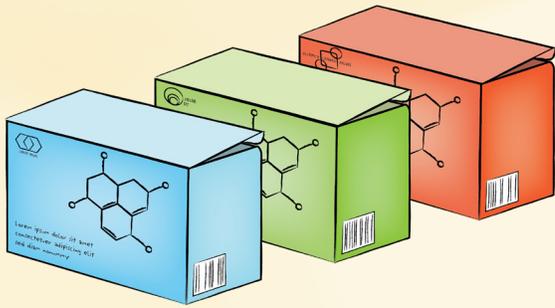


Biosimilar biologics in Canada – What inflammatory arthritis patients need to know

Second Edition

April 2021

Biosimilar biologics in Canada



A biosimilar biologic is highly similar to its originator biologic



After an originator's patent expires, other companies are allowed to produce their own biosimilar version of it. Because biosimilars are produced post-patent, biosimilar manufacturers do not have the same costs to bring the product to market and can therefore offer it at a lower price¹



There is no clinically, meaningful difference in safety, efficacy or quality



Health Canada has approved more than 33 biosimilars to help treat Canadians living with inflammatory arthritis, cancer, diabetes, inflammatory bowel disease and psoriasis



Biologic drugs make up some of public and private drug plans' largest drug expenditures. Even though less expensive biosimilars provide same therapeutic benefits as their originators, the uptake in Canada of biosimilars continues to be very low



Biosimilar biologics can improve access to biologics and produce significant savings for public and private healthcare systems



The Patented Medicines Pricing Review Board has estimated that private and public drug plans across Canada could save from \$332 million CDN to \$181 billion CDN in the third year following biosimilar entry across a portfolio of product²



Biosimilar savings can help improve non-medication elements of care that patients need, such as specialized nursing, counseling, physio- and occupational therapy



Biosimilars savings can modernize "special access criteria," removing the need for patients to fail on older therapies before approving reimbursement for biosimilars



Through the launch of biosimilar transition policies, British Columbia, Alberta and New Brunswick are using biosimilars savings to improve the sustainability of their drug plans by adding new medicine listings and boosting existing medication coverage for patients



Biosimilar savings can be reinvested into public and private drug plan budgets making it possible to add new medications

Transitioning to a biosimilar biologic



“Medical transition” occurs when a patient, not doing well on their current originator or biosimilar, is transitioned to another originator or biosimilar to regain maximum disease control



“Policy transition” occurs when a public or private drug plan’s reimbursement policy change necessitate patients to move from their originator to its biosimilar, usually because it is significantly less expensive

Transitioning is safe and effective



According to Health Canada: “Patients and health care providers can have confidence that biosimilars are effective and safe for each of their authorized indications. No differences are expected in efficacy and safety following a change in routine use between a biosimilar and its reference biologic drug in an authorized indication.”³



More than 170 research studies exist on patients with inflammatory arthritis, gastrointestinal and skin disease who have successfully policy transitioned from a TNF inhibitor originator to its TNF inhibitor biosimilar

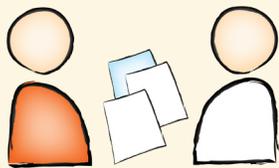


After transitioning to a biosimilar, patients will obtain their medication in the same or similar way as their previous biologic



Patients, in partnership with their rheumatologists, will monitor the safety and effectiveness of their biosimilars as part of routine care

Credible fact-based information on biosimilar biologics



The decision to start on a biologic (originator or biosimilar) is best made by a well-informed patient and their rheumatologist based on credible scientific evidence and in consideration of the safety, benefits and risks, patient treatment goals and preferences, accessibility of treatment and affordability



Patients can find more biosimilars information from a number of credible sources: Rheumatologists, rheumatology nurses and pharmacies, as well as their public or private drug plan and patient support programs

1 Canadian Agency for Drugs and Technologies in Health (CADTH): Biosimilar Drugs: Your Questions Answered
https://www.cadth.ca/sites/default/files/pdf/biosimilar_drugs_patient_en.pdf

2 Patented Medicine Prices Review Board – Biologics in Canada
<https://www.canada.ca/content/dam/pmprb-cepmb/documents/reports-and-studies/chartbooks/biologics-part1-market-trends.pdf>

3 Health Canada Fact Sheet on Biosimilars: Switching
https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/dhp-mps/alt_formats/pdf/brgtherap/applic-demande/guides/Fact-Sheet-EN-2019-08-23.pdf

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Foreword

Biosimilar biologics in Canada – What inflammatory arthritis patients need to know

Biosimilar biologics (“biosimilars”) have been approved for use in Canada since 2009, and in arthritis since 2014. Thirty-three biosimilars are currently approved by Health Canada for chronic diseases, including inflammatory arthritis, cancer, inflammatory bowel disease, diabetes and psoriasis. Since the European Union (EU) approved the first biosimilar in 2006, and in inflammatory arthritis in 2013, the EU has approved more than 72 biosimilars.

Based on scientific evidence and the lived experience of patients in North America and Europe, rheumatologists across Canada are now regularly prescribing biosimilars for newly initiated inflammatory arthritis patients. In full consultation with their patients, they are now also transitioning their experienced patients from originator biologic (“originator”) to its biosimilar.

Public and private drug plans have begun implementing policy transition (also called “non-medical switch”) requiring patients to move from their current originator to its biosimilar. Policy transition has been implemented in several Canadian provinces, including British Columbia, Alberta and New Brunswick.

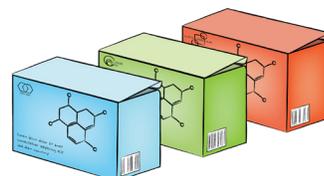
B.C. was the first province to implement biosimilars transition policy in May 2019 and has reported that thousands of patients living with inflammatory arthritis, inflammatory bowel disease and diabetes have been transitioned with no compromise to patient safety, effectiveness or quality of care.¹

In this guide, we discuss important biosimilars facts for patients to understand if they are starting on or transitioning to a biosimilar. If you have any questions or wish to share feedback, please contact us at feedback@jointhealth.org.

