outpatients with moderate-to-severe UC, infliximab, adalimumab, golimumab, vedolizumab, tofacitinib, or ustekinumab should be used over no treatment for the induction and maintenance of remission.[19] Notably, the AGA suggests *against* the use of thiopurines for moderately-to-severely active UC, as they have a slow onset of action and they may not be any more effective than placebo for inducing remission.

For patients with moderate-to-severe UC who have inadequate response or intolerance to conventional therapy, the ECCO guidelines recommend treatment with either anti-TNF agents (i.e., infliximab, adalimumab, and golimumab), vedolizumab, tofacitinib, or ustekinumab for induction of remission.[10] It is further recommended that for maintenance of remission, the same drug should be used in patients who have responded to induction therapy with that drug.[10] In developing the recommendations, the ECCO expert panel considered evidence of clinical response, clinical remission, endoscopic response, endoscopic improvement, steroid-free clinical remission, sustained clinical remission, improvement in quality of life, and safety.[10] These guidelines were published prior to the development of newer IL23p19 therapies (mirikizumab, risankizumab, and guselkumab), JAK-1 selective inhibitors (upadacitinib), and S1PR modulators (ozanimod and etrasimod). It should be noted that while current guidelines highlight the use of advanced agents in moderately-to-severely active UC, not all advanced treatments are directly comparable in clinical care. Treatment is personalized based on both patient-, drug-, and system-related factors (see *Treatment Gaps*) and there remains significant unmet medical needs for patients with UC who either cannot tolerate or fail to achieve remission with currently available options.

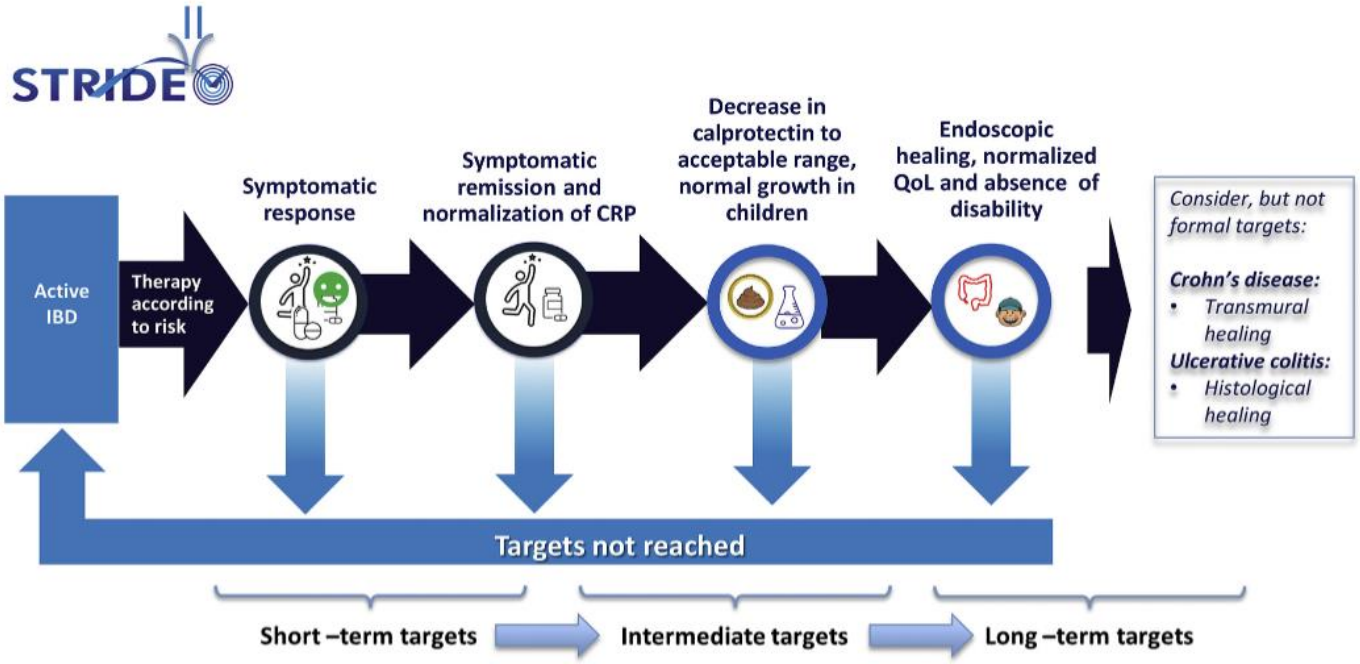
We believe that clinical practice guidelines for UC focus on Health Canada approved medical therapies, but do not always capture the breadth of treatment options discussed with patients, such as combining therapies or fecal microbiota transplantation. As such, our response has focused on medical treatments. Non-medical treatments, such as nutritional and psychological support, play an important role in the multidisciplinary approach to managing UC. As discussed earlier in this response, pharmacological treatment forms the basis of the treatment plan for patients with moderately-to-severely active UC. Despite the availability of advanced

targeted agents, up to 25% of patients with UC will eventually require hospitalization or surgery, underscoring the need for new medical treatments.[12]

Treatment Targets in UC

Due to the complexity of UC, there are multiple treatment goals to consider when developing a management plan, leading to the need to identify which are the most important to address. Many physicians rely on the STRIDE consensus recommendations and clinical algorithms of the STRIDE group to incorporate clinical targets and facilitate treatment of UC. The most recent initiative, STRIDE-II, proposed an updated, simple algorithm for using selected short-, intermediate-, and long-term treatment targets, with the timing of reaching the goals depending on the specific treatment, see Figure 1.[8]

Figure 1. Schematic of STRIDE II treatment targets.



