Biologic Coverage in Canada for Inflammatory Bowel Disease

Gastrointestinal Society
GI (Gastrointestinal) Society | www.badgut.org

As the Canadian leader in providing trusted, evidence-based information on all areas of the gastrointestinal tract, the GI Society is committed to improving the lives of people with GI and liver conditions, supporting research, advocating for appropriate patient access to health care, and promoting gastrointestinal and liver health. The Gastrointestinal Society is a registered Canadian charity that, in collaboration with its sister registered charity, The Canadian Society of Intestinal Research, has been actively involved in Canadian health care since 1976. Collectively they own the BadGut® brand.

**This Report**

We assembled this report card in association with gastroenterologists and other IBD medical experts living throughout the country. We formed recommendations using the most current evidence-based research on the appropriate management of IBD and on their clinical practices.

Gail Attara, Chief Executive Officer
Gastrointestinal Society
gail@badgut.org | 1-866-600-4875

**Why an IBD Report Card?**

About 1 in every 150 Canadians has inflammatory bowel disease (IBD), which is among the highest prevalence in the world. Of all digestive diseases, IBD is one of the most devastating. It is chronic, often challenging to manage, decreases quality of life, affects the ability to attend school or go to work, and can lead to death. The exact cause of IBD is unknown and there is currently no cure.

Patients affected by IBD need medications that work. Biologic medications are extremely beneficial for many patients with moderate to severe IBD, however, biologics used in IBD offer varied responses, depending on the patient; therefore facilitating biologic access is important to IBD patients. There is wide variation in provincial/territorial/federal drug plan coverage across Canada for IBD patients, preventing many from securing affordable access to the medications they need.

As of 2017, there is a new biologic on the market, called Inflectra®(infliximab), which is a biosimilar of Remicade®(infliximab). Unlike typical generic versions of medications, biosimilars can differ from the originator biologic because the medication is derived from biologic materials through a unique manufacturing process. At this point, Health Canada has determined the biosimilar to be safe and effective, and assures its quality but has not declared the biosimilar to be interchangeable with the reference originator biologic. Physicians can choose to prescribe either medication for treatment of IBD, however, due to the lower costs to produce the biosimilar, and its lower cost to public plans, most jurisdictions are insisting on starting a patient on Inflectra®, the biosimilar, but will allow those already taking Remicade®, the originator biologic, to stay on that product.

When an IBD 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.

There is wide variation in provincial/territorial/federal drug plan coverage across Canada for IBD patients, preventing many from securing affordable access to the medications they need.
Summary of Results

As demonstrated in Tables 1 and 2 of this Report Card, in most jurisdictions it is easier to obtain coverage for Crohn's disease than it is for ulcerative colitis. Specifically, coverage for Crohn's disease is more comprehensive in British Columbia, Manitoba, and Quebec while the guidelines for coverage for ulcerative colitis are more generous in Ontario, Saskatchewan, and Manitoba. However, this report also shows that long delays in making decisions to cover medications are problematic, especially in Ontario, which undermines its more favourable guidelines.

Canadian IBD experts recommend these pressing coverage improvements, applicable to most regions:

- Research suggests that, in cases of Crohn's disease, 5-ASA should not be considered a frontline treatment and that use of these medications should only be at the discretion of the prescribing gastroenterologist. Additionally, early azathioprine therapy is no more effective than placebo for newly diagnosed Crohn's disease and early azathioprine was not more effective in achieving a sustained steroid free remission than placebo. Furthermore, Health Canada Warning "IMURAN® (azathioprine) or PURINETHOL® (mercaptopurine) monotherapies are not authorized by Health Canada for the treatment of inflammatory bowel disease."

- Allow for dose optimization; the gastroenterologist should make this determination, based on individual patient need.

- Provide coverage for biologic indications Health Canada approves, based on evidence for that medication, for use in Crohn's disease and ulcerative colitis. Inflammatory bowel disease patients have so few treatment options; see page 10 for the complete list.

Public and private drug plans should provide coverage for all of these medications once approved by Health Canada. This way, physicians will have the right tools to manage the care of their many, varied inflammatory bowel disease patients. No patient will be on more than one biologic product and it makes absolute sense to have options, so that physicians can choose the right medicine for each patient, in the correct dose.

This Report Card represents a united, urgent appeal for systemic improvements so that inflammatory bowel disease patients have fair and appropriate access to biologic medication coverage in all parts of Canada.

This document evaluates publicly funded medication formularies based on the coverage of medically necessary biologic medications for IBD in two separate charts, for Crohn's disease and ulcerative colitis. Because these formularies change frequently, we encourage you to contact the Ministry of Health in your province or territory with questions you may have about medication listings of concern to you.