About the Author

Arthritis Consumer Experts (ACE) has produced the “Biosimilar biologics in Canada: What inflammatory arthritis patients need to know” guide to address those needs of patients who want information on biosimilar medicines. It provides answers to questions patients may have on biosimilars and the information tools they need to power and support their conversations with their rheumatologists and other health care providers to ensure science-based continuity of care. If you would like to read more about biosimilar medicines, there are references for further information at the end of this guide or visit jointhealth.org.

Arthritis Consumer Experts thanks Arthritis Research Canada for its review of the content in this guide.



Biosimilar biologics overview

What are biologics (originators and biosimilars)?

Over the past 20 years in Canada, biologics have improved the treatment for patients living with disabling and life-threatening chronic diseases, including inflammatory arthritis (IA), cancer, diabetes, inflammatory bowel disease and psoriasis.

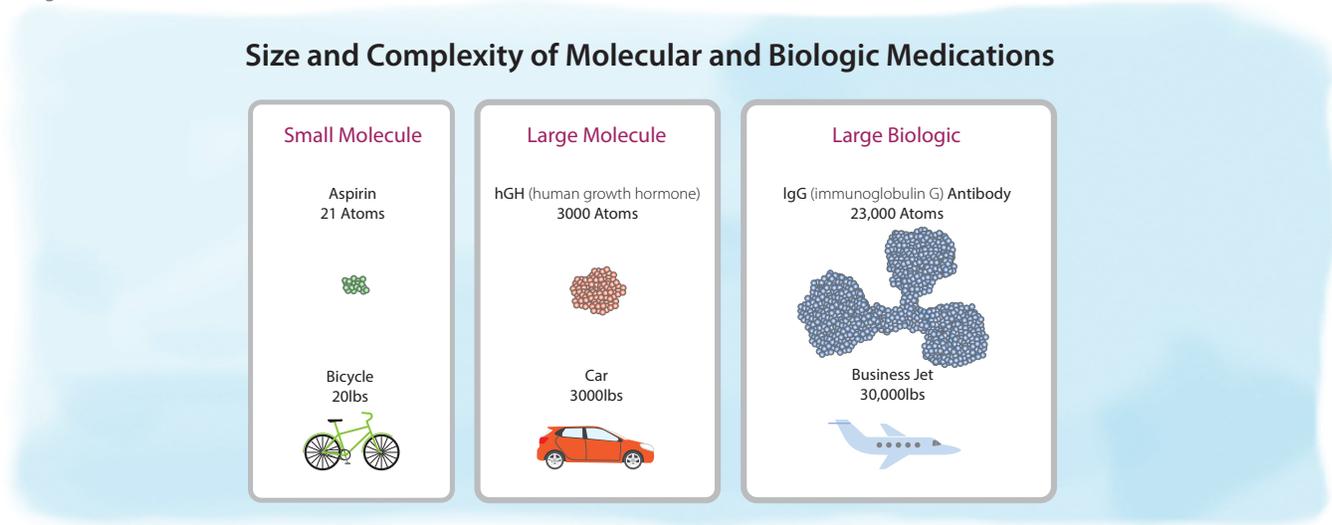
Rheumatologists prescribe biologics to IA patients whose disease does not respond, or respond well enough, to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) such as hydroxychloroquine or sulfasalazine. Biologics are proved to effectively address disease signs and symptoms – like swelling, pain and fatigue – but also may improve mortality and reduce heart disease and other complications of IA.

Biologic medicines are made from living organisms, such as living cells that have been modified using biotechnology. This allows these living organisms or cells to produce the active substance (the part that works to treat the disease) of the biological medicine. This active substance is then harvested from the cells. The active substance is commonly called a “protein.” Biologics are much larger and more complex in composition than conventional, small molecule medicines, like over-the-counter ibuprofen (e.g. Advil) or by-prescription methotrexate. (See figure 1)

Because of their complexity, biologics are expensive and time consuming to develop. This can make it difficult for the health care system to afford them and limit patients’ access to biologics. In 2018, three of the top five drug classes that accounted for the highest proportion of public drug plan spending in Canada were biologics.² And, in 2018, biologics used to treat diseases like rheumatoid arthritis and Crohn’s disease accounted for the highest proportion of public drug spending for the seventh consecutive year.³

Life-changing biologic medicines are complex, expensive to manufacture and continue to be a growing budget pressure for public and private drug plans.

Figure 1



What are biosimilar biologics?

When the patent of an originator expires, other manufacturers are allowed to make a biosimilar version of the medicine. A biosimilar has similar effectiveness, safety, and quality and delivers the same therapeutic benefits to patients as its originator.⁴

They are typically prescribed to inflammatory arthritis patients by a rheumatologist.