Source. Turner et al. 2021.[8]

According to STRIDE-II, the most important long-term treatment targets are achieving endoscopic healing, restoring QoL, and minimizing disability. A particularly important immediate goal is symptomatic relief, a target that is often rated highest by patients.[8] Given the debilitating nature of UC-related symptoms, patients have a need for treatments that can provide rapid relief to improve their quality of life that is significantly reduced by unpredictable relapses of diarrhea, abdominal pain, rectal bleeding, and bowel urgency, as well

as systemic symptoms, such as fatigue.[12] In 2024, the Canadian Society of Intestinal Research conducted a nation-wide survey on unmet needs in patients with IBD.[20] That survey reported that:

- 73% of patients self-reporting that IBD had a moderate to extreme impact on their QoL in the past year
- 19% of patients missed more than 6 days of work due to their IBD
- 29% of patients reported their IBD is uncontrolled with an additional 33% of patients being unsure
- **~ 24% of patients had to go to the Emergency Room for unplanned or unexpected care, which is a heavy burden to our healthcare systems**.
- In addition, patients commonly reported that they frequently experienced symptoms such as fecal incontinence, sleep interruption and tenesmus,
- **Only 18% of respondents indicated that they do not have any mental health condition**, highlighting the strong association between UC and the development of **psychological morbidity**

Overall, we concur with the STRIDE-II recommendations. In STRIDE-II, it was noted that histologic healing is a potential future therapeutic target, as there is increasing evidence that patients who achieve this most stringent level of healing have improved long-term outcomes.[21] The clinician group discussed that histologic remission in conjunction with endoscopic remission (histo-endoscopic mucosal improvement and histo-endoscopic mucosal remission) has become increasingly important for new drugs to achieve, because these measures are associated with a decreased likelihood of clinical relapse.[21] The International Organization for the Study of Inflammatory Bowel Disease (IOIBD) is presently working on the STRIDE-III guidelines and a statement including histology as a target has been added (Dr. Panaccione, Personal Communication, 2025). While there is variability in how histologic healing is incorporated in the clinic, achievement of this endpoint in clinical trials can be used to inform clinical practice and gives increased confidence around the potency of efficacy of treatment.

Aligned to patients wishes, we believe that rapid onset of symptom relief, durability of treatment, and safety of treatment are important treatment goals. However, the clinician group **emphasized that historically,** clinical trials in UC inadequately captured patient symptoms. The modified Mayo Score (mMS) and the full Mayo Clinic Score (MCS), which have been used to define patient populations and clinical remission for trials of all advanced therapies, only capture rectal bleeding and stool frequency.[22] While these are often considered hallmark symptoms in UC, they do not capture a broad range of other disease manifestations such as urgency, tenesmus, incontinence, abdominal pain, nocturnal stooling, and sleep disturbance, that are critically important to the patient experience with UC and require attention in clinical management.

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.

We believe that for moderately-to-severely active UC, conventional treatments for UC (5-ASA, corticosteroids, and thiopurines) are not associated with sustained efficacy and have long-term safety concerns. While advanced targeted agents are available with varying mechanisms of action and have

improved efficacy, a **considerable proportion (up to 20-30%) of patients do not respond to induction therapy (primary failure) or will lose response over time (secondary failure)**.[23] Secondary loss of response can occur with all therapies and can be due to a variety of mechanisms, including immunogenicity with anti-drug antibodies or breakthrough of the inflammatory response beyond the targeted mechanism of action.[24]–Up to 25% of patients with UC will eventually require hospitalization or surgery, underscoring the need for new medical treatments.[12] This is echoed in the IBD patient survey, which reported that 29% of patients believed their IBD to be uncontrolled.

While there are multiple options for advanced therapies in UC, **not all advanced therapies are directly comparable with each other.** Each has unique efficacy and safety concerns, which may limit their use in patients with UC. For example:

- Corticosteroids are often used to treat moderately to severely active UC, but they are not recommended for long-term use due to unacceptable AEs, including endocrine, neurologic, metabolic, dermatologic, psychologic, and infection-related complications.[25] Furthermore, corticosteroids are not effective for inducing or maintaining *endoscopic* remission, which is critical for changing the long-term natural history of UC. For example, in the CORE-II trial of budesonide MMX for UC, treatment with 9 mg budesonide MMX was not significantly better than placebo for achieving endoscopic improvement (OR 1.59 [95% CI: 0.88-2.86]).[26]

- It has been reported that 91% of patients experience suboptimal response to biologic therapy within 36 months of initiation.[27] Suboptimal therapy manifested as dose escalation (e.g., to a level twice that recommended), discontinuation, switching, augmentation (i.e., with a non-biologic therapy such as aminosalicylates, immunosuppressive therapy, or antibiotics) as an adjunct to the initial biologic treatment, steroid overuse, disease-related surgery, or disease-related urgent care.[27]

- *Vedolizumab:* While vedolizumab has a favorable safety profile, the efficacy profile is primarily in biologic-treatment naïve patients. There is limited data to support the use of vedolizumab after failure of other mechanisms of action, such as anti-TNFs. In addition, vedolizumab may not be efficacious against extra-intestinal manifestations (EIMs) that affect up to 1 in 3 patients with UC.[28] As discussed in earlier responses, patients rate symptomatic relief as their highest treatment goal; the slower onset of action of vedolizumab compared to other treatment options may pose a problem for maintaining an optimal patient-centered approach to UC management, and in clinical care, often requires co-induction with corticosteroids.[29]

