# Common Drug Review
## *Patient Group Input Submissions*

## Infliximab (Inflectra) for treatment of Crohn's disease and Ulcerative Colitis

| **Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.** |
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| Crohn's and Colitis Canada's Patient Group Input – permission granted to post |
| GI (Gastrointestinal) Society - – permission not granted to post |

**CADTH received patient group input for this review on or before May 2, 2016**

CADTH posts all patient input submissions to the Common Drug Review received on or after February 1, 2014 for which permission has been given by the submitter.

The views expressed in each submission are those of the submitting organization or individual; not necessarily the views of CADTH or of other organizations. While CADTH formats the patient input submissions for posting, it does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no personal information is included in the submission. The name of the submitting patient group and all conflict of interest information are included in the posted patient group submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

# Crohn's and Colitis Canada

## 1 General Information

### 1.1 Information Gathering

It was challenging to collect patient feedback for Inflectra considering that there are no people living with Crohn's disease and ulcerative colitis in Canada who are currently taking this treatment for clinical trials. Crohn's and Colitis Canada wants people living with IBD to have greater options, however the organization feels it is necessary to approve treatments based on evidence that demonstrates that the drug is safe and efficacious for each specific indication.

Information was drawn from the Crohn's and Colitis Canada (CCC) published reports, including the 2012 "Impact of Inflammatory Bowel Disease (IBD) Report" and educational brochures found on the organization's website. Experiences on the innovator drug were pulled from previous drug submissions made to CADTH. In addition, results from the Gastrointestinal Society survey on SEBs (2015) were used to highlight thoughts and concerns from Crohn's and colitis patients.

## 2 Information about the Submitting Patient Group

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| **Name of the drug** | Inflectra (Subsequent Entry Biologic) |
| **Indication of interest** | Crohn's disease and ulcerative colitis |
| **Name of the patient group** | Crohn's and Colitis Canada |
| **Name of the primary contact for this submission:** | [redacted] |
| Position or title with patient group | Manager, Public Policy & Stakeholder Relations |
| Email | [redacted] |
| Telephone number(s) | 416-920-5035 ext.229 |
| **Name of author (if different)** | |
| **Patient group's contact information:** Email | Same as above |
| Telephone | 416-920-5035 |
| Address | 600-60 St.Clair Avenue East, Toronto, ON |
| Website | www.crohnsandcolitis.ca |
| **Permission is granted for CADTH to post this submission** | **X Yes** ☐ No |

### 2.1 Submitting Patient Group

Crohn's and Colitis Canada is the only national, volunteer-based charity focused on finding the cures for Crohn's disease and ulcerative colitis, the two main forms of inflammatory bowel disease (IBD), and improving the lives of children and adults 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 $94 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 go-here.ca decal and free mobile app;
- raising awareness about these Canadian diseases with bilingual public advertising campaign via TV, print, radio and digital carriers;
- offering kids with Crohn's or colitis camp experience; and
- providing an online peer support program to newly diagnosed people.

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 45 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.

### 2.2 Conflict of Interest Declarations

***a) We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements:***

In the fiscal year 2014-2015, Crohn's and Colitis Canada received less than 11% of its total revenue from pharmaceutical companies. The non-restricted grants are used to sponsor patient education events, research and medical conferences, educational brochures, youth camps and post-secondary scholarships for inflammatory bowel disease (IBD) patients. The majority of Crohn's and Colitis Canada's funding comes from individual donors contributing to fundraising events including the annual Gutsy Walk.

***b) We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission:***

None of the pharmaceutical companies have played a role in contributing to this submission. This patient input submission was developed and prepared solely by the staff at Crohn's and Colitis Canada.

## 3 Disease/Condition and Current Treatment Information

### 3.1 Impact of Condition on Patients

Crohn's disease and ulcerative colitis are disabling, life-long gastrointestinal conditions that primarily affect working-age Canadians. These diseases are twice as common as multiple sclerosis or Parkinson's disease and are about as common as Type 1 diabetes or epilepsy. Sadly, Canada has a rate that ranks highest in the world. New evidence suggests that these diseases are now escalating in children at an alarming rate, especially those under 10 years old. Over the past 15 years, the number of children with Crohn's and colitis has increased by more than 40%. With an expected 10,200 new diagnoses every year, in addition to the nearly quarter of a million Canadians living with Crohn's and colitis, these diseases are becoming increasingly prevalent in Canada.