What the Grades Mean:

We have assessed all aspects of coverage (when applicable) and assigned a letter grade that represents overall access to coverage for each biologic medication approved by Health Canada.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Optimal</td>
</tr>
<tr>
<td>B</td>
<td>Acceptable</td>
</tr>
<tr>
<td>C</td>
<td>Needs Improvement</td>
</tr>
<tr>
<td>D</td>
<td>Not Acceptable</td>
</tr>
<tr>
<td>F</td>
<td>No Coverage</td>
</tr>
</tbody>
</table>
The Basics

Inflammatory bowel disease, which primarily attacks the digestive system, refers mainly to two related but distinct diseases – Crohn’s disease and ulcerative colitis. The key differences are the location of the inflammation, the extent of inflammation, and the presenting symptoms. This chart helps demonstrate the similarities and differences:

<table>
<thead>
<tr>
<th>Inflammatory Bowel Disease Overview</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Crohn’s Disease (CD)</strong></td>
</tr>
<tr>
<td>• the inflammation can be in multiple patches or one large patch, and may involve any area throughout the entire digestive tract, from the mouth to the anus (gum to bum), often affecting the last part of the small intestine (terminal ileum)</td>
</tr>
<tr>
<td>• inflammation can extend right through the entire thickness of the bowel wall, from the mucosa, through the muscle, and can even include the thin outermost layer of digestive tract cells (serosa)</td>
</tr>
<tr>
<td><strong>Ulcerative Colitis (UC)</strong></td>
</tr>
<tr>
<td>• only affects part or all of the large intestine (colon) and always begins at the anus, with the disease continuously progressing upward. In some cases, it can involve the entire large intestine (pancolitis)</td>
</tr>
<tr>
<td>• inflammation only involves the inner mucosa, which is the inner colon lining</td>
</tr>
</tbody>
</table>

**Shared Symptoms might include:**
- stomach/abdominal pain
- diarrhea
- rectal bleeding
- decreased appetite
- anemia
- eye inflammation
- kidney stones
- gallstones
- fever, night sweats
- liver & bile duct inflammation
- skin lesions
- primary sclerosing cholangitis
- arthritis & joint pains

**CD-Specific Symptoms**
- nutritional deficiency
- delayed growth in children
- weight loss
- nausea & vomiting
- weakness, fatigue
- perianal infection or abscess
- anal & perianal ulceration
- fistulising disease

**UC-Specific Symptoms**
- tenesmus
- more mucus and blood in stool

These are the typical symptoms, but it is very important to recognize that IBD can play out quite differently in different persons. The symptoms of IBD can come and go over long periods. Patients may experience periods of severe symptoms (or flare-ups), and go through periods when they have few or no symptoms at all (remission). Sometimes there can be no obvious symptoms and yet on examination of the GI tract via a scope, disease is present.

Medical professionals are not exactly sure why Crohn’s disease and ulcerative colitis happen, but it appears that some sort of environmental factor in genetically susceptible individuals causes the immune system to malfunction.

IBD can first appear at any time during life, from infancy into adulthood, with the bulk of diagnoses occurring in young people ages 15-25. There is a slightly increased risk for those who have a family member with the condition.

For an interesting, visual explanation of IBD, we encourage you to view our collaborative IBD video at www.badgut.org/ibd-video.
Treatment

Currently, there is no cure for IBD. Many of the treatments that effectively manage IBD target the immune system, so medications such as 5-ASA and corticosteroids, which help reduce inflammation, or immunosuppressants, are often used. However, not all of these medications are appropriate for every patient to try; physicians must be able to prescribe the right medication for each patient based on the individual’s specific disease circumstances and current, evidence-based research.

Medicines called biologics have become an important treatment option for those who have moderate to severe IBD. They work by using specially developed antibodies to selectively block the effects of molecules that are involved in the inflammation of the gut wall. Some of these medications move beyond symptom management and heal the mucosal lining, which can lead to remission and prevent future hospitalizations and surgery. Patients for whom biologics are the most appropriate option should have equal and adequate coverage for them, no matter where in the country they reside.

IBD can profoundly affect an individual’s life at home, at school, or in the workplace – physically, emotionally, socially, and financially. Having to go to the washroom more than 10 times a day, or even talking about your bowels, is challenging at any age, but perhaps particularly so for a young person, when this disease commonly strikes.