- *TNF antagonists:* While this treatment class has been used for over 20 years in treating UC, a substantial proportion of patients will not respond or lose response to TNF antagonists. There are concerns with this class of treatment with respect to long-term infection, lymphoma, and malignancy risk (which is reflected in the product monograph of these agents), and for patients, **this class of therapy has limited durability:** up to 50% of patients with UC develop immunogenicity to TNF antagonists, which requires either switching treatment, addition of immunomodulators, or dose intensification.[30] There are also concerns about the efficacy and safety of this class of treatment in UC: for example, adalimumab has been demonstrated to be *inferior* to vedolizumab in a head-to-head randomized controlled trial and only 10.9% of patients achieve clinical remission with standard

dosing.[31] In addition, a meta-analysis in CD patients that reported that anti-TNF therapy prior to elective surgery may increase the odds of postoperative infection.[32]

- *Ustekinumab:* Ustekinumab and mirikizumab both target the Th17/IL-23 pathway: ustekinumab targets IL12/23 through the shared p40 subunit whereas mirikizumab specifically blocks IL23p19.[33] These agents have well-established safety profiles, but their uptake in UC has been somewhat limited, particularly in Canada and the group identified that sparse real-world data was a concern. It has previously been demonstrated that ustekinumab is less effective in patients with more severe disease burden and patients who also required corticosteroids with induction were 50% more likely to require ustekinumab discontinuation within 12 months.[34] Ustekinumab dose optimization (either IV reinduction or optimizing to every 4-week maintenance therapy) is often done in clinical care but several controlled studies in IBD have shown that this practice is ineffective.[35,36] Finally, ustekinumab only achieved clinical remission in ~1 in 10 patients with prior exposure to biologic therapy, and in the phase 3 UNIFI clinical trial program, this was mostly limited to patients with prior TNF antagonist exposure and not other mechanisms of action, limiting generalizability.[37]

- *Mirikizumab*, targeting IL23p19, was demonstrated to be effective in moderately-to-severely active UC but has seen limited uptake in Canada. Long-term data on efficacy and safety are lacking. For patients, mirikizumab is often not a preferred agent due to the requirement to administer two subcutaneous injections for each maintenance dose. **Finally, the ability to induce clinical remission with mirikizumab in biologic or tofacitinib-failed patients was limited (15.2% vs. 8.5% in placebo, treatment difference not statistically significant).[38]**

- *Guselkumab,* also targets targeting IL23p19, has been shown to be more efficacious than placebo, however, no head to head studies are available comparing guselkumab with other agents target the IL-23 pathway in UC.[39]

- *Janus kinase inhibitors:* JAK inhibitors are effective therapies in UC but are the least comparable to risankizumab in the current treatment landscape due to unique safety considerations that must be evaluated in all patients. The pan-JAK inhibitor tofacitinib has a Serious Warnings and Precautions Box for serious infections, malignancies, thrombosis, and major adverse cardiac events (MACE).[40] A similar Serious Warnings and Precautions Box is applied to upadacitinib, a JAK-1 selective inhibitor. Accordingly, the patient population that may be considered for a JAK inhibitor is often limited by comorbidities, age, and smoking.

- S1P receptor modulators, such as ozanimod and etrasimod, binds with high affinity to S1P receptors 1 and 5, which are involved in regulation of the immune system.[41] However, there is no longer a patient support for ozanimod in Canada: to our knowledge, this is no longer a prescribed treatment in the Canadian UC landscape. Etrasimod is associated with increased susceptibility to infections (some of which may be serious, including cryptococcal infections which have been reported with this class of therapy due to its mechanism of action). Additionally, S1P receptor modulators are known to cause decreases in heart rate and atrioventricular conduction delays: therefore, all patients require electrocardiogram evaluation and the treatment cannot be used in patients with some pre-existing

cardiac abnormalities. Long-term, there have been signals that hypertension can occur with S1P receptor modulators, and there is an increased risk of macular edema for which patients with uveitis (a common EIM of UC) or diabetes must undergo ophthalmic evaluation. Finally, long-term adherence with oral therapy in UC has been demonstrated to be poor, which may limit the effectiveness of a daily pill option.[42] Thus, there are many patients for whom S1P receptor modulators are not a viable therapeutic option.

Taken together, there remains a significant medical need for additional efficacious, durable, and safe treatment options that provide symptom control and mucosal healing, improve quality of life, and reduce the risk of hospitalization and surgery in the long-term for patients with moderately to severely active UC who have inadequate response or intolerance to conventional or advanced therapies.

5. Place in Therapy

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

Risankizumab is a humanized monoclonal antibody that selectively binds with high affinity to the p19 subunit of human IL-23 cytokine and inhibits IL-23 signalling.[43] There is extensive literature including genetic studies, pre-clinical animal models, and human tissue expression analyses that demonstrate that IL23 expression is central to the pathogenesis of UC (and other immune-mediated diseases). Targeting IL23 specifically has been demonstrated to be superior to other mechanisms of action, including ustekinumab, in both psoriasis and in Crohn's disease.[44]

In reviewing the clinical data, the clinician group believes that risankizumab should be used as the first choice in patients with moderately-to-severely active UC who have failed or are not candidates for other conventional therapy, or who have failed one or more advanced therapies, as risankizumab addresses multiple unmet needs:

Robust Efficacy, including across multiple sub-groups

- The phase 3 clinical program includes two pivotal multicentre, double-blind, placebo-controlled clinical studies of which one is a Phase 2b/3 induction study (Study M16-067)[45], and one is a Phase 3 maintenance study (Study M16-066)[43].
- In the INSPIRE trial, induction therapy with risankizumab 1200 mg IV Q4w was highly efficacious when compared to placebo at Week 12. The primary outcome of clinical remission at Week 12 and all ranked (multiplicity-adjusted) secondary outcomes were met, demonstrating superiority of risankizumab 1200 mg IV over placebo. Secondary endpoints evaluated several types of improvement: symptomatic (clinical response), endoscopic, endoscopic-histologic, and patient-reported quality of life outcomes.

