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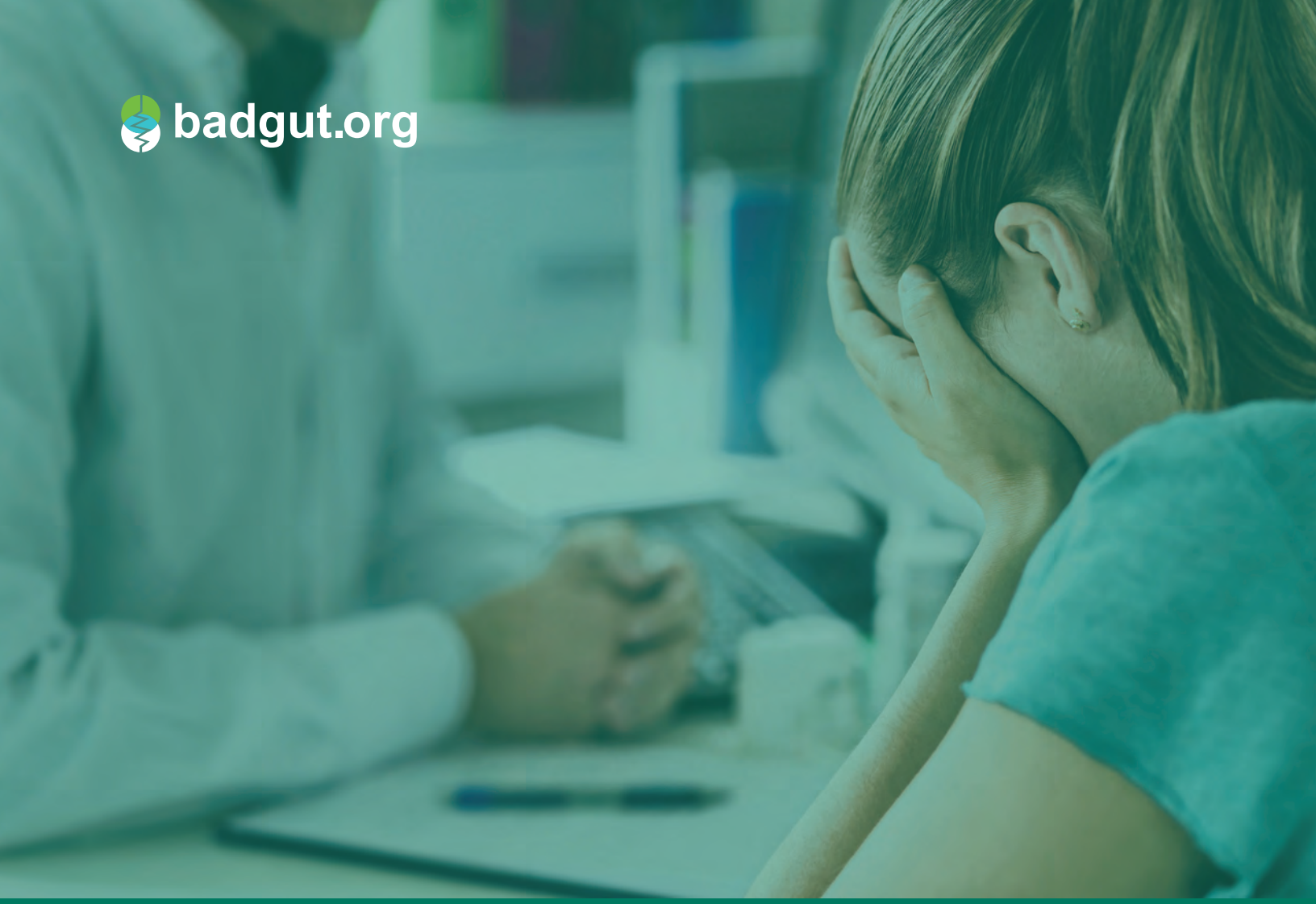


