



## Common Drug Review *Patient Group Input Submissions*

### **linaclotide (Constella) for irritable bowel syndrome with constipation**

**Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.**

GI (Gastrointestinal) Society — permission granted to post.

**Disclaimer:** 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.

## GI (Gastrointestinal) Society

### Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest	Constella® (linaclotide) for IBS-C
Name of patient group	GI (Gastrointestinal) Society
Name of primary contact for this submission:	██████████
Position or title with patient group	██████████
Email	██████████
Telephone number(s)	██████████
Name of author (if different)	
Patient group's contact information:	
Email	<a href="mailto:info@badgut.org">info@badgut.org</a>
Telephone	604-873-4876
Address	231-3665 Kingsway, Vancouver, BC V5R 5W2
Website	<a href="http://www.badgut.org">www.badgut.org</a>
Permission is granted to post this submission	Yes

#### 1.1 Submitting Organization

Our mission: As the Canadian leader in providing trusted, evidence-based information on all areas of the gastrointestinal tract, 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 health care, and promoting gastrointestinal and liver health.

Canadian health care professionals request more than 550,000 of our BadGut® Basics patient information pamphlets each year, and tens of thousands of Canadians benefit from our important quarterly publication, the *Inside Tract*® | *Du coeur au ventre*<sup>MC</sup> newsletter.

Our free BadGut® Lectures from coast to coast cover various digestive conditions for patients, caregivers, and other interested individuals. We also have dynamic websites in English ([www.badgut.org](http://www.badgut.org)) and French ([www.mauxdeventre.org](http://www.mauxdeventre.org)). Organized on a number of topics, GI Society support group meetings offer a wealth of information for those newly diagnosed with a gastrointestinal disorder, as well as those who have lived with a condition for years.

Our highly trained staff and volunteers offer additional patient resources, including responding to information requests and participating in community initiatives. Staff and advisors work closely with health care professionals, other patient groups, and governments at all levels on behalf of GI patients. The GI Society, along with its sister charity, the Canadian Society of Intestinal Research (founded in 1976), has supported a number of significant clinical, basic, and epidemiological GI research.

### 1.2 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:**

The GI Society receives financial contributions from pharmaceutical companies in support of our independent charitable work for Canadians affected by GI/liver conditions. Supporters have no input into the editorial content of our resource material, which is approved by the GI Society's Medical Advisory Council (made up of GI/liver health experts only). Pharmaceutical companies from whom we have received support of any kind, such as charitable donations or grants, sponsorships, subscriptions to *The Inside Tract*<sup>®</sup> newsletter, etc. in the last two years include:

Abbott Laboratories Ltd, AbbVie Corporation, Amgen Canada Inc, Actavis (as Aptalis Pharma, Forest Laboratories, and Warner Chilcott), AstraZeneca Canada Inc., Bristol-Myers Squibb Canada, Canada's Research-Based Pharmaceutical Companies (Rx&D), Ferring Inc., Gilead Sciences Canada Inc., GlaxoSmithKline Inc., Hoffmann-La Roche Ltd., Janssen Canada, Merck Canada Inc., Medical Futures Inc., Cubist Pharmaceuticals (as Optimer Pharma), Pfizer Canada Inc., sanofi-aventis Canada Inc., Takeda Canada Inc., and Vertex Pharmaceuticals (Canada) Inc.

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

None. The GI Society has solely prepared this submission entirely independently of any outside groups or individuals.

## Section 2 — Condition and Current Therapy Information

### 2.1 Information Gathering

The GI Society obtained information through printed sources, collective feedback from patients associated with the GI Society who suffer with chronic constipation and/or irritable bowel syndrome with constipation (IBS-C) via a website survey, interviews with patients who were part of the clinical trials for Constella<sup>®</sup>, and information written by physicians for our publications (newsletter, pamphlets, website).