For example:

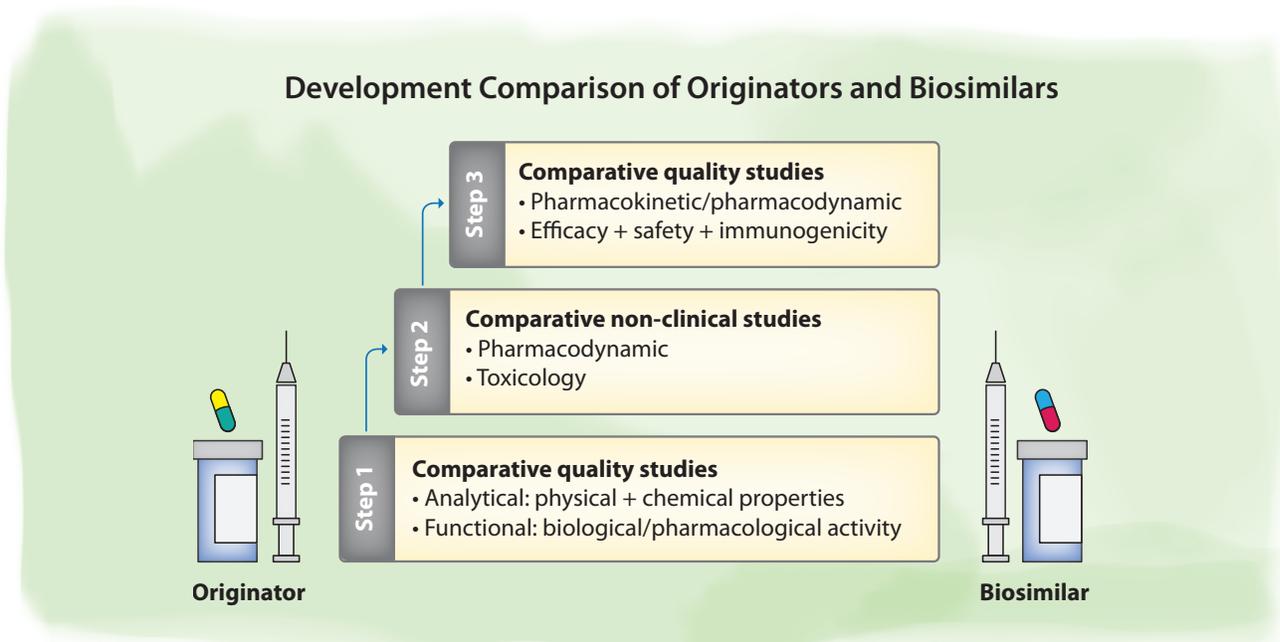
- adalimumab (Amgevita[®]), adalimumab (Hadlima[®]), adalimumab (Hulio[®]), adalimumab (Hyrimoz[®]), and adalimumab (Idacio[®]) are biosimilar versions of the originator adalimumab (Humira[®]);
- etanercept (Brenzys[®]) and etanercept (Erelzi[®]) are biosimilar versions of the originator etanercept (Enbrel[®]);
- infliximab (Inflectra[®]) and infliximab (Renflexis[®]) are biosimilar versions of the originator infliximab (Remicade[®]);
- rituximab (Riximyo[®]), rituximab (Ruxience[®]) and rituximab (Truxima[®]) are biosimilar versions of the originator rituximab (Rituxan[®]).

Due to the size, complexity and natural variability of biologic medications, a biosimilar and its originator can be shown to be similar, but not identical.

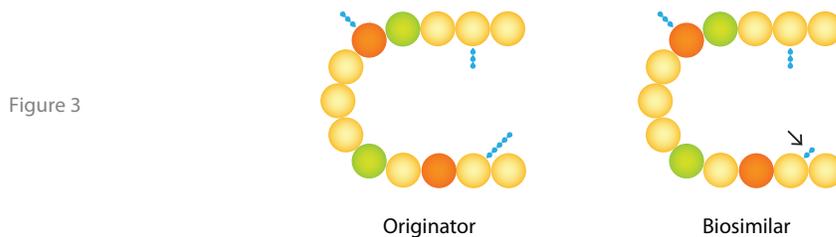
For example, the way that adalimumab, etanercept, infliximab, or rituximab are manufactured make it impossible to produce an exact copy of the molecules. This differs from other pill-form medications you may have taken before. Medications like methotrexate and ibuprofen are made of small chemical molecules, not proteins. When patents expire on small molecule medications and generic versions are authorized for manufacture, exact copies can be made.

When the patent of an originator expires, other manufacturers are allowed to make a biosimilar version of the medicine.

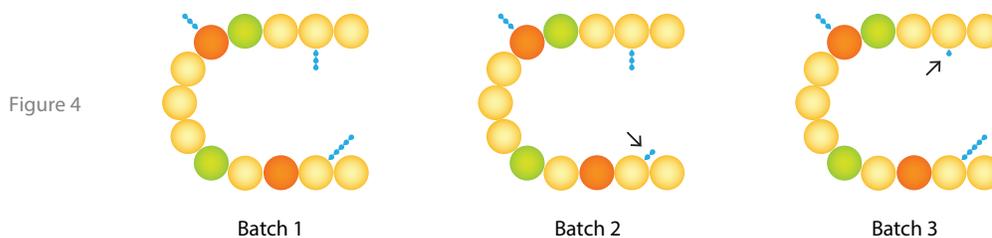
Figure 2



The diagram below (Figure 3) shows the slight differences that occur between originator and biosimilar because they are both made from living cell lines. The arrows in the diagrams below point to slight differences that do not involve the active or “medicinal” part of the biosimilar. The slight difference is called “glycosylation”, or simply put, sugar molecules. Minor differences between the originator and the biosimilar in clinically inactive components are acceptable and are not known to make a difference in the way the medicine works in the body.



Biologics – originators and biosimilars – are made in “batches”. Batches of originators are slightly different from each other (Figure 4), but those differences are minimal and are not known to affect safety, efficacy or patient outcomes. Health Canada carefully monitors the manufacturing processes of originators and biosimilars to ensure that they are consistent and acceptable.



Both originator and biosimilar biologics are made in “batches,” and Health Canada carefully monitors the manufacturing processes of originators and biosimilars to ensure they are consistent and acceptable.

Because biosimilars are produced post-patent, biosimilar manufacturers do not have the same costs to bring the product to market and can therefore offer it at a lower price.⁵ The potential savings generated by biosimilars may be reinvested into healthcare resources needed by Canadian patients.