Forced To Switch: Canadian Biosimilar Experience

SURVEY REPORT

December 2020 // **Gastrointestinal Society**

Preamble

On September 5, 2019, the government of British Columbia implemented Phase II of the Biosimilars Initiative, affecting many patients in the province living with inflammatory bowel disease (IBD), primarily Crohn's disease and ulcerative colitis.[1] This policy mandated that PharmaCare coverage for the infliximab originator biologic, Remicade®, would discontinue as of March 5, 2020, meaning that patients who wanted to continue infliximab treatment had to switch to an infliximab biosimilar, e.g., Inflectra® or Renflexis® (at the time) by the March deadline to have their medication covered under PharmaCare.

The Alberta government subsequently announced a similar switch policy. However, due to the COVID-19 pandemic, they postponed the deadline until January 14, 2021 to switch to a biosimilar to maintain coverage under public drug plans.[2] This will affect about 2,000 persons living with IBD in that province.[3]

Introduction

The Gastrointestinal Society conducted phone interviews with patients who contacted us because these policies negatively affect them. We also started an online survey in late 2019 to capture a pan-Canadian view of patients' experiences with originator biologics and biosimilars.

In this report, we look at the results of our 2020 survey and compare it to those from our 2015 survey on subsequent entry biologics (the former term for biosimilars).[4] In both years, most respondents contend that patient-physician consultation and consent for biologics (innovator and biosimilar) are vital components of care.

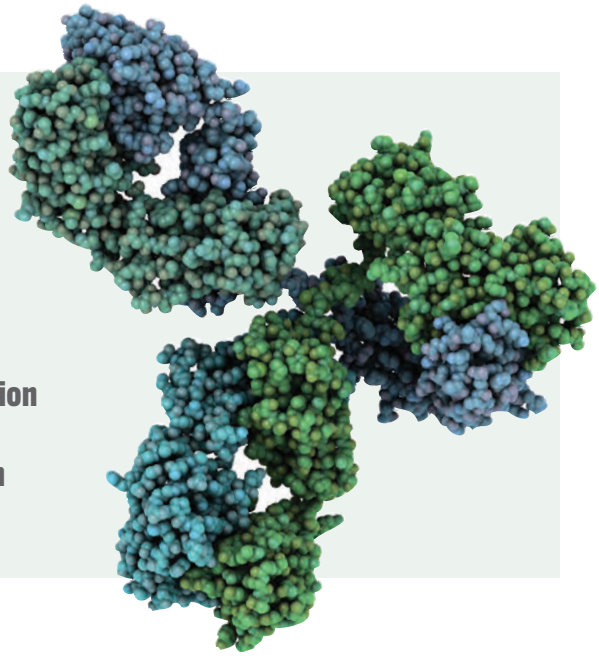
There is also an overview of what we heard directly from patients over the phone, which ranged from concerns with lack of timing for physician visits, a need for appropriate education around biosimilars, their specific difficulties with the policies and continuity of care, and more.

What are biologics?

Biologics are highly effective medicines made in living cells with complex molecular structures.

Their development and manufacturing processes are significantly more intricate than small-molecule drugs, which are simpler to reproduce or copy.

It is not possible to create an exact or "generic" version of an originator biologic. Instead, upon patent expiry, other manufacturers can produce a similar copy, known as a biosimilar.