### 2.2 Impact of Condition on Patients

It is normal to have a bowel movement as frequently as three times a day or as infrequently as three times a week, provided the stool is soft and comfortable to pass. A person with constipation has hard or lumpy stool that is difficult to pass and is often accompanied by bloating and abdominal pain. Almost everyone experiences constipation occasionally. 13-20% of Canadians are living with irritable bowel syndrome (IBS), which is a chronic, often debilitating, functional gastrointestinal disorder. When the predominant symptom is constipation, it is called IBS-C, and this group comprises about one third of IBS patients in whom the digestive system contracts slowly, delaying transit time for products of digestion.

Interestingly, in a recent study that we reported on in the *Inside Tract*, issue 181, researchers found that many IBS patients would, hypothetically, risk a 1% chance of immediate death for a 99% chance of a cure of their IBS symptoms. That study helped to show the degree of suffering these patients endure. Each person is unique; a normal bowel movement pattern for one person may be very different from those of family members or friends. Some individuals have an irregular pattern, never knowing what to expect.

**Seniors**, who are already often isolated due to health limitations, suffer further when they cannot participate in social interactions or maintain independence because they do not have effective relief of constipation.

**Children** may miss out on school and social opportunities, which can have adverse effects on their development. A **working parent** with IBS-C may have to miss work because of chronic constipation and/or be unable to effectively care for children or other family members who need them.

**Symptoms/Complications:** The increased length of time during which stool remains in the colon causes increased pressure on the bowels, leading to abdominal cramping and bloating. Rectal pressure or fullness, bloating, abdominal pain, and a sensation of incomplete evacuation are common symptoms of constipation. The slowdown

in the digestive tract may also cause poor appetite, back pain, and general malaise. Most complications result from the intense straining needed to pass stool. These include hemorrhoids, anal fissures, diverticular disease, rectal bleeding, and rectal prolapse.

Patients with chronic constipation problems like IBS-C have told us the following about how it affects their lives:

- “The irritation of feeling bloated, uncomfortable, and sick is tiresome and never ending.”
- “I can’t move and [I’m in] constant pain.”
- “Basic activities such as grocery shopping or sitting at a desk are painful and challenging.”
- “In the morning I can’t do anything and have to wait until the pain subsides.”
- “I hate going to dinner because I fear when I eat I will be stuck in the bathroom.”
- “I cannot do cardio exercise because it immediately causes severe and dramatic bloating and distention that literally take days to resolve.”
- “It’s caused severe pelvic floor dysfunction and I cannot have sex without pain.”
- “The more severe the constipation, the more fatigued I become, barely able to get through the work day and often spending the weekend resting.”
- “I lost my job because I was missing too much time. I would be in such pain and worry of needing the bathroom that I could not leave my house.”

### 2.3 Patients’ Experiences With Current Therapy

IBS-C is a serious problem that significantly impairs quality of life. IBS-C sufferers face public stigma and lack of understanding. There are many treatments available, but they all have drawbacks, especially concerning their long-term efficacy and safety. Overuse of laxatives can lead to intestinal paralysis, cathartic colon, lazy or laxative gut, pancreatitis, and other health problems. IBS-C patients need a treatment that is safe and that they can use for longer periods of time, if necessary.

**Diet/exercise:** Eating regular well-balanced meals and snacks with high-fibre content, as set in *Canada’s Food Guide*, and maintaining an adequate fluid intake, is the recommended approach to prevent and manage constipation. This often helps those affected by occasional or mild constipation, but is not sufficient to relieve IBS-C, a chronic condition. Though there is evidence that exercise assists with some constipation, it has more of an indirect benefit (e.g., improved mood and attitude) on IBS-C rather than a significant direct improvement of physical constipation symptoms.

**Physiotherapy:** Pelvic dysfunction physiotherapy may include bowel retraining, electrical stimulation, and posture correction. This treatment helps some patients, but usually in combination with other treatments (e.g., laxatives, which are not intended for long-term use).