## Crohn's and Colitis Canada's Patient Group Input to the Common Drug Review at CADTH

Overall, Canadians have more reasons to be concerned about Crohn's and colitis than anyone else in the world. With one in every 150 Canadians being diagnosed with Crohn's disease and ulcerative colitis - the two most common forms of Inflammatory Bowel Disease (IBD) - these conditions are becoming "Canada's diseases". Families new to Canada, predominantly those of South Eastern Asian descent, are developing Crohn's and colitis for the first time – often within the first generation. The burden that Crohn's disease and ulcerative colitis places on individuals and the healthcare system is significant and will continue to grow as the number of people diagnosed increases.

IBD symptoms include bloody diarrhea, bloating, abdominal pain and fatigue, however the aspect that the majority of interviewees pointed out as the most unbearable is the lack of control over their bowel movements, including the urgent and frequent need of the bathroom. This corresponds with results based on a Crohn's and Colitis Canada 2011 survey where 73% of respondents affected by IBD said they experienced between five to 20 or more bowel movements a day. Some expressed concern about the increased risk of colon cancer with longstanding IBD. During times of active disease (flare ups), patients spend a lot of time in the bathroom, feeling like they live in the bathroom. Even during times of remission, people with IBD feel that they can't be too far away from the bathroom. Blood in the stool and abdominal pain were noted as important aspects of the disease, however bathroom access dominated concerns since it changed people's lifestyle. As one interviewee stated, "when you have to go to the washroom 20 times a day, it impacts everything you do."
People living with Crohn's disease and ulcerative colitis must limit their activities. These diseases make it more challenging to work. "You simply can't lead a normal life of working and going to the office." Some of those interviewed had compassionate employers that allowed them to work from home, and others faced scrutiny from their bosses and colleagues for taking frequent 'bathroom breaks' or taking too many sick days of absence. These diseases result in episodic and invisible disabilities. Ignorance can easily set in at the workplace. Because of the stigma associated with these diseases, it is difficult for an individual to disclose their condition.

According to a Crohn's and Colitis Canada's 2012 publication, The Impact of IBD Report, 43% of employed people with Crohn's and colitis took time off work per year, and each employed person with either colitis or Crohn's disease took 7.2 days off per year due to their chronic condition. The report also highlights that people with colitis or Crohn's disease are more likely to have lower labour participation rates than the general population, ranging from three to 13% less employment. Caregiver work absences in Canada are estimated to cost $7 million per year for parents of paediatric IBD cases, plus $86 million per year for severely ill people with IBD.

When patients are not receiving effective treatments, they must also limit their leisure activities (such as going out to dinners, movies and concerts), doing physical activities and using the public transportation system. Thirty-four per cent of survey respondents frequently missed out on playing sports, 22% missed school trips, 20% skipped family vacations, 40% avoided parties and 22% did not attend special events, which includes, graduations or family weddings. One interviewee missed the first few months of her newborn son's life because she was hospitalized for colitis. This is time lost that she will never gain back.

### 3.2 Patients' Experiences With Current Therapy

**To date there are no SEBs that have been indicated for Crohn's disease and ulcerative colitis in Canada.**

Overall the patients interviewed for previous innovator biologic submissions said that they responded well to treatment. Where first line treatments have failed, innovator biologic drugs have been able to achieve remission in patients. Patients reported a reduction in the number of bowel movements, decreased fatigue and less pain. Remission also helped to alleviate the psychological stress associated with the inability to access washrooms.

Biologics offer people with severe forms of IBD a new treatment option, other than surgery, to help them manage their disease. One interviewee, when describing an innovator drug said, "[Biologics are] like insulin for diabetes." Another interviewee said, "with steroids I was at 60% but with [innovator biologic] I'm at 95%." According to those interviewed for previous drug submissions, these innovator biologics helped them achieve as close to a normal life as possible.

Overall, biologics are lowering surgery and hospitalization rates in Canada. A study explored the economic cost and shift in the burden of care for Crohn's disease. It compared hospitalization, outpatient and medication costs from 1994/1995 to a decade later from 2003/2004 and found that the costs of care (hospitalization and outpatient care) decreased between 1994/1995 from a mean of $12,417 per year [1] to a mean of $10,952 per year[2] in 2003/2004.

In 1994-1995 the mean of the costs of care was $12,417 per year. Here is the breakdown:

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| -Hospitalization | $7,115 (57.3%) |
| -Outpatient care | $4,858 (39.1%) |
| -Medications | $ 444 (3.6%) |

In 2003-2004 costs of care was a mean of $10,952 per year. Here is the breakdown:

| | |
|---|---|
| -Hospitalization | $2,593 (31.4%) ↓ |
| -Outpatient care | $2,753 (33.3%) ↓ |
| -Medications | $2,753 (33.3%) ↑ |

Biologics have also been attributed to lowering the rates of surgery. In one-quarter to one-third of patients with UC, surgery is recommended as a cost-effective treatment. Surgery may alleviate the symptoms experienced but it is not a cure and does not necessarily improve the quality of life. Patients can experience post-surgery complications including continence/soiling, poor pouch function, pouchitis and sexual dysfunction. Sadly, many females, who undergo surgery, are at an increased risk of losing fertility. One interviewee suggested that surgery should only be an option of last resort.