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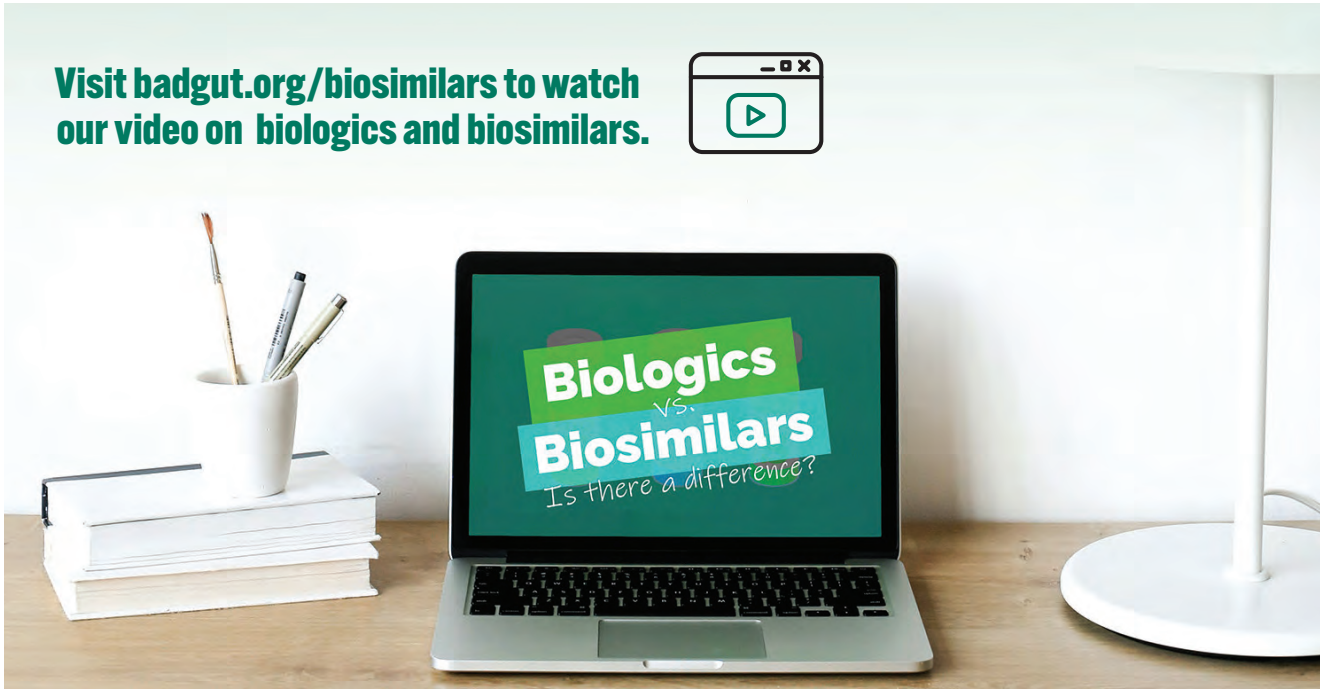
Background

Our federal authority, Health Canada, approves biosimilars as new drugs by comparison with an innovator (also called originator) reference biologic that they previously authorized for sale in Canada. They only approve biosimilars that are similar in quality, safety, and efficacy to the original reference product that demonstrate no clinically meaningful differences.

There are many biosimilars on the market, including many examples of multiple biosimilar products for each originator biologic that has reached the end of its patent. More are on the way in other therapeutic areas, as patents for originator biologics continue to expire.



What Switching Means

A gastroenterologist will need to write you a new prescription and connect you with a new biosimilar coordinator and a different patient support program. If you have private insurance, your healthcare team will discuss with you the terms of coverage and whether you can stay on the originator biologic or if you will have to switch to its biosimilar.

Gastroenterologists in Alberta calculated that, before the policy deadline, they will need to schedule a minimum of 650 clinic hours to process the treatment switch for all patients affected,[3] while ensuring that everyone receives their biosimilar infusions in a timely manner. This is because it is unsafe for infusion delays to occur as your body might form antibodies if the concentration level of the drug in your body drops too low, which can lead to consequences, including a return of IBD symptoms.

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Data Gathered Online

Online Survey

The Gastrointestinal Society represents patients on a variety of healthcare fronts, including access to medications. From September 26, 2019 to September 15, 2020 (extended timeline due to COVID-19), we hosted a survey on our English (www.badgut.org) and French (www.mauxdeventre.org) websites to capture a pan-Canadian review of patients' experiences with biologic medications.