Health Canada’s Biosimilar Biologic Drug web site page provides information about biosimilars including a fact sheet, relevant guidance documents, scientific advice meetings and links to approved drugs: <http://bit.ly/HealthCanadaBiosimilarEN>

The biosimilar biologic review process in Canada

A biosimilar can enter the market after an originator patent expires and after a thorough review by Health Canada. Health Canada defines a biosimilar as a biologic medicine that is highly similar to a biologic medicine that was already authorized for sale. There are no expected meaningful differences in efficacy and safety in the biosimilar compared to an originator biologic.

Health Canada does not require all studies with the originator repeated with the biosimilar. Because the safety and effectiveness of the biologic originator are already well known, if the biosimilar medicine is very similar in structure and works as well, not all clinical studies need to be repeated. Instead, studies aim to show that there are no clinically meaningful differences between the biosimilar and the originator (i.e. to demonstrate biosimilarity).⁶

The key principles that Health Canada uses to evaluate biosimilars are aligned with those of other regulators and international organizations such as the European Medicines Agency (EMA), the United States Food and Drug Administration (FDA), and the World Health Organization and the International Coalition of Medicines Regulatory Authorities (ICMRA). In July 2019, the ICMRA issued a statement on biosimilars, providing assurance on the regulatory processes for the authorization and monitoring of biosimilars medicines and highlighting the benefits they can provide for patients and healthcare systems in terms of increased treatment alternatives, access and cost competitiveness.⁷

Since the EU approved the first biosimilar in 2006, it has approved the highest number of biosimilars worldwide, amassing considerable experience of their use and safety. During this period, the EU monitoring system for safety concerns has not identified any relevant difference in the nature, severity or frequency of side effects between biosimilars and their originators.

There have been more than 700 million patient days of exposure to biosimilars in the EU and no new safety concerns have emerged that were not previously observed with the reference product. During this period the EMA states: “The evidence acquired over 10 years of clinical experience shows that biosimilars approved through EMA can be used as safely and effectively in all their approved indications as other biological medicines.”⁸



Reinvestment of biosimilar savings can improve the healthcare system for Canadians.

Benefits to patients and health care systems

Underlying Health Canada’s approach to authorizing biosimilars are the benefits to society the use of biosimilars can bring to patients and the health care system. Biosimilars can be used for the same therapeutic aim as their originator and offer an opportunity to reduce spending on more costly originators. These savings may be reinvested into improving the healthcare system for Canadians.

The Canadian Government’s Patented Medicine Prices Review Board has estimated that private and public drug plans across Canada could save from \$332 million to \$1.81 billion in the third year following biosimilar entry across a portfolio of products.⁹

Extrapolation

Once studies show that the biosimilar works as well as the originator medicine with no clinically meaningful differences, Health Canada can approve the biosimilar for the same diseases as its originator based on the previously established efficacy and safety of the originator in each disease.¹⁰ All the major health regulators around the world agree there is no need to repeat the clinical studies for each disease.

Post marketing surveillance: How the safety of biosimilar biologics is monitored after review and if approved

Tracking the efficacy, safety and value to patients and the health care system of both originators and their biosimilars is important. Patients and their physicians rely on this “real-world data” when they are making treatment decisions.

Health Canada monitors the safety of all medications on the market, including biosimilars. Specifically, Health Canada:

- Conducts market surveillance
- Monitors adverse reaction reports
- Investigates complaints and problem reports
- Takes action as appropriate

Each manufacturer must do its part for drug safety; including:

- Set up a system to monitor reported side effects;
- Report any new information received about serious side effects to Health Canada;
- Notify Health Canada about any studies with new safety information;
- Request authorization for any major changes to:
 - the manufacturing process,
 - dose regimen, or
 - recommended uses of the medicine.¹¹



Biosimilar biologics library

- Health Canada Fact Sheet: Biosimilar Biologics
<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html>
- Canadian Agency for Drugs and Technologies in Health (CADTH): Biosimilar Drugs: Your Questions Answered
https://www.cadth.ca/sites/default/files/pdf/biosimilar_drugs_patient_en.pdf
- Ontario Drug Policy Research Network: Current and Prospective Utilization of Innovator Biologics and Biosimilars in Ontario
<https://odprn.ca/wp-content/uploads/2020/01/Utilization-of-Innovator-Biologics-and-Biosimilars-in-Ontario.pdf>
- Patented Medicines Prices Review Board: Potential Savings from Biosimilars in Canada.
https://www.pmprb-cepmb.gc.ca/CMFiles/NPDUIS/2017_Conference_Posters/post_6_biosim.pdf
- pan-Canadian Pharmaceutical Alliance: Pan-Canadian Oncology Biosimilars Initiative
<https://www.cancercareontario.ca/en/programs/provincial-drug-reimbursement/oncology-biosimilars-initiative>
- International Coalition of Medicines Regulatory Authorities (ICMRA) statement about confidence in biosimilar products
http://www.icmra.info/drupal/sites/default/files/2019-07/ICMRA_statement_about_confidence_in_biosimilar_product_HCP.PDF
- European Medicines Agency and The European Commission: Biosimilars in the EU: Information Guide for Healthcare Professionals
https://www.ema.europa.eu/en/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf
- European Medicines Agency: Biosimilars Medicines: Overview
<https://www.ema.europa.eu/en/human-regulatory/overview/biosimilar-medicines-overview>
- FDA Biosimilars Home Page
<https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/biosimilars>

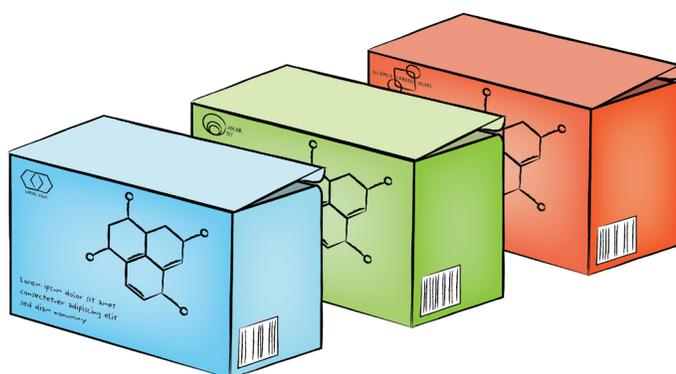
How do patients and health care systems benefit from biosimilar biologics?

