Biologics

Biologics are very specific, highly effective medicines made in living cells. They improve health in many complex conditions, including Crohn’s disease, ulcerative colitis, diabetes, rheumatoid arthritis, cancer, osteoporosis, psoriasis, HIV, multiple sclerosis, growth deficiencies, and more.

Some examples of biologics include hormones, blood products, cytokines, growth factors, vaccines, gene and cellular therapies, fusion proteins, insulin, interferon, and monoclonal antibody (mAb) products. Patients receive biologics by injection under the skin (subcutaneously) or by intravenous infusion and cannot take them orally, since the process of digestion breaks down the biologic, making it ineffective.

What are Biosimilars?

Biosimilars are brand name products that are highly similar to an already existing brand-name, original biologic (innovator or originator biologic) but, unlike a generic drug, are not identical. To understand why, we need to look at how biologics are different from other medicines.

**Small Molecule:** Most medicines, such as aspirin, are small molecule products, which means they have simple molecular structures. These simple structures make it easy to produce or copy. Once a patent expires, other companies can make copies of small molecule drugs by reproducing the exact same active ingredient (typically a chemical) as the original product. After Health Canada approval, they can then sell this as a generic version. The original product and the generic copies are considered bioequivalent because the active part of the medicines behave the same way in the body and produce equivalent levels of drug in the body. Clinical trials studying the effects of generic copies are often not needed for Health Canada to approve a generic drug.

**Biologics:** By comparison, biologics are very large and have complex molecular structures. They are produced by living cells, from highly specialized ingredients using a complex biotechnology process. It is impossible to produce an exact copy even when using the exact same ingredients, the same living cell lines, and identical manufacturing conditions. In fact, it is not possible to demonstrate that a batch of any biologic, originator or biosimilar, is identical to its previous batches; however, the same ingredients and processes might be used by the same manufacturer. Clinical trials in patients with the condition the biologic treats are required for Health Canada to approve a biosimilar. Different manufactures will not have access to the ingredients and manufacturing processes each use and; therefore, innovator biologics and biosimilars do not have the same manufacturing process. Health Canada ensures that the efficacy, safety and quality of biosimilars meet the measures required for them to be considered a biosimilar version of the original.

As with other medicines, once a patent expires for a biologic, it is legal for other manufacturers to reproduce the drug. However, the innovator company doesn’t have to share its patented manufacturing processes (which may include the room temperature, the type of cells that produce the biologic, and the food the cells use to grow), and since there is always variability in a live biological system, it is impossible for a biosimilar to be an identical copy. Since biosimilars are not identical, they are not generic versions of the biologic they are copying.

With small molecule drugs, there are often many generic versions, and they all work the same. For example, whether you buy name brand acetylsalicylic acid (Aspirin®) or one of the many generic versions, they are the same chemical and perform the same in the body. However, with biologics, there could be many different biosimilars all referencing one innovator medicine, and each have a different manufacturing process.
resulting in a similar molecule to the innovator biologic. Biosimilars are compared against the innovator reference biologic for approval by Health Canada, and are not studied or compared against another biosimilar. It is recognized that with any biologic product, one batch of a biologic drug may not be exactly the same as the next, but they are required to be within a tight range. Changes in manufacturing process deemed significant also require submission by the manufacturer and approval by Health Canada.

**Biologic and Biosimilar Regulations in Canada**

Health Canada regulates biosimilars as new drugs by comparison with an innovator reference product previously authorized and marketed in Canada. As the federal authority, Health Canada states that biosimilars are not generic biologics. Health Canada only approves biosimilars for marketing in Canada when the manufacturer demonstrates that their product is of similar quality, safety, and efficacy to the original reference drug. Health Canada describes a biosimilar as a drug that has been demonstrated to be highly similar to a reference biologic drug, with no clinically meaningful differences in safety and efficacy between them.

Currently, there are several biosimilars on the market (with more than one biosimilar version for each originator), with many more on the way, which Health Canada has approved so far for treatment in Crohn’s disease, ulcerative colitis, inflammatory arthritis (rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis), diabetes, and plaque psoriasis. Health Canada is expecting an influx of biosimilars as the patents for innovator biologics continue to expire.

Health Canada makes decisions to approve some biosimilars to treat conditions that the innovator biologic has approval for, through educated assumptions by extrapolating scientific evidence. Therefore, a biosimilar might have an indication to treat a specific disease without the manufacturers testing in that disease, but some biosimilars will not have the full array of indications for which the original reference product is approved. This may be due to patent protection for specific indications, that the process of gathering the data necessary for Health Canada is ongoing, or due to the manufacturer not requesting regulatory approval for a specific indication(s).

**Switching, Substitution, and Interchangeability**

Typically, if a patient has a prescription for a small molecule medication, a pharmacist may substitute a generic version without consulting with the patient’s physician. This is called interchangeability. However, biosimilars are not interchangeable with their originator biologic in Canada. A physician may choose to switch their patient from an originator biologic to the biosimilar product if they think it will be beneficial, but a pharmacist may not change the patient to a biosimilar. Switching refers to a one-time change from an originator biologic to its biosimilar, or the reverse. The decision to switch should only be made by patients in consultation with their physician, using the available clinical evidence and any relevant provincial or territorial policies.