- Extended induction treatment with risankizumab was also demonstrated to be highly efficacious. Comparable rates of clinical response per Adapted Mayo score to those achieved at Week 12 were observed at Week 24 following an additional 12 weeks of risankizumab treatment in patients who do not achieve initial response after 12 weeks of treatment.
- The efficacy of risankizumab was also displayed among advanced therapy inadequate responders (AT-IR) and non-advanced therapy inadequate responders (non-AT-IR) subpopulations during induction. Similar trends to the total study population were observed for the primary and secondary endpoints in both subpopulations regardless of having enrolled a highly refractory patient population. **Close to 75% of subjects were AT-IR and a third of them had previously failed more than 2 advanced therapies and 15% had failed a JAK inhibitor, reflecting IBD patients' realistic journey**. This is a clear differentiator for risankizumab as compared to other advanced therapies, which do not have data to support efficacy in this extent of prior treatment exposure.
- **The non-AT-IR population using risankizumab as first-line therapy showed remarkable efficacy in several key endpoints, notably in endoscopic improvement (EI) with 76.1% of the patients achieved this** endpoint. As such, risankizumab shows the highest percentage of patients achieving EI in the non-AT-IR population to date. This sets risankizumab apart in terms of first-line advanced therapy choice for biologic-naïve patients.
- Maintenance therapy with both doses of risankizumab 180 mg SC and 360 mg SC was highly efficacious and durable.
- Risankizumab is the first drug to demonstrate that patients achieving early symptom resolution also showed improved clinical, endoscopic, and HRQoL outcomes (including improvements in clinically meaningful and relevant patient-reported outcomes studied for the first time, see below) in the long-term.

Fast Acting

- Differences in clinical response were observed as early as Week 4.
- Early symptoms control was also achieved, as risankizumab demonstrated no nocturnal bowel movements, no tenesmus, and a reduction in fecal incontinence and sleep interruption at Week 12.

Long-term efficacy, including mucosal healing

- At Week 52, the primary outcome was met by both risankizumab doses (all $P < 0.001$). Across all ranked secondary outcomes, both doses of risankizumab showed a superior response compared with placebo.
- Treatment with risankizumab was able to display durable remission despite its re-randomization design, high placebo rate and the long duration of the trial (52 weeks).

- Risankizumab demonstrated longer-lasting pharmacodynamic effects post-induction studied in a post hoc analysis showing that treatment effects persist for up to 24 weeks post-induction in some patients, maintaining biomarker suppression (hs-CRP, fecal calprotectin).
- Risankizumab not only demonstrated efficacy in maintaining the treatment benefit gained from the induction treatment but also while discontinuing corticosteroid use.
- Risankizumab demonstrated the highest endoscopic improvement rate (76.1%) observed to date in an AT-naïve UC maintenance trial at Week 52 offering deep disease control, which sets risankizumab apart in terms of first-line advanced therapy choice for biologic-naïve patients.

Safety

- Across both trials, risankizumab was well tolerated and had an acceptable safety profile during induction therapy with 1200 mg IV Q4w and maintenance therapy with 180 mg SC and 360 mg SC Q8w. In general, the proportion of subjects with AEs in each risankizumab arm were generally comparable to the placebo arm with no consistent dose-dependant pattern between the risankizumab arms. Moreover, the safety profile of risankizumab was consistent with its known safety profile in plaque psoriasis, psoriatic arthritis, and Crohn's disease with no new safety signals identified. Extended induction treatment up to 24 weeks of risankizumab 1200 mg IV Q4w did not result in any new safety risk.

Reduction in UC-Related hospitalizations

- Risankizumab is **the first treatment to show statistically significant reduction in hospitalizations through week 12.** Induction treatment with risankizumab resulted in a statistically significant decrease in UC-related hospitalizations (percentage of patients with one or more UC-related hospitalization was 0.8% in the risankizumab vs. 5.5% in the placebo group, $p \leq 0.001$), which is an indicator of the severity of the patient population recruited in the phase 3 trials and its ability to reduce healthcare resource use.
    - Historically, 20–30% of hospitalized patients with severe acute UC undergo colectomy during their admission. Recent studies suggest that this rate remains elevated despite advancements in medical therapy.[5]

Patients' needs

- The treatment benefits of risankizumab also translated **into improvements in clinically meaningful and relevant patient-reported outcomes studied for the first time**, all of which were multiplicity-adjusted met statistical significance, such as reduced bowel urgency, sleep interruption, abdominal pain, nocturnal bowel movements and tenesmus, fecal bowel incontinence, and improved HRQoL as measured by the Inflammatory Bowel Disease Questionnaire (IBDQ) and the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) instruments.

- Risankizumab is the first advanced therapy to demonstrate improvements in PROs such as tenesmus, fecal incontinence, sleep disturbance, urgent bowel movements, reported to be outcomes of interest in the nation-wide survey on unmet needs in patients with IBD.[20]

There is a significant unmet need for patients with moderately-to-severely active UC whose disease is not adequately controlled with conventional medical treatments. Targeting IL23p19 has revolutionized the management of other immune mediated inflammatory diseases, with risankizumab demonstrating **superiority** over ustekinumab in both psoriasis and in Crohn's disease. The phase 3 risankizumab trials in UC demonstrate that this agent is also highly effective and safe in moderately-to-severely active UC. An ongoing randomized head-to-head trial will confirm whether risankizumab is superior to vedolizumab in UC; many Canadian sites including sites from clinicians on this panel are participating in this study. Based on the available efficacy and safety profile of risankizumab across multiple patient populations and multiple endpoints including those that are focused on addressing patient needs and those that are predictive of long-term outcomes, we believe risankizumab will likely become a widely used therapy for moderately-to-severely active UC across first- and second-line indications, in patients with comorbid immune mediated disease, and in patients with UC across the spectrum of moderate-to-severe disease activity.