Biologics take years to research, develop and manufacture, making them expensive when they come into the marketplace. Health care systems limit reimbursement access to biologics through “special access criteria” – a patient must be, or get, very sick before public or private drug plans will pay for them. As a result, all patients who medically need a biologic therapy may not qualify for reimbursement coverage because the criteria are too difficult to meet.

Since the entry of biologics into the Canadian market, the use of biologics has been higher in Canada than in most comparable international markets. In 2018, three of the top five drug classes that accounted for the highest proportion of public drug plan spending were biologics. One of these biologic drug classes, anti-TNF medicines, used to treat diseases such as rheumatoid arthritis and Crohn’s disease, accounted for the highest proportion of public drug spending for the seventh consecutive year.¹²

Biosimilars can be used for the same therapeutic aim as their originator and offer an opportunity to reduce spending on more costly originators. Biosimilars can create three main benefits to patients, the health care system, and society:

1. **Savings from biosimilars use can modernize “special access criteria”.** Currently, patients must try and fail treatment on older, less expensive medications. Because biosimilars are significantly less expensive, public and private drug formularies can remove the need for patients to fail on these older therapies before approving reimbursement for them.
2. **Savings from biosimilars use can be reinvested into public and private drug formulary budgets** making it possible to improve the sustainability of their drug plans by adding new medication listings and boosting medicine coverage for patients.
3. **Savings from biosimilars should be invested into non-medication types of care** that patients need, such as specialized nursing, counselling, physio and occupational therapy.



Biosimilar biologics: Frequently asked questions



Are biosimilar biologics generic medicines?

Biosimilar and originator medicines are not the same as the more common generic medicines such as aspirin or ibuprofen. Generic medicines are small molecules (usually “pills”) that are chemically synthesized. They contain identical medicinal ingredients to their reference products. When a drug patent expires, pharmaceutical companies can copy that branded drug, and sell it for significantly less as a generic.

If they meet Health Canada’s safety and efficacy requirements, biosimilars are allowed to enter the marketplace when the patent of the originator expires. Biosimilars and their originators can be shown to be highly similar, but not identical. This is because biologic medicines are often large and complex and are made from living cells rather than with chemicals and so are naturally variable.

My rheumatologist and I are thinking about choosing a biosimilar biologic for my treatment: Is it going to be safe and effective?

Patients understandably have many questions when prescribed a biologic, whether it’s an originator or biosimilar. This places a great deal of importance on the conversation about biologics between a patient and their healthcare provider.

A biosimilar is a biologic that has extremely similar effectiveness, safety, immunogenicity profile and quality, and delivers the same therapeutic benefits to patients as its originator.¹³

As with any treatment, it is important patients have a thorough conversation with their rheumatologist about all available therapeutic options, the safety, benefits and risks, patient treatment goals and the differences between the medications, before coming to a decision

Why do biosimilar biologics cost less than originator biologics?

A manufacturer of biologics must spend many years studying a new biologic medicine before it can be approved for sale in Canada. The company then holds a patent on the medicine that prevents other companies from selling that product. This allows the originator manufacturer to earn back the money it spent on bringing the product to market. When the patent of an originator expires, other manufacturers are allowed to make a biosimilar version of the medicine. Manufacturers that make biosimilars of other originator medicines do not have the same costs to bring the product to market and can therefore offer it at a lower price.¹⁴

What should I do if I think I have a side effect?

For people living with inflammatory arthritis, the greatest risk while taking a biologic is infection. Biologic medications – originator or biosimilar - may make it harder for these patients' immune system to fight off infections. The likelihood of experiencing infection or any other side effects vary from person to person.

As with any biologics (originator or biosimilar), in cases where you suspect you may have a side effect, both you and your rheumatologist or pharmacist should report it. This helps authorities to continuously monitor the safety of medicines in the wider population.

Why aren't all studies conducted by the originator biologic maker repeated with the biosimilar biologic maker?

Because the safety and effectiveness of the originator are already well known, if the biosimilar is very similar in structure and has the same biological activity, not all clinical studies need to be repeated.

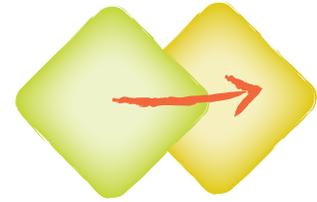
What is immunogenicity and how is it addressed for biosimilar biologics?

The immune system has evolved to recognize foreign proteins in the body. Biologics are usually given by injection, which can cause the body's immune system to react to them. This is referred to as immunogenicity. Sometimes immunogenicity can only be detected using sophisticated laboratory tests and has no impact on the patient. In other cases, immunogenicity can impact patient safety or how well the medication works. For these reasons, studies showing that there are no clinically meaningful differences in immunogenicity between the biosimilar and originator are required for authorization of a biosimilar. In addition, biosimilar manufacturers are responsible to monitor the immunogenicity potential of the biosimilar after it is used in Canada.¹⁶

Biosimilar biologic transition overview

Transitioning from an originator biologic to a biosimilar biologic

The leading regulators in the world – including the European Medicines Agency, Food & Drug Administration in the U.S and Health Canada – support well-controlled transitions (“switches”) to biosimilars. Patients need to know transition policy has been safely and effectively implemented over the past 12 years with tens of thousands of patients with autoimmune diseases such as inflammatory arthritis in many countries in Europe and North America with no compromise to patient safety, effectiveness or quality of care.



