

Biosimilar Drugs

As more biosimilar drugs come to the Canadian market, decision-makers need information to help guide prescribing and policy development. Are biosimilars the same as their reference drugs? Can they improve access for patients? What's the difference between interchangeability and switching? Read on for more information, or get our patient handout.

What are biologic drugs?

Biologic drugs, commonly known as biologics, are a class of drugs derived through the metabolism of living organisms, rather than being synthesized by chemical reactions.¹ Biologics include insulin analogues, interferons, erythropoietin, and monoclonal antibodies such as infliximab or adalimumab.

What is a biosimilar drug?

A biosimilar is a new, highly similar version of a biologic drug that comes to the Canadian market after the patent for the original product has expired. Biosimilars were previously called subsequent entry biologics (SEBs) in Canada.

Are biosimilars safe and effective?

Yes. Health Canada must review and approve all drug products before they can be sold in Canada. Biosimilars are treated as new drug products and require a full submission, including clinical trial data. All manufacturers must meet the same federal standards for good manufacturing practices. Authorization of a biosimilar by Health Canada means that the biosimilar and the reference biologic drug are highly similar and that there are no clinically meaningful differences in safety and efficacy between them.

What is a reference biologic drug?

A reference biologic drug (RBD) is the product to which a biosimilar is compared. Generally it is the first version of the drug that was approved for sale in Canada, and there is a body of evidence regarding its safety and efficacy.² An RBD may also be called an innovator biologic, innovator drug, or originator drug.

Is a biosimilar identical to its RBD?

No. Biologics are large molecules with complex manufacturing procedures. While the protein sequence is known, the manufacturing process is proprietary. So it is impossible to exactly duplicate all of its characteristics.³ In fact, there is even variation between batches of the same RBD.⁴ This is different from traditional generic drugs, which are small molecules that can be precisely replicated and deemed bioequivalent to the innovator drug. For more information on bioequivalence or generic drugs, please visit: cadth.ca/generics.

Is a biosimilar comparable to its RBD?

Yes. To be authorized for sale in Canada as a biosimilar, a drug must meet a detailed set of criteria from Health Canada (for example, similar biochemical structure; similar pharmacokinetic and pharmacodynamic characteristics) and must demonstrate safety and efficacy for each indication; in certain situations, it is possible to extrapolate therapeutic similarity from one indication to another indication. Because of the rigorous demonstration of similarity between the biosimilar and the RBD, Health Canada may authorize a biosimilar for use in more than one indication even if clinical studies were not conducted in each indication.^{2,3}

Is a biosimilar interchangeable with its RBD?

Interchangeability is not the same thing as bioequivalence or similarity to a reference product. Interchangeability allows one product to be substituted for another product at time of dispensing, and these decisions are made by each province and territory according to its own regulations.

What is the difference between interchangeability, substitution, and switching?

Interchangeability: Products that are so alike that the drug is expected to have the same clinical result as the reference drug in any given patient.⁵ **Decisions about interchangeability are made by provinces and territories.** Drugs deemed interchangeable may be noted on the provincial Drug Benefit List.

Substitution: The act of dispensing one product in place of another. *Automatic* substitution can occur whenever products have been deemed interchangeable and a pharmacist may dispense any of the interchangeable products. Health Canada does not support the automatic substitution of a biosimilar for its RBD.

Therapeutic substitution means substitution with a different medication from the same class that is expected to have the same therapeutic effect. This is less common than automatic substitution and usually pursuant to a medical or provincial directive. **Decisions to make a therapeutic substitution are generally made by pharmacists** based on a medical directive from a Pharmacy and Therapeutics Committee of a hospital or from an individual physician.

Switching: A decision to change a specific patient's medication. Individual patients who are already established on an RBD may consider switching to a biosimilar with consideration to the patient's unique situation and preferences. **Decisions about switching are generally made by individual patients and their practitioners based on the available clinical evidence.**

What is the benefit of biosimilars?

Increased competition among manufacturers decreases costs and increases choice, thereby improving access for patients. Biosimilars create savings that can be redirected elsewhere.

DISCLAIMER

This material is made available for informational purposes only and no representations or warranties are made with respect to its fitness for any particular purpose; this document should not be used as a substitute for professional medical advice or for the application of professional judgment in any decision-making process. Users may use this document at their own risk. The Canadian Agency for Drugs and Technologies in Health (CADTH) does not guarantee the accuracy, completeness, or currency of the contents of this document. CADTH is not responsible for any errors or omissions, or injury, loss, or damage arising from or relating to the use of this document and is not responsible for any third-party materials contained or referred to herein. This document is subject to copyright and other intellectual property rights and may only be used for non-commercial, personal use or private research and study.

Where can I find more information?

Health Canada provides detailed information on its [website](#). A **guidance document** explains how biosimilars are approved and details the information that manufacturers must submit. A **fact sheet** provides further information on key issues.

Bottom Line:

- Biosimilars are highly similar to the reference product in safety and efficacy, but not identical.
- Biosimilars offer a choice for patients and may improve access.
- Biosimilars create savings that can be redirected elsewhere.

References

1. Fact Sheet: Biosimilars [Internet]. Ottawa: Health Canada, 2016. [cited 2017 Jan 19]. Available from: (<http://www.hc-sc.gc.ca/dhp-mps/brgtherap/applic-demande/guides/biosimilars-biosimilaires-qa-qr-eng.php>)
2. Pandya N. Regulation of subsequent entry biologics. In: Fundamentals of Canadian regulatory affairs [Internet]. 4th edition. Rockville (MD): Regulatory Affairs Professionals Society; 2014. Chapter 19. p. 147-58.
3. Devlin SM, Bressler B, Bernstein CN, Fedorak RN, Bitton A, Singh H, et al. Overview of subsequent entry biologics for the management of inflammatory bowel disease and Canadian Association of Gastroenterology position statement on subsequent entry biologics. *Can J Gastroenterol* [Internet]. 2013 Oct [cited 2016 Sep 12];27(10):567-71. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3805336>
4. Renwick MJ, Smolina K, Gladstone EJ, Weymann D, Morgan SG. Postmarket policy considerations for biosimilar oncology drugs. *Lancet Oncol*. 2016 Jan;17(1):e31-e38.t
5. Chingcuanco F, Segal JB, Kim SC, Alexander GC. Bioequivalence of Biosimilar Tumor Necrosis Factor-alpha Inhibitors Compared With Their Reference Biologics: A Systematic Review. *Ann Intern Med*. 2016 Aug 2.

ABOUT CADTH

CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs and medical devices in our health care system.

CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Ce document est également disponible en français.

February 2017