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?

In Phase 3 trials, patients were selected based on eligibility criteria that broadly included a confirmed diagnosis of active UC with an Adapted Mayo score of 5 to 9 points and endoscopy subscore of 2 to 3 points, and demonstrated inadequate response to, loss of response to, or intolerance to at least one of: aminosalicylates, oral locally acting steroids, systemic steroids (prednisone or equivalent), immunomodulators and/or biologic therapies.[46,47]

We believe that risankizumab is best suited to treat any adult patient with moderately-to-severely active UC as per its use in clinical trials, who have had an inadequate response, loss of response, or were intolerant to conventional therapy, a biologic treatment, or a JAK inhibitor.

These patients are in the most need of intervention as they have active symptoms, lack long-term treatment options and are at high risk of disease progression. Once UC has progressed, patients are at higher risk of disabling digestive symptoms, emergency room visits, hospitalizations, and surgery.

With respect to risankizumab, efficacy was demonstrated across all subgroups. The most relevant subgroups to consider would be patients with limited vs. pancolonic UC disease extent, prior treatment exposure with advanced agents, and moderate vs. severe endoscopic disease activity. Patients across these different phenotypes could be effectively treated with risankizumab. Patients with EIMs or other immune mediated inflammatory diseases that are susceptible to treatment with IL23, such as psoriasis or psoriatic arthritis would be especially good candidates for risankizumab.

Issues with Diagnosis

Following an in-office consultation at presentation, patients require an endoscopy for a definitive UC diagnosis. Physicians also may use other modalities to comprehensively evaluate the disease, including but not limited to tests for complete blood count (CBC), albumin, C-reactive protein, fecal calprotectin, examination of stool for infectious organisms, and in some centers, intestinal ultrasonography. The diagnosis of UC is made based on clinical, endoscopic, and histologic features. There is a broad differential diagnosis to consider (e.g., Crohn's disease, other types of colitis – medication induced, infectious, ischemic colitis), but these are generally excluded based on other tests.

In patients with previously established UC, repeated endoscopy is often not conducted as it is invasive, requires bowel preparation, carries risks of procedural-related complications, and access may be limited with long wait times. Therefore, treatment decisions in patients with established disease may be made on the basis of symptoms and other objective measures such as fecal calprotectin, a non-invasive stool biomarker that is well correlated with endoscopic appearance.

Patients Not Suitable for Risankizumab

UC patients who have mildly-to-moderately active disease, or those with previous mildly-to-moderately active disease and whose remission can be adequately maintained with conventional treatments such as 5-ASA are least suitable for treatment with Risankizumab. IL23 therapies have limited efficacy in patients with axial spondyloarthritis – therefore, these patients may be better treated with another agent. In addition, patients that present with ASUC are not appropriate for initial therapy, as these patients require inpatient intravenous corticosteroids and are generally excluded from all outpatient moderate-to-severe UC trials.

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?

There is a need for novel targeted therapies with new mechanisms of action that provide sustained clinical and endoscopic outcomes, as well as exhibit improved benefit-risk profiles across different patient populations when used as long-term maintenance therapy. In clinical trials, outcomes are measured by the following endpoints: clinical remission, clinical response, disease activity, patient-reported symptoms, stringent endoscopic and histologic outcomes that included mucosal improvement and healing, as well as HRQoL outcomes. Data are available for 12 weeks (induction therapy), 24 weeks (extended induction therapy), and 52 weeks (maintenance therapy).[43,45]

In the INSPIRE trial, induction therapy with risankizumab 1200 mg IV Q4w was highly efficacious when compared to placebo at Week 12. The primary outcome of clinical remission at Week 12 and all ranked (multiplicity-adjusted) secondary outcomes were met, demonstrating superiority of risankizumab 1200 mg IV over placebo. Secondary endpoints evaluated several types of improvement: symptomatic, endoscopic, endoscopic-histologic, and patient-reported quality of life outcomes. Differences in clinical response were observed as early as Week 4. Early symptoms control was also achieved, as risankizumab demonstrated no nocturnal bowel movements, no tenesmus, and a reduction in fecal incontinence and sleep interruption at

Week 12, novel endpoints studied for the first time. Additionally, induction treatment with risankizumab resulted in a statistically significant decrease in UC-related hospitalizations in only 12 weeks. The efficacy of risankizumab was also displayed among advanced therapy inadequate responders (AT-IR) and non-advanced therapy inadequate responders (non-AT-IR) subpopulations during induction. Similar trends to the total study population were observed for the primary and secondary endpoints in both subpopulations. Although extended duration is not specifically mentioned in the risankizumab product monograph,[48] extended induction treatment with risankizumab was demonstrated to be efficacious. Comparable rates of clinical response per Adapted Mayo score to those achieved at Week 12 were observed at Week 24 following an additional 12 weeks of risankizumab treatment.

Maintenance therapy with risankizumab 180 mg SC and 360 mg SC was also highly efficacious and durable regardless of having enrolled a highly refractory patient population. Close to 75% of subjects were AT-IR and a third of them had previously failed more than 2 advanced therapies and 15% had failed a JAK inhibitor. At Week 52, the primary outcome was met by both risankizumab doses (all $P < 0.001$). Across all ranked secondary outcomes, both doses of risankizumab showed a superior response compared with placebo. Treatment with risankizumab was able to display durable remission despite its re-randomization design, high placebo rate and the long duration of the trial (52 weeks). Risankizumab not only demonstrated efficacy in maintaining the treatment benefit gained from the induction treatment but also while discontinuing corticosteroid use. The treatment benefits of risankizumab also translated into numerical improvements in novel patient-reported symptoms such as reduced bowel urgency, abdominal pain, nocturnal bowel movements and tenesmus, and improved HRQoL as measured by the Inflammatory Bowel Disease Questionnaire (IBDQ) and the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) instruments.