This survey builds on a similar study we did in 2015, which was limited to patients with inflammatory bowel disease (primarily Crohn's disease, ulcerative colitis, and indeterminate IBD).[4] Our 2015 survey received 423 responses (317 English and 106 French). In this survey, we opened it to all individuals in Canada diagnosed with any condition treated with biologic medications. 145 participated, 137 in English; 8 in French, but not everyone answered each question, as they were not mandatory. For comparison purposes, we asked a few of the same questions in each survey to determine whether there were any changes in patient perceptions regarding treatment decisions.

Even though there was a five-year time span, patients still believe that it is imperative for medication choices to reside between themselves and their treating physician.

Survey Demographics

Participants consisted of:

- 40% with Crohn's disease, 24% ulcerative colitis, 16% rheumatoid arthritis, 12% diabetes, 12% osteoporosis, 8% psoriasis, 8% ankylosing spondylitis, 5% hidradenitis suppurativa, 4% cancer, 2% psoriatic arthritis, 1% growth disorders, and 3% other
- all provinces, except Prince Edward Island
- the majority (67%) were female
- similar representation from all ages, with most respondents between 30-39 years old (21%) and 50-59 years old (23%)

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Understanding Originator Biologics & Biosimilars

Patients expressed their familiarity with biosimilars:

- 50% of respondents were very familiar with biologic medications, 30% were familiar, and 6% have heard of them
- a majority (76%) said they have heard of biosimilars and, among these individuals, most (23%) reported that they learned through sources such as traditional media, social media, health organizations, and word of mouth
- 19% listed self-study as to where they heard about biosimilars and 15% had a discussion with their physician
- 10% said they first heard about biosimilars when physicians prescribed a biosimilar product for them

We asked participants how they think biosimilars differ from originator biologics and a majority (46%) indicated the cost of medication, 35% said that it was how they are made, 28% reported that it was how patients react to them, 17% selected types of side effects, and 11% marked it as how they work. Interestingly, 27% said that they have no opinion on this matter.

When asked what factors are important in the regulation of biosimilars in Canada, most respondents indicated safety (68%) and efficacy (64%). Health Canada approves some biosimilars to treat conditions that the originator biologic has approval for, through educated assumptions by extrapolating scientific evidence. Yet, 52% of survey participants think that regulators should evaluate biosimilars by having clinical trials in all applicable diseases. We asked the same question in our 2015 survey and the results between then and now on this question were similar.

Medication Choice

92% of respondents indicated that it is important to have the sole authority to decide, together with their physician, the most suitable biologic medicine to use to treat their disease (77% very important and 15% somewhat important). 4% said that they were not sure and another 4% decided that it was not important.

When asked their level of concern if a pharmacist or government/private insurance plan made the determination on which biologic (innovator or biosimilar) to dispense to them on initiation of treatment, 68% found this to be very concerning, 21% somewhat concerning, 7% indicated that it is not concerning for them, and 4% were unsure.

Respondents were even more concerned by the idea of a pharmacist or government/private insurance plan choosing which biologic (innovator or biosimilar) to dispense to them during their treatment, including maintenance therapy (switch medicines without informing them); 81% viewed this as very concerning, 10% said it was somewhat concerning, 7% found it to be not concerning and 2% were unsure. In addition, 62% found it to be very concerning and 18% somewhat concerning if they were doing well on biologic therapy yet they were forced to switched for non-medical reasons.

Mental Health

Mental health issues came across strongly. We suspect that this is due to the anxiety surrounding destabilization of their care, as all would have had to switch their patient support programs and go to a different clinic for their infusions, coupled with the fact that this switching crossed over into the COVID-19 pandemic. 66% of respondents said they experience mental health related conditions (currently or ever), such as insomnia, anxiety disorders, and mood disorders.