Why Surgery is NOT a Solution for UC

The colon’s primary function is to extract water from bowel contents, so when it is surgically removed, elimination remains frequent and is mostly liquid. Afterward, patients could experience cramping and as many as 20 bowel movements a day. Extra-intestinal complications include continual, debilitating disease symptoms, secondary illnesses such as arthritis, skin lesions, depression and anxiety disorders, and decreased family/social interactions.

Surgery has a 1.5% mortality rate and a 27% morbidity rate and leads to unnecessary usage of health care resources (e.g., additional hospital stays, further surgeries, diagnostic procedures, other medications) and a ripple effect of financial burden on the patient, government, and taxpayers (e.g., through inability to work, long-term disability claims, biologic-related expenditures, and even bankruptcy). If a patient has a surgically-created pouch to hold stool before elimination, it can become inflamed, a condition called pouchitis, which requires further medical attention.
<table>
<thead>
<tr>
<th>Jurisdiction</th>
<th>Coverage</th>
<th>Criteria¹</th>
<th>Efficacy Assessment¹; Renewal Period</th>
<th>Grade</th>
<th>Canadian IBD Experts Recommend</th>
</tr>
</thead>
<tbody>
<tr>
<td>BC PharmaCare</td>
<td>No new starts</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>UR 5-ASA, corticosteroids trial and either dependant, resistant, or intolerant Current HBI ≥ 8</td>
</tr>
<tr>
<td>Alberta Health</td>
<td>No new starts</td>
<td>Yes</td>
<td>UR</td>
<td>Yes</td>
<td>UR 5-ASA, glucocorticoids immunosuppressants HBI ≥ 7</td>
</tr>
<tr>
<td>Saskatchewan Drug Plan</td>
<td>Yes</td>
<td>Yes</td>
<td>ES</td>
<td>Yes</td>
<td>UR 5-ASA, glucocorticoids immunosuppressants</td>
</tr>
<tr>
<td>Manitoba Pharmacare</td>
<td>No new starts</td>
<td>Yes</td>
<td>UR</td>
<td>Yes</td>
<td>UR 5-ASA, corticosteroids immunosuppressants</td>
</tr>
<tr>
<td>Ontario Public Drug Programs</td>
<td>No new starts</td>
<td>Yes</td>
<td>Yes</td>
<td>6 months</td>
<td>preferred</td>
</tr>
<tr>
<td>Régie de l’assurance maladie du Québec</td>
<td>No new starts</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>ME corticosteroids immunosuppressants</td>
</tr>
<tr>
<td>New Brunswick Prescription Drug Program</td>
<td>No new starts</td>
<td>Yes</td>
<td>UR</td>
<td>Yes</td>
<td>UR 5-ASA, corticosteroids immunosuppressants</td>
</tr>
<tr>
<td>Nova Scotia Pharmacare</td>
<td>No new starts</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>UR 5-ASA, corticosteroids immunosuppressants</td>
</tr>
<tr>
<td>PEI Pharmacare</td>
<td>No new starts</td>
<td>Yes</td>
<td>UR</td>
<td>Yes</td>
<td>UR 5-ASA, glucocorticoids immunosuppressants HBI ≥ 7</td>
</tr>
<tr>
<td>Newfoundland and Labrador Prescription Drug Program</td>
<td>No new starts</td>
<td>Yes</td>
<td>UR</td>
<td>Yes</td>
<td>UR 5-ASA (Humira® only) corticosteroids immunosuppressants</td>
</tr>
<tr>
<td>NIHB</td>
<td>No new starts</td>
<td>Yes</td>
<td>UR</td>
<td>Yes</td>
<td>UR 5-ASA, glucocorticoids immunosuppressants</td>
</tr>
</tbody>
</table>

1. Criteria for approval of biologics vary by jurisdiction and may include evidence of efficacy, reduction in disease activity, and evidence of benefit beyond the initial recommendation.

2. Renewal periods for biologics are typically 1 year, but may be extended based on the criteria and the specific drug.

3. UR indicates ‘under review’ or ‘to be determined’.

4. 5-ASA refers to 5-aminosalicylic acid, a non-steroidal anti-inflammatory drug commonly used in the treatment of inflammatory bowel diseases.

5. HBI stands for Harvey-Bradshaw Index, a widely used tool for assessing disease activity in Crohn’s disease.

6. CDAI stands for Crohn’s Disease Activity Index, another tool used to assess disease activity.

7. Humira® is a brand name for the drug adalimumab, a biologic approved for the treatment of Crohn’s disease.

8. NIHB stands for National Institute for Health and Biomedical Innovation, which provides funding and support for Canadian health research and innovation.
The Harvey-Bradshaw Index consists of a few questions that allow physicians to quickly categorize the severity of Crohn’s disease and detect remission. This index is especially useful for data collection. Harvey and Bradshaw first published the index in The Lancet, in 1980, as a shorter, simpler alternative to the standard categorization technique called the Crohn’s Disease Activity Index. Patients answer the following five questions, and are given a score based on the severity of their symptoms.