Across both trials, risankizumab was well tolerated and had an acceptable safety profile during induction therapy with 1200 mg IV Q4w and maintenance therapy with 180 mg SC and 360 mg SC Q8w. In general, the proportion of subjects with AEs in each risankizumab arm were generally comparable to the placebo arm with no consistent dose-dependent pattern between the risankizumab arms. Moreover, the safety profile of risankizumab was consistent with its known safety profile in plaque psoriasis, psoriatic arthritis, and Crohn's disease with no new safety signals identified. Extended induction treatment up to 24 weeks of risankizumab 1200 mg IV Q4w did not result in any new safety risk.

The duration of treatment is highly dependent on the therapy and on the patient's disease activity and personal preferences. Further, as discussed in earlier responses, some treatments have more rapid onset of action than others and this should be considered before deciding a treatment has failed. In general, we believe that a treatment should be used for three months, at which point a determination of treatment response can be made.

Overall, the clinical trial outcomes indicate that a broad range of use is possible in clinical practice – from first line advanced therapy to treatment of patients with inadequate response or intolerance to multiple advanced therapies. Importantly, the robust clinical, endoscopic, QOL and hospitalization data could translate into changing the course of disease with risankizumab. Risankizumab also

breaks the efficacy ceiling in several key primary and secondary endpoints in the non-AT-IR population. Most of the Group indicated that it should be the treatment of choice in most patients with Ulcerative Colitis due to the favorable benefit-risk ratio and its ability to achieve key primary and endpoints early and during maintenance.

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

The risankizumab development program aligned with what is done in clinical practice, including a patient population that was both advanced therapy-naïve and heavily pre-treated (75% were AT-IR and >25% of patients had two or more prior advanced therapies) and aligns with disease management strategies outlined in STRIDE-II.[8] The Canadian IBD Physicians Group recommends that management strategies strive for complete remission, which is defined as both symptomatic and endoscopic remission and align with Canadian Consensus Guidelines.

In the first three months of therapy, a meaningful improvement in symptoms as measured by elements of the PRO2 (stool frequency and abdominal pain) should be demonstrated. Patients would be expected to be in symptomatic remission and off corticosteroids by six months. The extended induction data from the clinical trial indicates that up to half of patients who have not yet symptomatically responded by 3 months can achieve a meaningful benefit by continuing treatment to 6 months. Therefore, unless there is worsening in the first three months of therapy, the group felt that treatment should be continued for a minimum duration of six months to evaluate response.

Symptomatic improvement should be accompanied be a decrease in biomarkers (C-reactive protein and fecal calprotectin) of inflammatory activity in the first six months. Although, the program demonstrated robust endoscopic response in the first three months, **the Group would not assess endoscopic activity until 9-12 months into therapy**. In addition, the consensus Group recognized that because of the substantial impact of UC on a patient's daily life activities and HRQoL, it is imperative to consider the patient's perspective when making treatment decisions. In many instances, factors that influence patient decisions relating to therapy choice and goals of therapy are not the same as those of the treating clinician.

The Canadian IBD Physicians Group would recommend discontinuing treatment with risankizumab if there is worsening of symptoms or if there is an inadequate response, but this is not broadly anticipated based on available clinical data demonstrating that a large proportion of patients will respond to therapy over the first six months. In instances where there is an inadequate response to risankizumab as first line biologic therapy in moderate to severe UC, then a switch to another class of agents is warranted.

5.5 What settings are appropriate for treatment with risankizumab? Is a specialist required to diagnose, treat, and monitor patients who might receive risankizumab?

In the clinical experience of the Canadian IBD Physicians Group, risankizumab would need to be administered in clinic by a trained health care professional during the induction phase under the supervision of a healthcare professional experienced in the management of patients with UC. Patients would be trained to use the on-body injector for maintenance therapy and would require training to be comfortable with the device which will happen during their last visit to the infusion clinic during induction.

6. Additional Information

Canada has one of the highest prevalence rates of IBD in the world and although the arrival of previous biologic agents has reshaped the UC disease management landscape, there remains a significant unmet need. Based on a patient survey, 29% of patients reported that their IBD is uncontrolled with an additional 33% of patients being unsure, 73% of patients self-reporting that IBD had a moderate to extreme impact on their QoL in the past year. **Approximately 24% of patients reported having to go to the Emergency Room for care, which is a heavy burden to our healthcare systems**. In addition, the clinical relapse rates remain high with available biologic agents approved for use in UC and patients continue to experience a loss of response in the first year during maintenance treatment.

There is an alarmingly frequent need for dose escalation using available biologics to levels that are off label to achieve treatment response. This is a reality in clinical practice for an estimated 30-50% of patients Canada wide. The prevalence of this practice in the clinic introduces unnecessary delays in the patient treatment journey while driving up costs of care. The current advanced therapies were approved on their ability to improve symptoms and it is acknowledged that this is not enough to change the course of disease.

The mechanism of action seen with risankizumab provides sustained clinical and endoscopic outcomes across different patient populations when used as induction and maintenance therapy. The unparalleled degree of clinical and endoscopic response could help reduce and delay many other long-term, downstream consequences of UC, including hospitalizations, surgical interventions, steroid use, and loss of functioning in daily life activities. Thus, the favourable efficacy, safety, and durability profile of risankizumab makes it a prime candidate for the treatment of patients with moderate to severe UC. Nationwide availability and coverage of this biologic agent is expected to mark the next leap forward in the current treatment landscape.