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Data Gathered by Phone & Email

Phone Calls and Emails

We documented close to 100 calls and emails to our office by inflammatory bowel disease patients who expressed anxiety and concern surrounding their care, causally related to switching to a biosimilar. We were able to classify 53 of these calls into 4 categories and will expand on the other issues later in this report. We logged these calls from BC patients between 2019-11-13 and 2020-02-06. By classifying and summarizing them, we are not lessening their importance to the patients who called us:

- 18 experienced delays with biosimilar dose, so patients needed an additional Remicade® dose
- 24 expressed a lack of correspondence from biosimilar patient support program
- 9 patients had no biosimilar dose available at scheduled infusion date
- 2 experienced lack of coverage issues for the biosimilar

Physical and Mental Health

The impact of a mandated, non-medical switch for patients with IBD included poor timing of the policy implementation and insufficient patient consultation. There was a distinct lack of education on biosimilars, and there were delays at the new patient support programs, which were unprepared for the volume of patients switching. In some cases, patients had to travel great distances to access the different infusion clinics. Patients found that the special authority program (which potentially would allow them to stay on the originator biologic) was of little benefit to them, as the criteria were too strict. All these factors lead to the conclusion that forced non-medical switching from an originator biologic to a biosimilar (and then even to a different biosimilar if the first one failed) jeopardizes the physical and mental health of thousands of patients who are affected by this policy.

Many patients who we spoke with have been on the originator biologic for years. As examples, one has been on the originator biologic for at least 3 years and another has been receiving it for 13 years. The originator biologic (Remicade® in this case) gave them the ability to go about their daily lives without difficulty, to work fulltime jobs, to care for their families and loved ones, to exercise, and more. Patients who do not want their medication switched had tried a range of drugs before starting on the originator biologic and none had worked as effectively. Thus, their options are extremely limited, so patients experience fears and worries about the stability of their health when switching to a biosimilar that is not identical to the drug that has helped them. Patients expressed stress, anxiety, and depression due to the uncertainties and consequences of non-medical switching. The COVID-19 pandemic might further decrease their health and wellbeing.

Alberta

The biosimilar policy announcement by the Alberta government in early December 2019 prompted a number of patients in the province to contact the GI Society to learn more about the non-medical switch process, how they can stay on the originator biologic, and ways to increase their advocacy efforts with the provincial government. The temporary suspension of various healthcare services and other measures taken to address the COVID-19 pandemic has also brought a myriad of challenges and may have prevented individuals from accessing necessary health services. Alberta gastroenterologists are also in dialogue with the GI Society, expressing their concerns. However, it is too early to measure the impact of switching medication during the pandemic.

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Key Issues

Timing and Consultation

Patients were genuinely concerned with the lack of time provided by the government to switch their medicines. They needed to consult their healthcare team, learn what biosimilars are and how they will affect their health, and consider the logistics of transferring to a new patient support program. Patients also felt that they did not receive fair or appropriate notice about the switch. Most didn't learn of it directly from their gastroenterologist or members of their healthcare team, but rather in the form of letters from Janssen, the makers of Remicade®. One patient heard about it because he was watching the news when the BC Minister of Health made the announcement, while another received a call from her daughter's patient support program confirming whether she was aware of the changes. Patients who contacted us in January 2020 were still waiting to meet with their gastroenterologist to speak about the switch.

Here are direct quotes from BC patients:

> ***My next Remicade is scheduled for January 29. My specialist told me I would hear from the biosimilar co-ordinator for my new biosimilar infusion place, date, and time. Still nothing. The doctor said to call my Remicade co-ordinator for help. She said she can't help me and to call the doctor. I'm still panicking as no one can answer my questions.*** *~Abbotsford, BC*

> ***[I'm] switching to Inflectra come the deadline. Knowing that the forced switch was coming, I asked my GI [gastroenterologist] if I could make the switch back in September as sunny/warm weather was always when I was healthiest. No joke, he declined because "there's a large amount of paperwork that comes with the change, and I want to do everyone's at once at the deadline." Now that I'm riding the edge of a flare with the switch a couple months away, I'm a bit unsure how the transition will go.*** *~BC*

For Albertans, both patients and IBD physicians did not receive adequate, if any, consultation leading up to the government's policy announcement on December 12, 2019. As a result, gastroenterologists who were not aware of the incoming policy had already refilled prescriptions for the originator biologic for the upcoming year.

