Biologics and Biosimilars

We have been using biologic medicines since 1796, when scientists created the first rudimentary vaccines for smallpox. Biologics have continued to evolve throughout the years into powerful medicines that have revolutionized treatment for debilitating diseases, giving patients a new chance for a life.

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 or infusion and cannot take them orally, since the process of digestion breaks down the biologic, making it ineffective.

Biosimilars

How are these Different?

Biosimilars are products that are **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.

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 without using the exact same ingredients, the same living cell lines, and identical manufacturing conditions.

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 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, but not necessarily as similar to each other.

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.

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 a few biosimilars on the market, 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), 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.

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 made by a physician, and should only be made if it is in the **patient's best interest** and if the patient agrees. Little is known about switching between biosimilar products at this time.

Immunogenicity

Because biologics are proteins, the body can develop antibodies to them over time, which might affect how they work. This immune response, also called immunogenicity, might increase when switching from one biologic to another or back again, and is a strong reason for a discussion with your health care provider before switching among biologic products. Whether immunogenicity increases with switching is still unknown and requires further study.

Naming Biosimilars

Currently, biosimilars use the same international non-proprietary name (INN) as the originator biologic, even though they are not the exact same product. Health Canada and other similar groups internationally are looking into options for distinguishing between biologics and their biosimilars. The World Health Organization has been considering adding what they term a Biological Qualifier to all biologic products, but opinions on this are mixed, and there is no definite timeline of when they would implement this in Canada.

Patient safety is paramount and there is a strong regulatory need in Canada for distinguishable INNs between innovator biologics and their biosimilar medications. A biosimilar is not the same as the biologic it is similar to, and giving the products the same INN might cause further confusion. For now, the words 'biosimilar' or 'originator' often precedes the INN, and each drug has a unique Drug Identification Number (DIN) The DIN is the 8-digit number located on the label of prescription and over-the-counter drug products that have been evaluated by the Therapeutic Products Directorate branch of Health Canada and approved for sale in Canada.

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, given that fewer clinical trials are required for biosimilars. 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 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

approval for the innovator biologics.

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.

Conclusion

Biosimilars are not generic versions of originator biologics, but they are affordable alternatives that work similarly. For patients who have not begun an original biologic, biosimilars may be a useful alternative for physicians to prescribe. **However, only qualified health care professionals should be allowed to switch a patient from an innovator biologic to a biosimilar, and only if it is best for the patients' health.**

Questions to Ask Your Health Care Provider about Biosimilars

Are you considering talking to your health care provider about biosimilars or has your health care provider already talked to you about biosimilars?

As patient organizations, we have put together some questions that might be helpful to be part of a conversation with your health care 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 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.)
If I am going from infusion to subcutaneous (or vice versa), will I be provided with training and support?

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

If I administer the biosimilar myself, are there any 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?

Is there a cost difference between the brand name biologic and its biosimilar(s)? What will the biosimilar cost me?

When your health care 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 brand name biologic?

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