Transitioning terminology

“**Transitioning**” or “**switching**” means a patient is moved from one medication to another. In the case of biologics, there are two types of transitions:

“**Medical transition**” occurs in the case of a patient not doing well on their current originator or biosimilar who is transitioned to another originator or biosimilar, based on a decision by the patient and their rheumatologist, in order to regain maximum disease control.

“**Policy transition**” (sometimes referred to as “non-medical switch”) occurs when a public or private drug plan’s reimbursement policy necessitate patients move from their current originator to its biosimilar.

Even though less expensive biosimilar provide the same therapeutic benefits as their originators, the uptake in Canada of biosimilars continues to be very low.

Biosimilar biologic transitioning experience in Canada

For the past six years, federal, provincial, territorial and private insurance drug plans have mandated the use first of biosimilar versions ahead of their originators for treatment-naïve patients (patients who have not previously received the biologic in question). Since 2019, public drug plans have also begun implementing biosimilar transition policies that change coverage for specific biologic medicines.

In the context of biosimilar use, Health Canada considers “switching between authorized products to refer to a change from routine use of one specific product to routine use of another specific product. Patients and healthcare providers can have confidence that biosimilars are effective and safe for each of their authorized indications. No differences are expected in efficacy and safety following a change in routine use between a biosimilar and its reference biologic drug in an authorized indication.”¹⁷

During the period of transition policy implementation, the drug plans cover both originator and biosimilar medicines for the affected diseases, providing time for patients to understand the biosimilar transition and their treatment options with their specialists. Following the end of a transition period, the drug plans only cover the biosimilar versions for the treatment

When considering a transition to biosimilar, Health Canada states: “No differences are expected in efficacy and safety following a change in routine use between a biosimilar and its reference biologic drug in an authorized indication.”

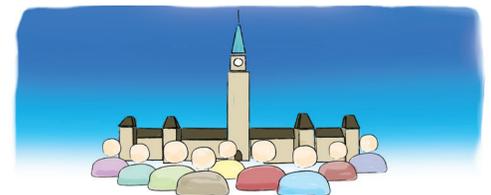
of diseases affected by the transition policy. Patients unable to transition or who have an adverse response to the biosimilar can seek exceptional “special authority” coverage for the originator.¹⁸

Patients will continue to be supported and obtain their biosimilar in the same way as they did for the biologic they were previously taking. Rheumatologist will provide patients the name of the patient support program for their biosimilar and will help organize reimbursement and other patient needs. Your rheumatologist or rheumatology nurse will monitor the safety and effectiveness of your biosimilar as part of your routine care.

As patients have already been successfully treated with the originator, they are unlikely to experience any new side effects after transitioning. As always, rheumatologists will monitor patient treatment carefully, just like they did with the previous biologic, whether it was an originator or a biosimilar. If patients feel they are experiencing a significant side effect, they should contact their rheumatologist who will be able to assess whether it is the medication or some other reason causing it.

Biosimilar biologic policy in Canada

In April 2021, New Brunswick became the third province in Canada to implement biosimilars transition policy after British Columbia and Alberta. Under New Brunswick’s new policy, coverage for certain originator medicines through the New Brunswick Drug Plan is changing and may require patients to transition from the originator medicine that they are currently on to a biosimilar version of that medicine.¹⁹



In May 2019, British Columbia was the first province to implement biosimilars transition policy, which moves patients from their current originator to its biosimilar. Since implementation, B.C. has reported that thousands of patients living with inflammatory arthritis, diabetes and inflammatory bowel disease have been safely transitioned.²⁰ Through the launch of its biosimilars switching policy, British Columbia stated it is improving the sustainability of its PharmaCare program by adding new medicine listings and boosting existing medication coverage for patients.²¹

In December 2019, Alberta announced its Biosimilar Initiative to expand the use of biosimilar medications through transition policy, explaining “patients will continue receiving the same safe and effective treatment, but at a lower cost.”²²

A key benefit of transitioning patients is hundreds of millions of dollars in cost savings to the health care system. Biosimilars have the potential to improve access to biologics (both originators and biosimilars) and save public and private healthcare systems billions of dollars now, and over the coming year.

At the announcement of the expansion of its Biosimilars Initiative program in August 2020, the B.C. government stated the third phase would allow it to put another \$30.7 million over the next three years, in addition to the \$96.6 million from earlier phases of the Biosimilars Initiative, back into BC’s health care system.²³ In April 2021, the B.C. government added another biosimilar (adalimumab) for provincial coverage, citing additional savings of over \$100 million over three years.²⁴

When it announced its biosimilars transition policy in December 2019, the Alberta government claimed switching to biosimilars would save between \$227 million and \$380 million over the next four years once fully implemented.²⁵

Transition experience and policy in Europe

Policy transition has been successfully implemented in many European countries over the past 12 years and in tens of thousands of patients living with inflammatory arthritis and inflammatory bowel disease with no compromise to patient safety, effectiveness or quality of care.

European Union (EU) member countries generally agree that EU approved biosimilars are considered alternative therapeutic options to their respective originators, under the supervision of a clinical decision maker. The majority of countries, including England, Norway, Denmark, Germany, Netherlands, Belgium, France, and Portugal support physician led transitioning for biosimilars.

In the EU, like in Canada, the ruling regulatory body (European Medicines Agency, the European equivalent to Health Canada) leaves the decision on biosimilar transitioning to individual member countries (comparable to federal, provincial and territorial jurisdictions or private drug plans decision making in Canada).