> ***My gastroenterologist didn't even know much about the switch when I came to see her after receiving the Janssen letter. I asked my primary doctor about it too and they had no information, so I faxed them a copy. Because my GI [gastroenterologist] wasn't aware, she had already written me a refill of Remicade® for the new year.*** *~Edmonton, AB*

> ***I only see my GI [gastroenterologist] once a year and the next time I see him is March 2020 in Edmonton, should I reschedule an earlier appointment with him?*** *~St. Albert, AB*

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Biosimilar Education

Most patients interviewed also expressed that their healthcare team gave them little to no information about biologics and biosimilars.

> ***[My gastroenterologist] told me that Remicade and Renflexis was the same drug. He compared it to 2 different brands of bananas; that if you cut both in half, they would look the same.*** *~Errington, BC*

Patients in Alberta, so far, seem to have received more help, information, and support from their gastroenterologists about the non-medical switch policy than did patients in BC. Some gastroenterologists even recommended that their patients contact their local MLA to oppose the policy. They specifically advised this action to patients who were stable on the drug and have limited therapeutic options, in that they have failed other drugs before.

> ***I want to stay on Remicade® so my doctor told me to keep writing to my local MLA. I also wrote to the Health Minister, Tyler Shandro, and Health Canada. I only got an acknowledgement letter from my MLA.*** *~Edson, AB*

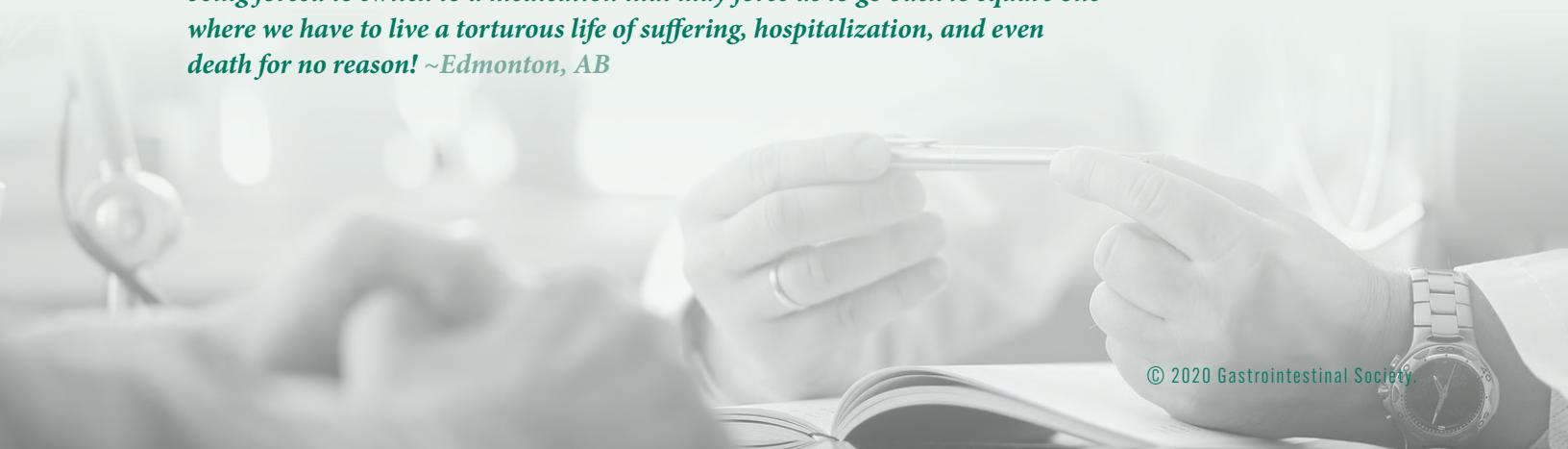
Patients who were frustrated or unsatisfied with the amount of information they received about biosimilars conducted research on their own to learn more. (Dr. Google.) They understand the reasoning for cost-savings but were disappointed in the government for enforcing the switch policy on patients who are stable on the originator biologic.