### 3.3 Impact on Caregivers

Caring comes with challenges for caregivers affected by Crohn's disease and ulcerative colitis. Absences from work, high costs of care, fatigue and stress can take a toll on the caregiver's mental health and physical wellbeing. Caregivers often act as advocates for loved ones and take on the burden of care,

[1] Feagan *et al*., American Journal of Gastroenterology, 2000; 95:1955-60.
[2] Kappelman *et al*., Gastroenterology, 2008; 135:1907-13.

including financial out-of-pocket costs associated with managing these diseases. The overall cost of caregiving for people living with severe forms of Crohn's and colitis is estimated to be at $86 million annually.

With increasing numbers of children being diagnosed with IBD, parents play an important caregiver role. Based on the Impact of IBD Report, the caregiver costs for parents of children living with Crohn's and colitis totalled $7 million for the estimated 5,900 children with IBD in Canada in 2012

# 4 Information About the SEB Being Reviewed

### 4.1 What Are Patients' Expectations for the SEB?

Ultimately patients want to **improve their quality of life**. This encompasses symptom relief, clinical remission and alleviation from the anxiety and stress that comes from needing a washroom. People affected by IBD want to lead as normal a life as possible. They want to be engaged in their family life and active in their career development or education. They want to be able to manage life without interruptions (short or long term absences) due to a flare-up. However, people affected by IBD also want to ensure that the drug prescribed is proven to be safe, efficacious and clinically proven in patients with IBD. Patients want SEBs to be held to the same rigour of review as their reference innovator drug. In addition, patients want to feel empowered and engaged in the treatment choices they make with their medical practitioner – many factors may weigh in when patients and their caregivers decide on a treatment path (including the mode of drug delivery, support programs, frequency of dosage, etc…).

The introduction of SEBs, if indicated for Crohn's disease and ulcerative colitis, will **increase treatment options**, prevent surgeries and decrease episodes of active disease (flare-up). Currently, the alternative to failed biologic treatments is often surgery. SEBs may provide more therapeutic options for patients. And for patients who have failed on current available biologic treatment, the introduction of SEBs, if clinically proven, provides patients and their gastroenterologists with alternative treatment options.

However, patients express concern on the **safety and efficacy of SEBs**. This is correlates to the results from the recent survey on SEBs. When asked about important factors for SEB regulation in Canada, survey respondents identified the following factors, ranked in order of priority:

1) Safety
2) SEB review and approval should be identical to originator
3) SEB tested for all indications/diseases
4) More treatment options
5) SEBs clinically tested in Canadians

Manufacturers of SEBs have yet to **demonstrate clinical rigor and scientific evidence for indications of Crohn's disease and ulcerative colitis**. According the Health Canada guidelines, manufacturers of SEBs are not required to provide the same level of clinical and non-clinical results as their innovator biologic counterparts, since information submitted for the drug review process will rely on information of the biologic innovator. While the safety and efficacy of the SEB must be shown to be sufficiently similar to that of the reference biologic drug, there is also a combination of "analytical testing, biological assays, non-clinical data, and clinical data that is used in the final determination of similarity." Though the formula may be similar, there is still no understanding on how slight alterations in these molecules

(resulting from differences in manufacturing processes) may affect patients. Furthermore, the relatively sparse clinical data available to researchers and medical practitioners may limit understanding the efficacy and safety of a particular SEB. This process is concerning to patients, even if similarity to the reference biologic drug is shown.

As one interviewee in a former drug submission said, "in the construction business when I have a flare up, I get tired and work becomes harder to do, staying home is not an option. In this work environment I don't get 'understanding' or 'empathy' from colleagues when I want to go the bathroom…For people like me there is no coverage from work. You have to look at the drug from the benefit it provides rather than the costs because when you are at 100% you don't need to worry about being sick, feeling tired and wondering about who is going to take care of your kids."

It is also concerning that the results from the clinical and non-clinical testing can be used to **extrapolate the findings to other diseases**. For example, the SEB that is currently under review in Canada has undergone clinical trials in patients with rheumatoid arthritis and ankylosing spondylitis and will be extrapolated to use and treat patients with psoriatic arthritis. There is concern that extrapolation to other conditions that were not originally indicated, including Crohn's disease and ulcerative colitis, may occur. SEBs should have the appropriate clinical evidence in order to understand its specific effect on the diseases for which it is prescribed. Patients may feel particularly vulnerable if they have a disease in which the SEB has not been clinically tested – they are real world clinical trial participants without the same level of medical support, monitoring, and informed consent that a clinical trial requires and provides.