The Canadian IBD Physicians Group foresees a broad range of use for risankizumab, including first line advanced therapy and to treat patients with inadequate response or intolerance to multiple advanced therapies. Critically, the robust clinical, QOL, hospitalization, endoscopic data and mucosal healing seen with Risankizumab could well translate into changing the course of disease in moderate to severe UC. Risankizumab also breaks the efficacy ceiling in several key primary and secondary endpoints in the non-AT-IR population. The Group would strongly recommend that

patients with moderate to severe UC be given access to this favourable treatment option.

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.

   <Enter Response Here>

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.

   <Enter Response Here>

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. Christopher Ma
Position: Associate Professor, Departments of Medicine and Community Health Sciences University of Calgary Inflammatory Bowel Disease Unit
Date: 23-03-2025

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

Table 1: Conflict of Interest Declaration for Clinician 1

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AbbVie				X
Alimentiv Inc.				X
Amgen		X		
AVIR Pharma Inc.	X			
Celltrion			X	
Domain Therapeutics	X			
Eupraxia	X			
Eli Lilly				X
Ferring				X
Forte Biosciences		X		
Fresenius Kabi			X	
Gilead		X		
Janssen			X	
Mirador Therapeutics	X			
Pendopharm		X		
Pfizer				X
Sanofi			X	
Takeda			X	
Tillotts Pharma		X		

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

Declaration for Clinician 2

Name: Dr. Remo Panaccione
Position: Gastroenterologist, Professor of Medicine, University of Calgary
Date: 23-03-2025

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

Table 2: Conflict of Interest Declaration for Clinician 2

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Abbvie				X
Alimentiv				X
Amgen			X	
AnaptysBio		X		
Astra Zeneca	X			
Bristol Meyers Squibb			X	
Boehringer Ingelheim	X			
Eli Lilly			X	

Ferring	X			
Fresenius Kabi	X			
Galapagos	X			
Gilead Sciences		X		
Glaxo-Smith-Kline	X			
JAMP Biomed	X			
Janssen				X
Merck			X	
Mylan	X			
Oppilan	X			
Organon	X			
Pandion Pharma	X			
Pfizer			X	
Progenity	X			
Protagonist Therapeutics	X			
Roche			X	
Satisfai Health			X	
Sandoz		X		
Sanofi			X	
Takeda Pharmaceuticals			X	
Ventyx		X		

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

Declaration for Clinician 3

Name: Dr. Cynthia Seow
Position: Professor of Medicine, University of Calgary
Date: 26-03-2025

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

Table 3: Conflict of Interest Declaration for Clinician 3

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

Takeda		x		
Pfizer		x		
Fresenius Kabi	x			
Bristol Myers Squibb	x			
Pharmascience	x			

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

Declaration for Clinician 4

Name: Dr. John Marshall
Position: Professor of Medicine
Date: 28-03-2025

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

Table 4: Conflict of Interest Declaration for Clinician 4

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
AbbVie				X
Amgen		X		
Avir Pharma	X			
Bausch Health	X			
Celltrion			X	
Janssen			X	
Lilly			X	
Organon		X		
Pfizer			X	
Pharmascience	X			
Sandoz	X			
Sanofi		X		
Takeda			X	

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

Declaration for Clinician 5

Name: Dr. John Igoe
Position: Assistant professor of medicine, Dalhousie University, The Moncton Hospital
Date: 26-03-2025

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

Table 5: Conflict of Interest Declaration for Clinician 5

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
AbbVie			X	
Janssen	x			
Takeda		x		
Merck	x			
BioJamp		x		
GSK		x		
Eli Lilly	x			

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

Declaration for Clinician 6

Name: Dr. Jesse Siffledeen
Position: Gastroenterologist, Covenant Health, Edmonton AB
Date: 25-03-2025

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

Table 5: Conflict of Interest Declaration for Clinician 6

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

Celltrion				X
Eli Lilly		X		
Ferring		X		
Fresenius Kabi		X		
Jamp			X	
Janssen			X	
Lupin	X			
Organon	X			
Pendopharm	X			
Pfizer		X		
Pharmascience	X			
Sanofi		X		
Takeda			X	

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

Declaration for Clinician 7

Name: Dr. Brian Bressler
Position**:** Staff Gastroenterologist
Date: 24-03-2025

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

Table 5: Conflict of Interest Declaration for Clinician 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**
Abbvie				x
Alimentiv				x
BMS		x		
Celltrion	x			
Eli Lilly		x		
Janssen				x
Organon		x		
Pfizer				x
Sandoz	x			

Takeda				x

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

Declaration for Clinician 8

Name: Dr. Sundeep Singh
Position: Gastroenterologist, Vancouver General Hospital
Date: 24-03-2025

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

Table 5: Conflict of Interest Declaration for Clinician 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**
Abbvie		X		
Takeda		X		
Pfizer		X		
Eli Lilly		X		
Celltrion		X		

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

Declaration for Clinician 9

Name: Dr. Mark MacMillan
Position: Medical Director of Endoscopy
Date: 24-03-2025

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

Table 5: Conflict of Interest Declaration for Clinician 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**
AbbVie	X			
Janssen	X			

Takeda	X			
Organon	X			

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

Declaration for Clinician 10

Name: Dr. Mark Borgaonkar
Position: Gastroenterologist, Newfoundland and Labrador Health Services
Date: 26-03-2025

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

Table 5: Conflict of Interest Declaration for Clinician 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**
Amgen	X			
Abbvie		X		
Janssen		X		
Astrazeneca	X			
BMS	X			
Celltrion	X			
Biojamp	X			
Pfizer	X			
Lilly		X		
Takeda		X		
Sandoz	X			
Innomar	X			
Organon	X			