They were outraged at the government because they learned from Janssen, the manufacturers of Remicade®, that they were willing to match the price of the biosimilar. **So why would the government force them to switch when they could have the same level of savings by accepting the lower price from Janssen? Patients are frustrated that the government is forcing them to switch their medication for no rational reason.**

> ***BC PharmaCare is not going to save money. It is going to cost more to stabilize everyone again. I bet the suicide rate will go up also. This is my option. 33% of patients switched over to biosimilar had allergic reactions in only two months. This is a complete disaster.*** *~Errington, BC*

> ***I have done well on Remicade and would prefer to stay on it if the price was going to be the same.*** *~Fort St. James, BC*

> ***[Minister Shandro,] please accept Janssen's offer so I, like so many others can continue our Remicade treatment and living healthy lives instead of being unnecessarily being forced to switch to a medication that may force us to go back to square one where we have to live a torturous life of suffering, hospitalization, and even death for no reason!*** *~Edmonton, AB*



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Issues with Patient Support Programs Led to Stress and Anxiety

Infusion clinics have exclusivity contracts with pharmaceutical companies who supply either the originator biologic or a biosimilar. As we've learned from patients in BC, clinics that supply a biosimilar have limited capacity and availability, including hours of operation, geographic location, and staffing. Switching to a new clinic typically also means a different healthcare team for patients. Accessibility issues increase in rural areas.

Patients were extremely worried about not receiving their biosimilar infusion on time, since missing one infusion might trigger a flare and adverse outcomes. As you can see in the summary of phone calls and emails above, many biosimilar clinics were struggling to offer prompt care. One person reported that the biosimilar clinics in their area aren't open on weekends, which makes it difficult for her because she works fulltime and must book days off work whenever she receives her infusions. The nearest ones were in cities that required an hour transit trip each way.

Evidently, some clinics were overwhelmed, understaffed, and were not as widely available and accessible to patients. However, this was the status report in the pre-COVID-19 era. Clinics and healthcare services have taken measures to implement safety protocols to minimize the risk of exposure to COVID-19 and this has increased stress and anxiety for patients in accessing the medication that is keeping them well.

We understand that, at the time of authoring this paper, some infusion clinics in Canada are beginning to offer infusion for any biologic, whether originator or biosimilar, but this is not yet widespread.

Special Authority Is Not a Viable Option

Most patients from both provinces were unaware that their physician could apply for special authority for them to stay on Remicade®. This is concerning since patients expressed strong concerns to their gastroenterologists about switching to a biosimilar and yet they did not inform them of this possibility. As the policy unfolded in BC, gastroenterologists expressed to us that they changed their behaviours so that they only rarely completed the special authority requests because of the increased work involved and the high likelihood that the special authority will be denied. (As demonstrated in BC PharmaCare's special authority stats.)

While Alberta's policy automatically excludes pediatric patients and pregnant women from switching, this exclusion is not available for BC patients. A BC gastroenterologist reported that there are children in BC who received temporary special authority for the originator biologic. However, their coverage for the originator biologic only lasted until November 2020.

> ***Instead of the medication that our 15 year old daughter has been on for the past seven years, showing great success in preventing very dangerous complications of her disease and often gave her the ability to fit in and maintain comfort while keeping up with her peers; the government would like us to switch her to a similar medication that has never been tested on children.*** *~Kitimat, BC*

> ***My gastroenterologist applied for special authority to extend my Remicade® coverage. However, PharmaCare has confirmed they are not accepting breastfeeding as an eligible exemption for covering Remicade® for me.***
> ***They have stated, "based on available information it is not clear why one version of infliximab would be more safe in breastfeeding than another version of this medication" despite it clearly stating on the drug monograph… that Inflectra is not recommended to take while breastfeeding.*** *~Kamloops, BC*

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Of most concern is the lack of clarity surrounding the criteria used to qualify for special authority. Despite considerable reporting of side effects and adverse reactions to biosimilars, approval rates for these requests in BC are low. According to a Calgary gastroenterologist's sources, only 1 in 400 received approvals for exemptions in Alberta, meaning that only 55 out of the estimated 22,100 (0.24%) patients affected were approved coverage to remain on the medication that made them well.

