Biosimilars: Frequently Asked Questions

What is a biologic?

Biologics are medicines to treat chronic diseases and are made from living organisms. Biologic medicines are generally larger and more complex in composition than chemically produced medicines.[1]

What is a biosimilar?

As patents and data protection expire for original-brand medicines, other manufacturers may produce new versions of the biologic medicines called biosimilars. To receive Health Canada authorization, a biosimilar must demonstrate it is highly similar and has no clinically meaningful differences in efficacy and safety compared to an original-brand ("reference") biologic.[2]

The type of data required to support biosimilar approval differs from that required for an original-brand biologic medicine. Biosimilar manufacturers do not have to recreate the original-brand biologic's research and development. Instead, biosimilar manufacturers must perform comparative studies to demonstrate similarity.[3] This means manufacturers that make biosimilars of other original-brand biologic medicines typically do not have the same costs to bring the product to market and can therefore offer it at a lower price.[4]

Since 2009, Health Canada has authorized 37 biosimilars of 15 original-brand medicines.

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[1] **Health Canada Biosimilars Fact Sheet: Biologic drugs and their uses**
https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html
[2] **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
[3] **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
[4] **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

What is an original-brand (reference) biologic medicine?

An original-brand biologic is a medicine that has been authorized for sale by Health Canada. It is also called a “reference” biologic because it is the medicine to which a biosimilar is compared. When the patents and data protection expire for an original-brand medicine, other manufacturers may produce new versions of the biologic medicine called biosimilars.

Why do biosimilars cost less than original-brand biologics?

A manufacturer of biologics must spend many years studying a new biologic medicine before it can be authorized for sale in Canada. The company then holds a patent on the medicine that prevents other companies from selling that product. This allows the original-brand manufacturer to earn back the money it spent on bringing the product to market. When the patent of an original-brand biologic expires, other manufacturers are allowed to make a biosimilar version of the medicine. Manufacturers that make biosimilars of other original-brand biologic medicines typically do not have the same costs to bring the product to market and can therefore offer it at a lower price.[5]

How are biosimilars different from generic medicines?

Biosimilar and original-brand biologic medicines are not the same as the more common generic medicines. Generic medicines are small molecules that are chemically synthesized. They contain identical medicinal ingredients to their reference products. They are also administered, usually in pill form, in the same way as the original medications.

A biosimilar and its original-brand biologic medicine, administered by injection or infusion, can be shown to be highly similar, but not identical. This is because biologic medicines:

- are often large and complex
- are made from living cells rather than with chemicals and so are naturally variable

Compared to generics, more studies are needed for the regulatory approval of a biosimilar in order to demonstrate that it is highly similar to its reference biologic medicine.

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[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

How is similarity between a biosimilar and its original-brand biologic shown?

Biosimilar manufacturers must provide information to Health Canada comparing the biosimilar with the original-brand biologic medicine. Similarity is demonstrated beginning with structural and functional studies and continuing with human clinical studies. Because the purpose of these studies is to demonstrate similarity, "the type of data Health Canada requires to support biosimilar authorization differs from that required for a stand-alone biologic drug."[6]

What is "switching"?

For the past five years, provincial drug plans across Canada have listed biosimilar brands ahead of original-brand biologics for treatment-naïve patients (patients who have not previously received the original-brand biologic). Since 2019, some provincial formularies have begun implementing "switch" policies that change coverage for specific biologic medicines. In May 2021, Quebec became the fourth province in Canada to implement biosimilars transition policy, following the implementation of similar initiatives by Quebec, New Brunswick, Alberta and British Columbia.[7] Under a switch policy, patients and their prescribers have a certain period to discuss switching from an originator brand to a biosimilar brand. Patients unable to switch or who have an adverse response to the biosimilar can seek exceptional "special authority" coverage for the original-brand biologic.[8]

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."[9]

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[6] **Health Canada Biosimilars Fact Sheet**:
https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html

[7] **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
Alberta Blue Cross: Government Sponsored Biosimilars Initiative
https://www.ab.bluecross.ca/government-plan/biosimilar-initiative.php
New Brunswick Biosimilars Initiative
https://www2.gnb.ca/content/gnb/en/departments/health/MedicarePrescriptionDrugPlan/NBDrugPlan/biosimilars.html
Government of Quebec: Prescription Drug Insurance – Coverage of Biosimilar Drugs
https://www.ramq.gouv.qc.ca/en/citizens/prescription-drug-insurance/know-conditions-coverage

[8] **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

[9] **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

Prior to switching, both physicians and their patients must be fully informed and have all available information about the biosimilar medicine, such as details about the reimbursement policy, patient support program information, including contact names and phone numbers.