Overall, the clinical research examining the impact of switching for two specific biologic molecules, infliximab and etanercept, suggests that a one-time switch from originator biologic to biosimilar is likely safe and does not carry a significant risk of adverse drug reactions. These studies, along with recent real-world evidence reports using patient registry data, have provided valuable insight regarding non-medical switching from originator biologic to biosimilar, including: (1) the need to develop disease-specific exclusion criteria by professional societies for vulnerable patients, (2) the need to closely monitor patients if they have been switched, and (3) the impact of requiring non-medical switch studies, i.e., clinical trials or patient registries, when considering new biosimilar products for switch. A non-medical switch is when this change in the version of medication is done for a financial reason, such as savings for the patient and/or the payer for the medication, rather than medical need. These savings in drug spending may be used in other ways, depending on the provincial or territorial policies.

**Immunogenicity**

Because biologics are proteins, the body can develop antibodies to them over time, which might affect how they work. This immune response, called immunogenicity, can also occur with biosimilar products and should be discussed with your healthcare provider before initiating therapy or switching among biologic products. Although initially there were theoretical concerns that a switch may enhance the development of immunogenicity, studies have not demonstrated this to be occurring.

**Naming Biosimilars**

The naming of biosimilars has been a complicated issue. Typically, each version of the same small molecule medication uses the same international non-proprietary name (INN) because they are the same molecule. However, biologics aren’t identical, yet we still use the same INN for innovator biologics as well as biosimilars. Because of this, Health Canada and other similar groups internationally have looked into options for distinguishing between biologics and biosimilars. As of 2019, Health Canada has settled on a biosimilars naming convention that involves identifying the products by their INN along with their unique brand name, without the addition of a product-specific suffix. The World Health Organization is still deliberating on a global position.

**Benefits of Biosimilars**

The cost of pharmaceuticals, particularly biologics, is an important consideration as experts look at ways to make pharmaceutical care sustainable. Because they are complex and have revolutionized the treatment for many diseases, biologic medicines are costly and consume a large portion of
public and private drug spending. In most cases, biosimilars are less costly than the innovator biologic for a number of reasons, including that fewer clinical trials are required for biosimilars, the costs of discovery and initial development of the drug is not needed, and additional competition might help explain the cost differences. Biosimilar manufacturers can extrapolate scientific evidence from one indication to another, which leads to fewer development costs. Biosimilar manufacturers focus on manufacturing processes that result in a highly similar product as well as studies demonstrating clinical similarity to the innovator biologic. These approaches are less expensive than the clinical trials required for initial drug discovery and approval for the innovator biologics. However, good negotiating by payers could result in lower cost for the originator as well.

Treatment options are very important for patients who have serious health conditions. With appropriate regulations in place around approval, advertising, and post-market monitoring, as well as private and public insurance coverage, products that demonstrate a safe and effective track record offer new treatment options for patients.

Biosimilars are safe and effective medicines that provide additional, lower-cost options for patients who are newly-prescribed biologics. However, prescribing medicines to treat chronic conditions should remain a decision between patients and their physicians, and should not occur for purely financial reasons. Your physician or pharmacist can provide additional information and discuss the options with you and play an important role to ensure your condition is well treated with the least adverse effects.

**Conclusion**

Biosimilars are not generic versions of originator biologics, but they are affordable alternatives that work similarly and are shown in studies to have equivalent outcomes. For patients who have not begun an original biologic, biosimilars may be a useful alternative for physicians to prescribe. However, only a physician should be allowed to switch a patient from an innovator biologic to a biosimilar, and only if it does not adversely affect the patient’s health.

**Questions to ask your healthcare provider about biosimilars**

Are you considering talking to your healthcare provider about biosimilars or has your healthcare provider talked to you already about biosimilars? As patient organizations, we have put together some questions that might be helpful to be part of a conversation with your healthcare provider about biosimilars and originator biologics.

**Will the biosimilar provide me with similar benefits and risks as my current biologic (if you are currently on one)? If not, what might be different? How would I know if I have an adverse reaction (to a biosimilar or biologic)?**

**Can I go back to the original medication I was on if the biosimilar does not work as well for me, or if I experience different side effects?**

**What is the name of the biosimilar(s) that could be taken instead of the originator biologic?** (Note that medications have two names – one the manufacturer gives it, which is also called the brand name, and one that is its non-proprietary or chemical/molecule name.)

**How will I take the biosimilar? If I take it by infusion, will I need to go to a different infusion centre from where I go now?** (You should note if the infusion centre is easier to get to or more difficult to get to than your current centre.)

**What is the dosing schedule – will it be the same as my current biologic?**

**If I administer the biosimilar myself, are there any different special storage requirements? Will I be provided with everything I need to administer the biosimilar?**

**Does this biologic have the same delivery method as my current biologic, i.e., is it by injection or infusion?**

**Is the patient support program different from the one I am currently on? If it is, how so?**

**Will I be able to get the biosimilar at the same pharmacy?**

**Is there a cost difference between the brand name biologic and its brand name biosimilar(s)? What will the biosimilar cost me? What does my private healthcare plan cover and is there a yearly or lifetime maximum drug coverage?**

When your healthcare provider starts a conversation with you about biosimilars, you may also choose to ask these additional questions along with those that are listed above:

**Why are you recommending this biosimilar for me?**

**What if I don’t want to change to the biosimilar? What are the consequences or options? Is there a cost to me if I choose to stay on the innovator biologic? Does my private healthcare plan cover any part of the innovator biologic?**
Who We Are

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