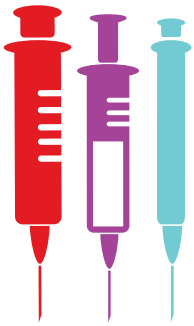
# Switching to a Biosimilar May Decrease Adherence



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Biologics are very specific, highly effective, large molecule drugs made in living cells. They have revolutionized treatment in complex diseases, including inflammatory bowel disease (IBD) – Crohn's disease and ulcerative colitis – and many other conditions, such as diabetes, rheumatoid arthritis, cancer, osteoporosis, psoriasis, HIV infection, and multiple sclerosis.

For context, it is important to know that most medications are small molecule drugs. This means that they have simple chemically-based molecular structures that are easy to reproduce and copy. You will often encounter both name brand and generic versions of these medicines sold side-by-side and dispensed interchangeably by pharmacists. All products made with the same active medical ingredient (molecule) will work the same. Generic substitution involves automatically replacing the name brand version with a generic medication made from the same molecule. Occasionally, this causes issues, such as if a patient has an allergy or sensitivity to an additive in the generic pill that wasn't in the original formula. However, the patient is receiving the exact same medical ingredient, so generic substitution usually saves money in the health care system without compromising patient health.

The GI Society has worked on various advocacy projects over the years, and one area that we have focused on is therapeutic substitution. This is when a patient must switch treatment from a molecule that is working for them to a different molecule in the same therapeutic class, for reasons such as cost, rather than efficacy. These products are sufficiently different to warrant a new brand name, but work in a similar way. Although therapeutic substitution is intended to save money, switching among different chemical, small molecule products in a therapeutic class has had negative outcomes in Canada in the past. In the case of patients with gastroesophageal reflux disease prescribed proton pump inhibitors, switching medications was unsuccessful for 23% of the population, and this amounted to increased cost to the British Columbia health care system in excess of $43 million over three years.[1]

On the other hand, with large molecule biologics, it is impossible to produce an exact copy even when using the exact same ingredients, the same living cell lines, and identical manufacturing conditions. When other brands make copies of an originator biologic, it is a similar product, but it is not the same. This is why federal regulators have designated these medications as biosimilars with their own brand names, rather than generic versions.

We need to take greater care when switching from an originator biologic to its biosimilar and must consider such things as the capacity to monitor and capture a patient's response after switching, development of exclusion criteria by professional associations, and the number of therapeutic options available if treatment failure occurs.

Patient support programs, which are unique to Canada, are an especially important factor to consider when analyzing data from other countries, as they add a major and complex variable when switching from a biologic medicine to a biosimilar.

Several recent studies of patients agreeing to and being aware of a switch from the originator biologic to a biosimilar (open-label) have reported higher discontinuation rates than anticipated.[2,3,4] Previous clinical trial data where patients were not aware if they were being continued on the originator biologic therapy or switched to the biosimilar (blinded) indicated similar continuation rates in patients who were switched to the biosimilar and those who were not switched (approximately 90%).[5] In the more recent open-label studies, only 72-76% of patients continued on therapy at approximately 30 weeks after switching.

One of the major reasons suggested for the higher discontinuation rates of patients in the open-label studies is the nocebo effect, or the concept that a patient's negative thoughts or experience may, in part, drive a less than optimal response and/or outcome. Recent surveys have captured patient concerns regarding the safety and efficacy of biosimilar drugs and also highlighted patient unease at prescription of biosimilar drugs by regulatory agencies (i.e., as policy) rather than their treating physician.[6,7] In 2015,

the Gastrointestinal Society conducted a survey with 423 Canadian respondents and the majority did not want these medications simply because they might be less expensive than the originator medications. These individuals were concerned about switching therapy between the originator biologic and a biosimilar, particularly if the government or private insurance plans mandate use of these drugs without their consent. Not surprisingly, 95% said that it was important for their physician to have the sole authority to decide, together with them, the most suitable biologic medicine to use to treat the disease. This patient directive is very strong and could account for the ultimate success or failure of a treatment.[8]

The limited number of therapeutic options for patients with IBD, compounded with the somewhat conflicting body of data around discontinuation rates of biosimilars post-switching, highlights the need for further studies in this area to determine the impact of switching on long-term adherence of medication.


1 Skinner, BJ *et al.* Increased health costs from mandated Therapeutic Substitution of proton pump inhibitors in British Columbia. *Alimentary Pharmacology & Therapeutics.* 2009;29(8):882-91.

2 Avouac J *et al.* Systematic switch from innovator infliximab to biosimilar infliximab in inflammatory chronic diseases in daily clinical practice: The experience of Cochin University Hospital, Paris, France. *Seminars in Arthritis and Rheumatism.* 2018;47(5):741-748.

3 Scherlinger M *et al.* Switching from originator infliximab to biosimilar CT-P13 in real-life: The weight of patient acceptance. *Joint, Bone, Spine.* 2017. Doi: 10.1016/j.jbspin.2017.10.003.

4 Tweehuysen L *et al.* Subjective Complaints as the Main Reason for Biosimilar Discontinuation After Open-Label Transition From Reference Infliximab to Biosimilar Infliximab. *Arthritis and Rheumatology.* 2018;70(1):60-68.

5 Jørgensen, KK *et al.* Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial. *Lancet.* 2017;389(10086):2304-2316.

6 Peyrin-Biroulet L *et al.* Patient Perspectives on Biosimilars: A Survey by the European Federation of Crohn's and Ulcerative Colitis Associations. *Journal of Crohn's & Colitis.* 2017;11:128-133.

7 Wilkins AR *et al.* Patient Perspectives on Biosimilar Insulin. *Journal of Diabetes Science and Technology.* 2014;8(1):23-25.

8 Gastrointestinal Society. Survey Results: Subsequent Entry Biologics (Biosimilars) 2015. Available at: https://www.badgut.org/survey-results-biosimilars/. Accessed 2018-08-20.


# Retention Rates Post-Switch

Original patient population switched from infliximab originator to biosimilar **(100)**

Fail to achieve/ loss of therapeutic response post-switch **(30)**

Achieve response post-switch **(70)**

Develop symptoms post-switch **(15)** *must be switched back to originator infliximab or to new originator molecule

Fail to respond to infliximab **(15)**, expected even without switch

**Note:** Data utilized for projections was gathered in countries without patient support programs (i.e., infusion site and health care personnel administering medication remained constant). This must be considered when extrapolating data for Canada. Estimates based off of three recent real-world evidence publications: Avouac J *et al. Semin Arthritis Rheum.* 2018 Apr;47(5):741-748, Scherlinger M *et al. Joint, Bone, Spine.* 2017 Nov 14. doi: 10.1016/j.jbspin.2017.10.003, and Tweehuysen L *et al. Arthritis Rheumatol.* 2018 Jan;70(1):60-68. *These studies reported higher discontinuation rates than have previously been captured. The conflicting body of data around discontinuation rates of biosimilars post-switching highlights the need for further investigation.



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