What are the risks using a biologic (original-brand or biosimilar)?

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 that takes into consideration benefits and risks, patient treatment goals and tolerance for side effects.

For people living with inflammatory bowel disease, rheumatoid arthritis, spondyloarthropaties, and psoriasis, 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.[10] The likelihood of experiencing infection or any other side effects vary from person to person.

Health Canada requires all biologic manufacturers to monitor the safety profile of their medication and ensure that the product monograph (label) for each of their medications is up to date and supports effective and safe conditions of use.[11] The product monograph is also where patients and healthcare providers can find specific information about potential risks.

Health Canada, in collaboration with the Public Health Agency of Canada, also monitors biologic adverse events, investigates complaints and problem reports, maintains post approval surveillance, and manages recalls, as required.

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[10] **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-Arth%20ritis-ENG.pdf

[11] **Health Canada Fact Sheet on Biosimilars: Safety related updates to biosimilar product monographs** https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html

What should you do if a healthcare provider offers you a biosimilar medicine?

Deciding on a treatment option is a crucial one and should be based on a discussion between the clinician and patient that takes into consideration benefits and risks, patient treatment goals and tolerance for side effects, accessibility of treatment and affordability.

Your specialist or pharmacist will have valuable information about biosimilars. You should also look for additional evidence-based information from your provincial drug plan or private health insurer, patient groups or pharmaceutical manufacturers. Patients who feel they understand their treatment option, who trust their healthcare professionals, and who understand that there is a support plan in place are likely to achieve better outcomes.

Biosimilars Glossary

Biologics (original-brand biologics and biosimilars)

Biologic medicines come from living organisms or from their cells and are often made using biotechnology. They are used to treat diseases and medical conditions including anemia, hormone deficiency, inflammatory arthritis, certain types of cancer, diabetes, inflammatory bowel disease and psoriasis. Biologics are generally larger and more complex than chemically produced medicines.

Biosimilars

As patents expire for originator medicines, manufacturers may produce new versions of the biologic medicines called biosimilars.

To receive Health Canada's authorization for sale, a biosimilar must demonstrate that there are no clinically meaningful differences in terms of physiochemical structure, function, efficacy and safety and immunogenicity. Clinical efficacy studies must demonstrate that the therapeutic effects of the biosimilar (both risk and benefit) are consistent.[12]

After a medicine is authorized for sale, post-market analyses and studies can further demonstrate no meaningful differences in clinical efficacy between a biosimilar and the original-brand biologic.[13]

Since 2009, Health Canada has authorized for sale 37 biosimilars of 15 original-brand medicines.

Original-brand biologic

Original-brand biologics are biologic medicines already authorized for sale (also known as the reference biologic). When the patent of an original-brand biologic expires, pharmaceutical manufacturers are allowed to make a biosimilar version or follow-on medicine of the original-brand biologic.

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[12] **Health Canada Biosimilars Fact Sheet: Roles of structural and functional, non-clinical and clinical studies** https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html

[13] **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

Authorization

Medicines are authorized for sale in Canada once they have successfully gone through the drug review process. This process involves the review of a drug application by scientists in the Health Products and Food Branch of Health Canada, and on occasion, outside experts, to assess the safety, efficacy and quality of a medicine.[14]

Throughout the process, the safety and well being of Canadians is the paramount concern.

Generics

Generic medicines are small molecules that are chemically synthesized and are equivalent to the original-brand name products both pharmaceutically and therapeutically. In other words, they feature the same amount of active ingredient(s) and the same dosage forms and also meet the same applicable (and other) standards of strength, quality, purity and identification. They are also administered, usually in pill form, in the same way as the original medications.