Gastroenterologists, general practitioners and pharmacists as well as patients doing well on a biologic innovator drug should be aware of the risks and benefits of substitution. Without scientific evidence and clinical data on the safety and efficacy of SEBs for IBD indication, we **caution against the therapeutic substitution or interchangeability**, in accordance with Health Canada's recommendations. Further clinical research is needed to demonstrate the potential effects and impact switching may have on patients living with Crohn's disease and ulcerative colitis.

# 5 Key Messages

Please provide the key points of your submission, in up to five bullet points.

- SEBs offer greater choice and treatment options for patients.
- Crohn's disease and ulcerative colitis are complex diseases that require individualized treatment plan and care.
- SEBs have yet to demonstrate clinical rigor and scientific evidence for indications of Crohn's disease and ulcerative colitis.
- Provincial drug plans must not introduce switching to those who are currently responding well to the innovator drug. These effects are yet unknown, and switching may negatively lead to a drop in remission rates and increased hospitalization and surgery rates.
- Due to a lack of scientific evidence, patients express concern on the safety and efficacy of SEBs and caution against switching.
- We understand that provinces face a difficult financial situation, and we all need to ensure that healthcare expenditures are judicious with demonstrated improvement in outcomes. We urge the

provinces to carefully consider all the factors mentioned in this submission when approving SEB use for Crohn's disease and ulcerative colitis.

# 6 Additional Information

**Providing Experiential Information**

Crohn's and Colitis Canada has received inquiries from the patient population regarding SEBs. The organization will hold patient education webinars in both languages to help provide a balanced educational session on SEBs. It is important to note however that there continues to be significant concern around the switching from a current innovator to an SEB. Patients are telling us that they do not wish to be forced to switch from a drug that is working well and keeps them in remission. Crohn's and Colitis Canada believes it is imperative that we share these concerns with public drug programs

# 7 Comments on Potential Ways SEBs Can be Used

**CDR reviewers and CDEC members will not review or use information in Section 8; however, drug plans may consider this information in their decision-making.**

Briefly provide your comments on the following scenarios or you may wish to provide other comments.

Overall, people affected by Crohn's disease and ulcerative colitis want greater treatment options available to them but, they want to ensure that prescribed drugs have been validated for efficacy and safety for their disease indication. A recent survey[3] on SEBs demonstrated that nearly all respondents rate safety and efficacy as the most important factors for SEB regulation in Canada. Nearly 80% of respondents said that **they, together with their physician**, should have sole authority to decide the most suitable biologic medicine to treat their disease.

- The SEB will be used instead of the originator (reference/brand name) product with physician approval before patient receives any treatments.

  Crohn's and Colitis Canada believes that patients should have choice and greater options in treatment. This scenario can occur with informed consent by the patient, together in consultation with their physician. If the patient and the physician feel that the innovator biologic is the most appropriate treatment, then they should have that choice available to them.

- The SEB would be replacing the originator product with physician approval once the patient has been on the originator product for a period of time, i.e. a one-time switch

  Again, patients doing well on a drug should not be switched. The patient must be informed on the potential consequences and make this decision together in consultation with their physician.

[3] Gastrointestinal Society, Subsequent Entry Biologics Survey, August 2015, n=423)

- The SEB will be used instead of the originator product without physician approval before patient receives any treatments

  No, this must not occur at any cost. Patients must be informed and make these decisions together with their doctor. We do know that people living with Crohn's disease and ulcerative colitis have strong concerns about switching treatments that work well for them. On average, it takes a long time for patients to find treatments (and treatment combinations) that work well and keep them in remission. We do not want patients to be switching if their treatments successfully achieve remission.

- The SEB would be replacing the originator product without physician approval once the patient has been on the originator product for a period of time

  No, absolutely not. Again, all drug decisions must be made by an informed patient, together with their physician.

- Back and forth replacement between SEB and originator product without physician consent.

  No, absolutely not, there are many unknowns in the use of SEBs for IBD and the effects of switching.

# GI (Gastrointestinal) Society

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| **Name of the drug** | Inflectra™ (infliximab) |
| **Indication of interest** | Crohn's disease and ulcerative colitis |
| **Name of the patient group** | GI (Gastrointestinal) Society |
| **Name of the primary contact for this submission:** | [redacted] |
| Position or title with patient group | [redacted] |
| Email | [redacted] |
| Telephone number(s) | [redacted] |
| **Name of author (if different)** | |
| **Patient group's contact information:** Email | [redacted] |
| Telephone | [redacted] |
| Address | [redacted] |
| Website | [redacted] |
| **Permission is granted for CADTH to post this submission** | □ Yes ✓ No |