The EU Consortium of Individual Regulators in 2017 concluded that because of the high similarity, there is no reason to believe that the body's immune system would react differently to the biosimilar compared with the originator upon a switch. This view is supported by the current experience with biosimilars on the market and by literature data. (Kurki et al. – Interchangeability of biosimilars: A European perspective)

<http://bit.ly/InterchangeabilityBiosimilars>

Transition Studies

- Cohen HP, Drugs, 2018: Switching Reference Medicines to Biosimilars: A Systemic Literature Review of Clinical Outcomes <http://bit.ly/CohenSwitchingRef>
- Edwards CJ et al. Switching to biosimilars: current perspectives in immune-mediated inflammatory diseases. *Expert Opinion on Biological Therapy* (2019) doi.org/10.1080/14712598.2019.1610381
- Gisbert and Chaparro. Switching from an originator anti-TNF to a biosimilar in patients with inflammatory bowel disease: Can it be recommended? A systematic review. *Gastroenterol Hepatol.* (2018) <https://doi.org/10.1016/j.gastrohep.2018.04.005>
- McKinnon et al. Biosimilarity and interchangeability: Principles and Evidence: A systematic review. *BioDrugs* (2018) 32:27-53
- Moots et al. Switching between reference biologics and biosimilars for the treatment of rheumatology, gastroenterology, and dermatology inflammatory conditions: Considerations for the clinician. *Curr Rheum Rep*

What is the NOCEBO effect?

Transitioning patients from originators to biosimilars is associated with the potential for a “nocebo” effect, a phenomenon that occurs when a patient’s negative expectation causes a treatment to have a more negative effect than it otherwise would—essentially, the opposite of the placebo effect.

The way in which rheumatologists and other healthcare providers communicate with patients about transitioning to a biosimilar is key to preventing the nocebo effect. Patients should be informed about the transition well in advance, and the availability of research-based information is important for patient understanding and empowerment. Finally, an appointment with a rheumatologist to discuss biosimilar transitioning should ideally allow enough time with the patient to understand the concept of biosimilars and transitioning and to address any concerns properly.

Having a fact-based biosimilar biologic transition conversation with your healthcare professional

Based on real-world experience, prior to transitioning patients, both rheumatologists and their patients must be fully informed about the policy requiring the transition and have all available information about the biosimilar.

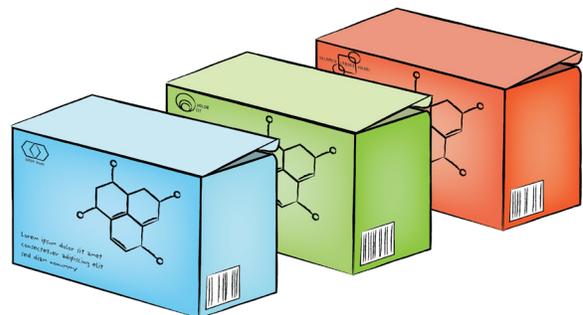
The key for patients going through policy transition is to be able to access science-based information to support their conversations with their healthcare team. Healthcare professional should be able to provide the patient education materials in “easy-to-read”, objective language to help them understand the principles of biosimilars and the reasons for transition and the scientific evidence that supports it.

There are several other credible places patients transitioning from one biologic to another (whether from originator to biosimilar, originator to originator, or biosimilar to originator) can go for information and support:

- Patient support program
- Public or private drug plan web sites
- Patient organizations such as Arthritis Consumer Experts
- Patient created biosimilars resources, such as the Biosim•Exchange

<http://bit.ly/BiosimExchangeEN>

Based on real-world experience, prior to transitioning patients, both rheumatologists and their patients must be fully informed about the policy requiring the transition and have all available information about the biosimilar.



- 1 B.C. Ministry of Health: Biosimilars Initiative Switch Data**
<https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/biosimilars-initiative-prescribers>
- 2 Canadian Institute for Health Information - Prescribed Drug Spending in Canada, 2019**
<https://www.cihi.ca/sites/default/files/document/pdex-report-2019-en-web.pdf>
- 3 Canadian Institute for Health Information - Prescribed Drug Spending in Canada, 2019**
<https://www.dropbox.com/s/8axt6loyw19t65r/Screenshot%202020-02-21%2014.51.24.png?dl=0>
- 4 Health Canada Fact Sheet on Biosimilars**
<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html>
- 5 Canadian Agency for Drugs and Technologies in Health (CADTH): Biosimilar Drugs: Your Questions Answered**
https://www.cadth.ca/sites/default/files/pdf/biosimilar_drugs_patient_en.pdf
- 6 Health Canada Fact Sheet on Biosimilars: Information requirement for initial authorization of a biosimilar**
<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html>
- 7 ICMRA statement about confidence in biosimilar products (for healthcare professionals):**
http://www.icmra.info/drupal/sites/default/files/2019-07/ICMRA_statement_about_confidence_in_biosimilar_product_HCP.PDF
- 8 European Medicines Agency: Biosimilars in the EU**
https://www.ema.europa.eu/en/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf
- 9 Patented Medicines Prices Review Board. Potential Savings from Biosimilars in Canada. Date modified: 2018-02-05**
https://www.pmprb-cepmb.gc.ca/CMFiles/NPDUIS/2017_Conference_Posters/post_6_biosim.pdf
- 10 Health Canada: Biosimilar biologic drugs in Canada: Fact Sheet – Authorizing Indications**
<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html#a9>
- 11 Health Canada: Biosimilar biologic drugs in Canada: Fact Sheet – How we monitor the safety of biosimilars after they have been authorized**
<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html#a9>
- 12 Canadian Institute for Health Information - Prescribed Drug Spending in Canada, 2019, page 9**
<https://www.dropbox.com/s/8axt6loyw19t65r/Screenshot%202020-02-21%2014.51.24.png?dl=0>
- 13 Health Canada Biosimilars Fact Sheet: Biosimilars Explained**
<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html>
- 14 Canadian Agency for Drugs and Technologies in Health (CADTH): Biosimilar Drugs: Your Questions Answered**
https://www.cadth.ca/sites/default/files/pdf/biosimilar_drugs_patient_en.pdf