Switching

For the past five years, provincial drug plans across Canada have listed biosimilar brands ahead of original-brand biologics for treatment-naïve patients (patients who have not previously received the original-brand biologic). Since 2019, some provincial formularies have begun implementing “switch” policies that change coverage for specific biologic medicines.[15]

Under a switch policy, patients and their prescribers have a certain period to discuss switching from an originator brand to a biosimilar brand. Patients unable to switch or who have an adverse response to the biosimilar can seek exceptional “special authority” coverage for the original-brand biologic.[16]

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[14] **Health Canada: How Drugs are Reviewed in Canada**
https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/fact-sheets/drugs-reviewed-canada.html

[15] **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
Alberta Blue Cross: Government Sponsored Biosimilars Initiative
https://www.ab.bluecross.ca/government-plan/biosimilar-initiative.php
New Brunswick Biosimilars Initiative
https://www2.gnb.ca/content/gnb/en/departments/health/MedicarePrescriptionDrugPlan/NBDrugPlan/biosimilars.html
Government of Quebec: Prescription Drug Insurance – Coverage of Biosimilar Drugs
https://www.ramq.gouv.qc.ca/en/citizens/prescription-drug-insurance/know-conditions-coverage

[16] **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

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]

Prior to switching, both physicians and their patients must be fully informed and have all available information about the biosimilar medicine, such as details about the reimbursement policy, patient support program information, including contact names and phone numbers.

Immunogenicity

The immune system has evolved to recognize foreign proteins in the body. Biologics are usually injected into the body and the immune system often reacts to them. This reaction is referred to as the immunogenicity of the product.

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.

Health Canada is addressing immunogenicity as part of the comparative clinical trials required for authorization of biosimilars. In addition, biosimilar manufacturers are responsible to monitor the immunogenicity potential of the biosimilar after it is on the Canadian market.[18]

Interchangeability

In Canada, interchangeability often refers to the ability for a patient to be changed from one medicine to another equivalent medicine by a pharmacist, without the intervention of the doctor who wrote the prescription when it has been deemed interchangeable by a Provincial or Territorial regulatory body. For instance, this is a common practice for medicines that are off patent and have been deemed interchangeable with their generic equivalent.

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[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] **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

At present and as it relates to biosimilars, Health Canada has declared biosimilars not to be interchangeable with their originator biologic.[19] Health Canada's authorization of a biosimilar is independent of provincial, territorial, or private drug plan decisions regarding its formulary listing and reimbursement or any decision as to interchangeability between these medicines.

According to the new guidance from Health Canada, interchangeability decisions rest with provincial or territorial governments, which also regulate pharmacy substitution practices.

Extrapolation

Once studies show that the biosimilar is highly similar to the reference biologic medicine with no clinically meaningful differences, Health Canada can authorize the biosimilar for the same indications as the reference biologic medicine, based on the previously established efficacy and safety of the reference biologic medicine in each indication.[20]

This concept is often called extrapolation or extension of indications, and it avoids the unnecessary repetition of clinical studies.

An indication is a term that means the use of a medicine to treat a specific disease or medical condition. Many biologic medicines are authorized for more than one indication. Authorization of each indication is also supported by scientific knowledge and the medical literature about the:

- biosimilar
- reference biologic medicine
- mechanism of action of the medicine in the specific diseases or medical conditions involved

Patients and prescribers can have confidence in the use of a biosimilar in each indication authorized by Health Canada.

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[19] **Health Canada: Biosimilar biologic drugs in Canada: Fact Sheet - Interchangeability**
https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html#a9

[20] **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

Post-marketing surveillance

After a medicine is authorized for sale, post-market analyses and studies can further demonstrate no meaningful differences in clinical efficacy between a biosimilar and the originator.

Health Canada monitors the safety of all medicines on the market, including biologics (original-brand and biosimilar).[21]

Health Canada:

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

Health Canada also requires medicine manufacturers to monitor for biologics (original-brand and biosimilar) safety:

- 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 approval for any major changes to
    - the manufacturing process,
    - dose regimen, or
    - recommended uses of the medicine [22]

Health Canada also receives drug safety information from other jurisdictions including the United States and the European Union.

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[21] **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

[22] **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