**Harvey-Bradshaw Index Questions**

1. **Patient’s general well-being** (for the previous day)
   
   (0 = very well, 1 = slightly below par, 2 = poor, 3 = very poor, 4 = terrible)

2. **Abdominal pain** (for the previous day)
   
   (0 = none, 1 = mild, 2 = moderate, 3 = severe)

3. **Number of liquid stools per day** (for the previous day)
   
   (score 1 per movement)

4. **Abdominal mass**
   
   (0 = none, 1 = dubious, 2 = definite, 3 = definite and tender)

5. **Complications** (score 1 per item)
   
   - joint pain (**arthralgia**)
   - inflammation of the middle layer of the eye (**uveitis**)
   - inflammation of fat cells that results in tender red nodules on shins (**erythema nodosum**)
   - ulcers in the mouth (**aphthous ulcers**)
   - condition that causes tissue to become necrotic (**pyoderma gangrenosum**)
   - tear in the tissue that lines the anus (**anal fissure**)
   - a newly formed channel between the end of the bowel and the skin around the anus (**fistula**)
   - swollen tissue with an accumulation of pus (**abscess**)

**Harvey-Bradshaw Index Score**

- Remission: <5
- Mild Disease: 5-7
- Moderate Disease: 8-16
- Severe Disease: >16
### Table 2 – Ulcerative Colitis

#### REPORT CARD - PROVINCIAL & FEDERAL DRUG PLAN COVERAGE OF BIOLOGICS FOR ULCERATIVE COLITIS

<table>
<thead>
<tr>
<th>Jurisdiction</th>
<th>Coverage?</th>
<th>Criteria</th>
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<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Alberta Health</td>
<td>No new starts</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>UR</td>
</tr>
<tr>
<td>Saskatchewan Pharmacare</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>UR</td>
</tr>
<tr>
<td>Manitoba Pharmacare</td>
<td>No new starts</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>UR</td>
</tr>
<tr>
<td>Ontario Public Drug Programs</td>
<td>No new starts</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>UR</td>
</tr>
<tr>
<td>Régie de l’assurance maladie du Québec</td>
<td>No*</td>
<td>No*</td>
<td>UR*</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>New Brunswick Prescription Drug Program</td>
<td>No new starts</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>UR</td>
</tr>
<tr>
<td>Nova Scotia Pharmacare</td>
<td>No new starts</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>PEI Pharmacare</td>
<td>No new starts</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>UR</td>
</tr>
<tr>
<td>Newfoundland and Labrador Prescription Drug Program</td>
<td>No new starts</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>UR</td>
</tr>
</tbody>
</table>
Assessment for Ulcerative Colitis Activity

The Partial Mayo Scoring Index is similar to the Harvey-Bradshaw Index, but instead of measuring Crohn’s disease it measures ulcerative colitis. The Partial Mayo Scoring Index consists of a few questions for the patient to answer, and one question for the physician to answer. The numerical results provide a score that represents an estimate of ulcerative colitis disease severity.

Patients complete these questions:
Number of daily bowel movements you have when in remission/number of daily bowel movements you had before your diagnosis or symptoms of ulcerative colitis began (this number will be Your Normal):
1. **Stool Frequency** (based on the past 3 days)
   - normal number of stools = 0
   - 1-2 stools more than normal = 1
   - 3-4 stools more than normal = 2
   - 5 or more stools more than normal = 3

2. **Rectal Bleeding** (based on the past 3 days)
   - no blood seen = 0
   - streaks of blood with stool less than half the time = 1
   - obvious blood with stool most of the time = 2
   - blood alone passed = 3

Physician completes this question:
3. **Physician’s Global Assessment**
   - normal (sub scores are mostly 0) = 0
   - mild disease (sub scores are mostly 1) = 1
   - moderate disease (sub scores are mostly 1 to 2) = 2
   - severe disease (sub scores are mostly 2 to 3) = 3

*The Physician’s Global Assessment acknowledges the sub scores, the daily record of abdominal discomfort and functional assessment and other observations such as physical findings, and the patient’s performance status.