15 Arthritis Research Canada: Biologics and Biosimilars for the Treatment of Inflammatory Arthritis

<https://arthritis.ca/getmedia/d77ec1aa-62ee-496d-9902-b82f3df88eb8/Biologics-and-Biosimilars-for-Treatment-of-Arthritis-ENG.pdf>

16 Health Canada: Biosimilar biologic drugs in Canada: Fact Sheet - Immunogenicity and how we address it for biosimilars

<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html#a1>

17 Health Canada Fact Sheet on Biosimilars: Switching

<https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html>

18 BC Biosimilars Initiative for Patients

<https://www2.gov.bc.ca/gov/content/health/health-drug-coverage/pharmacare-for-bc-residents/what-we-cover/drug-coverage/biosimilars-initiative-patients>

19 New Brunswick Biosimilars Initiative

<https://www2.gnb.ca/content/gnb/en/departments/health/MedicarePrescriptionDrugPlan/NBDDrugPlan/biosimilars.html>

20 B.C. Ministry of Health: Biosimilars Initiative Switch Data

<https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/biosimilars-initiative-prescribers>

21 British Columbia Ministry of Health: Biosimilars Initiative

<https://news.gov.bc.ca/releases/2019HLTH0080-001072>

22 Alberta Health: Biosimilar Drugs

<https://www.alberta.ca/biosimilar-drugs.aspx>

23 B.C. Government News: B.C. expands biosimilar program

<https://news.gov.bc.ca/releases/2020HLTH0257-001569>

24 B.C.'s biosimilars program expands

<https://news.gov.bc.ca/releases/2021HLTH0067-000653>

25 Alberta Biosimilars Initiative

<https://www.alberta.ca/biosimilar-drugs.aspx>

About ACE

Arthritis Consumer Experts (ACE) is a national organization that provides free science-based information and education programs in both official languages to people with arthritis. ACE serves people living with all forms of arthritis by helping them take control of their disease and improve their quality of life. Founded and led by people with arthritis, ACE actively advocates on arthritis health and policy issues through ACE's JointHealth™ family of programs and the Arthritis Broadcast Network. ACE is guided by a strict set of guiding principles established by an advisory board comprised of leading scientists, medical professionals and informed arthritis consumers.

ACE has been a leader in biosimilars discussions and education since 2009, sharing information with stakeholders across Canada through free research-based workshops, webinars and education programs. Drawing from this experience, ACE has created the Biosim•Exchange, an information hub for consumers to get the latest biosimilars news and background analysis. <http://bit.ly/BiosimExchangeEN>.

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ACE also receives unsolicited donations from its community members (people with arthritis) across Canada.

ACE thanks funders for their support to help the nearly 6 million Canadians living with arthritis.

ACE has produced a special biosimilars education video series, where ACE speaks to medical experts on key patient questions around biosimilars and transitioning from originators to biosimilars: Go to <https://biosim.jointhehealth.org/resources> and click on "Biosimilars education videos."

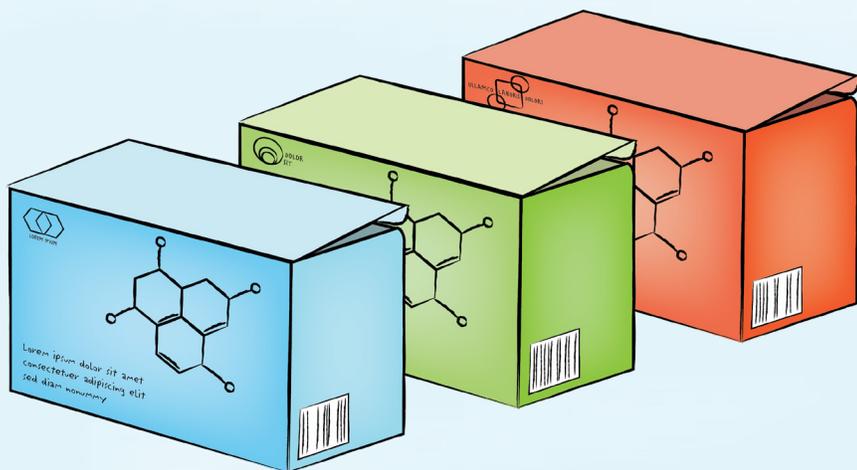
About this Guide

This guide has been prepared by Arthritis Consumer Experts (ACE) in collaboration with its advisory board comprised of leading scientists and medical professionals and will be updated and improved regularly as new research and information on biosimilars become available.

This guide was published in 2021. This information will be updated online and available for download in PDF format at <http://biosim.jointhehealth.org>.

Disclaimer

The material contained in this guide is provided for general information only. This guide should not be relied on to suggest a course of treatment for a particular individual or as a substitute for consultation with qualified health professionals who are familiar with your individual medical needs. It is meant to inform the discussion that you have with health care professionals, as well as others who play a role in your treatment and care. Should you have any health care related questions, you should contact your physician.



Biosimilars biologics in Canada – What inflammatory arthritis patients need to know

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Arthritis Consumer Experts thanks Arthritis Research Canada for its review of the “Biosimilar biologics in Canada – What inflammatory arthritis patients need to know” guide.

Visit the Biosim-Exchange:

<http://biosim.joinhealth.org>

Discover Arthritis Consumer Experts online:

www.joinhealth.org

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