When switching over, I was assured that the multiple test phases would cause a seamless transition over to Inflectra as most people don't suffer from the change. Unfortunately, this seems untrue for me. I was admitted to the hospital on December 24th with a small bowel obstruction. After being treated, without surgery, I was able to go home a few days later. My GI and I had spoken and he was confused as to what had caused it as all my levels were in good standing and I was in remission. *~Vancouver, BC*

I've now had a flare for three months straight and have been denied coverage twice for switching back to Remicade through BC Pharmacare and I feel very overwhelmed and afraid. When I asked the nurse why they denied me, she seemed frustrated and couldn't answer any of my questions. Now they've put me on Entyvio® and I hope it'll work for me, but I know that the risk of damage is too great to fail. *~Bowen Island, BC*

These are only a few of the stories we received from patients. Others reported experiencing side effects that they never experienced on the originator biologic, such as headaches, flu-like symptoms, pain, and severe bowel cramping from diarrhea and constipation. **For every patient who contacted us, BC PharmaCare denied their physician's request for special authority to remain on Remicade®.** BC PharmaCare has stated publicly that they have approved only 1% of special authority requests.

Patients looked to their healthcare team for answers on why BC PharmaCare denied their applications. Despite the support of their doctors and nurses for a special authority request, no one could give them answers, leaving patients hopeless and in fear of their future health outcomes.

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Conclusions

In these surveys of patients – online, by phone, and by email – we heard individual experiences with switching medication for non-medical reasons. They were forced to switch because the government in charge of the public reimbursement plan decided that they should.

For our online survey, we asked some of the same questions as in our 2015 survey to determine any changes in patient perspectives regarding treatment decisions. Despite the five-year time span and the wider eligibility of the 2020 survey to a variety of therapeutic areas, results between the two data sets were highly similar.

Patients still believe that it is crucial for medication choices to reside between themselves and their treating physician throughout their care. In fact, most respondents were familiar with biologic medications, with 77% taking a biologic, including biosimilars. Compared to the number of biologics for other inflammatory conditions, such as rheumatoid arthritis, IBD has only a few options, so it makes sense that 84% also thought that it was important to have biologic medications that have diverse ways of working (mechanism of action) to treat IBD (55% very important, 29% somewhat important).

In our open-ended questions, most responded that they understand the need to achieve healthcare savings through biosimilars. However, there are dire health consequences if government policies or insurance plans switch patients for non-medical reasons from biologic medications that are effective in treating their disease. Efficacy, safety, and doctor's recommendation were the top three factors respondents selected when choosing a biosimilar treatment, whereas cost considerations were less significant.

Provinces across the country continue to implement different policies on biosimilar coverage. Treatment options are also increasingly available to patients across other disease areas. However, patients maintain the position that they, along with their physician, should have the sole authority to decide the best biologic medication for their disease.

With vaccines for COVID-19 still in the future, additional hospital and clinic visits may increase a person's risk of exposure. We, along with gastroenterologists across Canada,[5] strongly recommend that governments halt any biosimilar policy changes or implementation during the pandemic.

In our view, a fair and equitable biosimilars policy is to set one price for reimbursement for all originator biologics and their respective biosimilars. Originator companies could lower their prices to compete and thereby governments would not need to force patients to switch their medications. We believe that this is the most viable option and encourage all Canadian jurisdictions to implement such a policy so that patients don't have needless suffering. This "lowest cost alternative" form of pricing policy is widespread in Canada for brand name and generic products and gives governments the cost-savings they desire.

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Acknowledgements

We thank the Canadian Society of Intestinal Research (CSIR) who collaborated with us on this survey. We received no external funds or support of any kind for this independent project.

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Gastrointestinal Society's Mission

We're committed to improving the lives of people with gastrointestinal and liver conditions, supporting research, advocating for appropriate patient access to healthcare, and promoting gastrointestinal and liver health.

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