**Bulk Forming Agents (e.g., Metamucil®, Benefibre®, Prodiem®):** Are safe for long-term use but are not quick-acting and can result in negative effects such as abdominal pain, bloating, and flatulence.

**Enemas:** Provide fast-acting relief but are not appropriate for long-term use.

**Stool Softeners (e.g., Colace®):** While safe for long-term use, they have limited effectiveness in IBS-C.

**Lubricants (e.g., mineral oil):** These products should not be used for longer than a week, as some have been shown to cause vitamin deficiencies and medication interactions. They are also not appropriate for pregnant women or for persons who have difficulty swallowing.

**Stimulants (e.g., Ex-lax®, Dulcolax®, castor oil, senna tea, and Senokot®):** These are useful only for very short-term situations and under the recommendation of a physician or pharmacist, because repeated use could cause the digestive tract to become stimulant-reliant. They are also not recommended for pregnant women. Laxatives are insufficient for the IBS-C patient.

**Hyperosmotics:** There are four main types: Saline (e.g., Royvac®), magnesium preparations (e.g., Phillips'® Milk of Magnesia), sulfate salts, and sodium phosphate; Lactulose; Polymer (e.g., polyethylene glycol - PegaLAX®); and Glycerine. Some of these laxatives can cause electrolyte imbalances if they draw out too many nutrients and other substances with the water. They can increase thirst and dehydration.

Patients who have tried the above treatments have told us:

- “One by one they become ineffective over time. I have to constantly track bowel movements and escalate treatment.”
- “[I] was using OTC laxatives on a daily basis, which made the situation worse. The side effects of those completely destroyed any chance of a normal life.”
- “The challenges were the treatments either didn’t work or they left me housebound because the results were so severe that I couldn’t chance leaving the house.”
- “I spent far more than I could afford on products.”
- “They did not work.”
- “Some actually worsened the constipation.”

### 2.4 Impact on Caregivers

When treatment does not provide effective relief, patients require more frequent use of hospital resources, increasing the public health care burden and disempowering individuals. In addition, caregivers may need to devote more resources to a family member suffering from IBS-C who is unable to complete day-to-day tasks such as errands, cooking, hygiene, etc., because of unresolved constipation problems.

## Section 3 — Information about the Drug Being Reviewed

### 3.1 Information Gathering

See 2.1.

### 3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had to Date With the New Drug?

When the available treatments do not provide effective relief, patients are unable to meet the normal responsibilities in their lives – toward their employers, families, and communities. We expect the patient population specifically affected by IBS-C will receive Constella® enthusiastically. Those who we spoke to who were part of the clinical trials or who have had other access (via private drug plans) were astounded by the change they felt once using Constella®. Here are some of the direct quotes on experience using Constella for IBS-C:

- **“Constella improved my whole system.”**
- **“There was a huge difference in my life... for the better.”**
- **“My stool went from rock hard to normal.”**
- **“Finally, I went from having bowel movements once a week to every day and the bloating diminished almost completely.”**
- **“Now it’s rare to feel bloated or crampy.”**

Constella® appears to be an easy and more reliable option for the IBS-C patient. This treatment could result in patients being able to resume their normal lives without the constant physical, emotional, and financial burden involved in juggling numerous – mostly-ineffective – treatments, such as laxatives and other short-term solutions with long-term potential consequences.

Many of the patients who use the GI Society resources say that they have used a wide variety of dietary/lifestyle strategies, bulk-forming agents, and laxatives in their struggle to normalize their bowel experiences. They continue to find those treatments inadequate for their IBS-C problems and they are desperately seeking a better option.

If Constella® is the safe, long-term solution for those suffering from IBS-C that the research suggests, then it would mean that more patients could return to work, and to the leisure activities that improve their social relationships

## **Patient Group Input Submissions**

---

and sense of wellbeing. The ripple effect of effective treatment for IBS-C would be fewer hospital visits, lessening the public health care burden.

Constella® could fill a crucial treatment gap for IBS-C patients.

## **Section 4 — Additional Information**

None