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

Declaration for Clinician 11

Name: Dr. Vivian Huang
Position: Gastroenterologist, Associate Professor, University of Toronto
Date: 30-03-2025

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

Table 5: Conflict of Interest Declaration for Clinician 11

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Abbvie			X	
Amgen	X			
BioJamp	X			
Celltrion		X		
Eli Lilly	X			
Ferring	X			
Fresenius Kabi		X		
Johnson and Johnson			X	
Organon	X			
Pfizer	X			
Takeda			X	

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

Declaration for Clinician 12

Name: Dr. Daniel Green
Position: Gastroenterologist
Date: 30-03-2025

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

Table 5: Conflict of Interest Declaration for Clinician 12

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Abbvie		x		
Amgen	x			
Celltrion	x			
Ferring	x			
Janssen		x		

Knight	x			
Lilly	x			
Pfizer	x			
Takeda	x			

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

Declaration for Clinician 13

Name: Dr. Yvette Leung
Position: Gastroenterologist, St Paul's Hospital, IBD Centre of BC
Date: 01-04-2025

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

Table 5: Conflict of Interest Declaration for Clinician 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**
Pfizer			X	
Abbvie			X	
Takeda			X	
Eli Lilly			X	
Janssen		X		

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

Declaration for Clinician 14

Name: Dr. Chadwick Williams
Position: Assistant Professor, Dalhousie University,
Date: 31-03-2025

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

Table 5: Conflict of Interest Declaration for Clinician 14

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	
Janssen		X		
Takeda			X	

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

Declaration for Clinician 15

Name: Dr. Edmond-Jean Bernard
Position: Asso Professor , Gastroenterology CHUM, Université de Montreal
Date: 30-03-2025

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

Table 5: Conflict of Interest Declaration for Clinician 15

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	
Janssen			X	
Pfizer			X	
Takeda	X			
Celltrion	X			
Organon	X			
Fresenius Kabi	X			
Pendopharm	X			
Merck	X			
Amgen	X			

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

Declaration for Clinician 16

Name: Dr. Christopher Sheasgreen
Position: Assistant Professor, Dalhousie University
Date: 02-04-2025

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

Table 5: Conflict of Interest Declaration for Clinician 16

	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			
Janssen	X			
Takeda	X			
Organon	X			
BioJamp	X			
Eli Lilly	X			

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

Declaration for Clinician 17

Name: Dr. Michael Stewart
Position: Assistant Professor
Date: 01-04-2025

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

Table 5: Conflict of Interest Declaration for Clinician 17

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Celltrion	X			
Eli Lilly	X			
Pfizer	X			
Janssen			X	
Takeda	X			
Abbvie			X	

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

Declaration for Clinician 18

Name: Frank Hoentjen
Position: Professor of Medicine, IBD Director.
Date: 31-03-2025

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

Table 5: Conflict of Interest Declaration for Clinician 18

	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			

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

Declaration for Clinician 19

Name: Neeraj Narula
Position: Director of IBD Clinic at Hamilton Health Sciences
Date: 30-03-2025

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

Table 5: Conflict of Interest Declaration for Clinician 19

	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	
Janssen		X		
Takeda		X		
Eli Lilly	X			
Fresenius Kabi	X			
Pfizer		X		
Viatris	X			
Sandoz	X			
Iterative Health			X	
Innomar Strategies		X		

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

Declaration for Clinician 20

Name: Jeffrey McCurdy
Position: Assistant professor, University of Ottawa
Date: 01-04-2025

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

Table 5: Conflict of Interest Declaration for Clinician 20

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Pfizer		X		
J&J		X		
AbbVie		X		
Takeda		X		

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

Declaration for Clinician 21

Name: Waqqas Afif
Position: Associate Professor of Medicine, Gastroententology and Hepatology Division Director McGill University Health Center
Date: 01-04-2025

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

Table 5: Conflict of Interest Declaration for Clinician 21

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	
Johnson & Johnson			X	
Sanofi			X	
Eli Lilly			X	
Pfizer		X		
Takeda		X		
Celltion		X		
Amgen	X			
Avir	X			
Merck	X			

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

Declaration for Clinician 22

Name: Talat Bessissow
Position: Associate Professor of Medicine, Gastroenterologist.
Date: 01-04-2025

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

Table 5: Conflict of Interest Declaration for Clinician 22

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	
Johnson & Johnson			X	
Pfizer			X	
Takeda			X	
Alimentiv			X	
Iterative scope			X	
CSF Vifor, ,		X		
Eli Lilly		X		
Sandoz		X		
BMS	X			
Celltrion	X			
Ferring	X			

Fresenius Kabi	X			
Gilead	X			
Merck	X			
Mirium	X			
Pendopharm	X			
Roche	X			
Sanofi	X			

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

Declaration for Clinician 23

Name: Dr Marc Bradette,
Position: Clinical Professor of Medicine at Université Laval, Québec and Head of the Gastroenterology Department, Centre Hospitalier Universitaire de Québec
Date: 31-03-2025

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

Table 5: Conflict of Interest Declaration for Clinician 23

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Takeda	X			
AbbVie	X			
Pfizer	X			
Janssen	X			
EI Lilly	X			

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

Declaration for Clinician 24

Name: Dr. David Pearson
Position: Clinical Assistant Professor UBC
Date: 02-04-2025

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

Table 5: Conflict of Interest Declaration for Clinician 24

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

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

Declaration for Clinician 25

Name: Brian Gordon Feagan
Position: Self Employed MD
Date: 04-03-2025

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

Table 5: Conflict of Interest Declaration for Clinician 25

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

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

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