**Total Partial Mayo Index Score**
Remission: 0-1
Mild Disease: 2-4
Moderate Disease: 5-6
Severe Disease: 7-9
Economic Benefits of Biologics in IBD

Overview

Canada has the highest prevalence and incidence rates of IBD in the world.¹ There are close to 233,000 Canadians living with IBD: 129,000 with CD and 104,000 with UC. Physicians diagnose more than 10,200 new cases of IBD each year, comprising approximately 5,700 cases of CD and 4,500 cases of UC.

Burden of IBD

Health economists estimated the direct medical costs for individuals with IBD to be $1.2 billion in Canada in 2012.¹ However, there are many other costs associated with IBD, and these indirect costs are higher than the direct medical costs.¹ Excluding disability leaves, IBD patients take 7.2 days off work per year on average, because of their illness.¹³ In addition, 28.9% of IBD patients report labour force nonparticipation.¹⁴ This leads to a vast lack of productivity from people who wish they could be fruitful. We can reduce or eliminate these burdens by ensuring that individuals with IBD receive proper treatments.

Biologics Increase Productivity

The productivity of individuals with IBD increases greatly when they receive biologic medications to manage their disease. A systematic review of 8 studies for work-related outcomes in CD and UC patients with biologics found that biologics had a positive effect on employment status after 24 weeks of treatment. 64% of UC patients were employed at baseline, and that number grew to 69% after treatment. In individuals with CD, after 54 weeks, 31% of patients who experienced remission were employed and only 16% of those who did not reach remission were employed. In addition, they found that patients treated with biologics significantly improved their productivity. The amount of absenteeism reduced by 7-15%, presenteeism reduced by 15-20%, and total work productivity impairment reduced by 19-21%.¹⁵

<table>
<thead>
<tr>
<th>Drugs</th>
<th>CD</th>
<th>UC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entyvio® vedolizumab</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Humira® adalimumab</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Inflectra® infliximab (biosimilar)</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Remicade® infliximab</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Simponi® golimumab</td>
<td>✓</td>
<td>-</td>
</tr>
<tr>
<td>Stelara® ustekinumab</td>
<td>✓</td>
<td>-</td>
</tr>
</tbody>
</table>

Use of Health Care Resources

A recent study found that IBD patients who used a biologic in the previous year were 3.8-5.6% less likely to be hospitalized and 2.4-6.1% less likely to require a visit to the ER than individuals with IBD who were not using biologics.¹⁶ In UC patients, adalimumab lead to a reduction of close to 50% in the risk of hospitalization.¹⁷ In CD patients, infliximab demonstrated a decrease in the annual incidence of all surgeries (38%) and endoscopies (43%).¹⁸
References


iv A patient must fail (or not tolerate) these medications before being eligible to apply for coverage of a biologic medication.

v All jurisdictions require assessment with Harvey Bradshaw Index (HBI) with moderate to severe disease severity.

vi This recommendation arises because in this particular jurisdiction, the dosing escalation is either not allowed, regardless of physician recommendation, or the jurisdiction permits it only for some medications.

vii Research suggests that in cases of Crohn's disease, 5-ASA should not be considered a frontline treatment and that use of these medications should only be at the discretion of the prescribing gastroenterologist. Additionally, early azathioprine therapy is no more effective than placebo for newly diagnosed Crohn's disease and early azathioprine was not more effective in achieving a sustained steroid free remission than placebo. Furthermore, Health Canada Warning "IMURAN" (azathioprine) or PURINETHOL" (mercaptopurine) monotherapies are not authorized by Health Canada for the treatment of inflammatory bowel disease." Panés J et al. Early azathioprine therapy is no more effective than placebo for newly diagnosed Crohn's disease. Gastroenterology. 2013;45(4):766-74.

viii For patients on biologics who are transitioning from private insurance, and for continuity of care between physicians.

ix The Non-Insured Health Benefits (NIHB) program provides coverage for approximately 831,090 eligible registered First Nations and recognized Inuit with a limited range of medically necessary health-related goods and services not provided through private, provincial, or territorial health insurance plans. The process to apply for coverage is convoluted, time-consuming, unfair to patients, and does not have a feedback loop to inform physicians regarding approval or denial of coverage.

x Nunavut = Nunavut Extended Health Benefits. Nunavut uses the NIHB criteria, which the NIHB administers.

xi NWT = Northwest Territories Extended Health Benefits for non-Natives and Métis >60 years of age. NWT uses NIHB criteria, which Alberta Blue Cross administers.

xii Régie de l'assurance maladie du Québec (RAMQ) will review applications on a case-by-case basis for coverage for all indicated biologics in UC, which are routinely approved, but only after the patient has tried and failed Inflectra®.


