What you need to know about biosimilar drugs
A fact sheet for healthcare professionals

What are biologics?
- Biologics are complex protein molecules created inside a living cell. [1]
- Biologics have become mainstays in the treatment of many types of cancer, including breast, gastrointestinal, lung, ovarian and other cancers.

What are biosimilars?
- A reference biologic is the original branded product approved by Health Canada.
- When the patent for a reference biologic expires, manufacturers can sell highly similar copies of the reference biologic, known as biosimilars.
- A biosimilar is not necessarily identical to its reference biologic (see question below), but based on Health Canada’s guidelines and approval standards for the pharmacokinetics, pharmacodynamics, safety and clinical efficacy of biologics, the two are highly similar. [1-3]
- Health Canada says that there are no clinically meaningful differences between biosimilars and their reference biologic drugs. [1]

How do biosimilars differ from generic drugs?
- The active ingredients in generic drugs are exactly the same as the brand name drug, while biosimilars are highly similar but not exact copies.
- The natural variability and more complex manufacturing of biologics does not allow an exact replication of a biologic molecule.

How are biologics and biosimilars manufactured?
- Since biologics and biosimilars are made inside living cells, every batch of biologics and biosimilars made is slightly different.
- The variability between batches is supervised by Health Canada.
- When a manufacturer makes changes to the process of how a biologic is made, they need to prove that the product is highly similar to the previous product and that there is no adverse impact upon safety or efficacy. [3]
How are biologics and biosimilars regulated in Canada?
- Biosimilars are regulated as new drugs under the Food and Drugs Act and the Food and Drug Regulations. [1]

- For a drug to be called a biosimilar, the drug manufacturer must provide information to Health Canada to show that the biosimilar and the reference biologic drug are highly similar, and that there are no clinically meaningful differences in terms of safety and efficacy between them. [4]

- Health Canada's decision to authorize a biosimilar for sale is based upon a benefit/risk assessment after considering all of the data submitted by the manufacturer. [4]

- Health Canada's rigorous standards for authorization mean that patients and healthcare providers can rely upon the quality, safety and efficacy of a biosimilar, just as for any biologic drug. [4]

Do biosimilars work as well as the reference biologic?
- Biosimilars have been shown to be equivalent to the reference biologic in properly designed clinical trials. These trials must have a sensitive and homogenous patient population, an appropriate clinical design and useful study endpoints.

- Biosimilars have been studied in large numbers of patients. As an example, trastuzumab biosimilars have been trialed in 6 independent Phase 3 clinical trials that had at least 500, and as many as 800 patients in each clinical trial. [5-10]

- Biosimilars work in the same ways as their reference biologic. It is expected that if a patient is transitioned to, or started on, a biosimilar, they will have the same outcome as if they were treated with the reference biologic.

How are biologics and biosimilars monitored?
Health Canada monitors the safety of all drugs on the market, including biosimilars. [1] Health Canada and manufacturers both play a role in monitoring drug safety.

Health Canada:
- conducts market surveillance
- monitors adverse reaction reports
- investigates complaints and problem reports [1]
Manufacturers:
- 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 authorizations for any major changes to the manufacturing process, dose regimen or recommended use of the drug [1]

What is switching?
- Switching generally refers to a one-time change from a reference biologic drug to a biosimilar [1] but can also refer to a change from a biosimilar to a reference biologic or another biosimilar.

Will patients currently on a reference biologic be switched to a biosimilar?
- Each provincial cancer agency will decide whether to switch patients to biosimilars.
- Deciding to switch the product at the pharmacy level (i.e. interchangeability) is up to each province. Health Canada does not designate any product (biologic or non-biologic) as interchangeable. [1]
- Healthcare providers should be prepared to answer questions from patients about changing from one biologic drug to another.

What does it mean to extrapolate indications?
- Extrapolation is often used to refer to the authorization (by a regulatory body, like Health Canada) of a drug for indications where clinical studies were not done. [1] For example, rituximab (Truxima) was studied in non-Hodgkin lymphoma yet was also approved for chronic lymphocytic leukemia.
- Extrapolation also refers to the use of a drug for indications that are not approved by Health Canada. In some instances, these indications are publicly funded.

Is it safe to use a biologic for an indication that has not been approved by Health Canada?
- Health Canada states that a biosimilar can have an indication different from what was studied for its approval as long as there is a good scientific rationale.
- Health Canada does not make any safety recommendations for off-label use of approved medications. However, certain medications in Canada (e.g. bevacizumab (Avastin)) are funded for indications where there is not an approved indication (cervical cancer).
• In other regions (e.g., Europe) all indications for the reference biologic are extrapolated to the biosimilar. [11]

How will biosimilars impact the health system in Canada?
• Biosimilars can save money for the health system.
  
• Biologic drugs are very expensive to the health system. In 2016, Canada spent more than $3.6 billion on these drugs. [12]
  
• Biosimilars can be sold at a much lower price than the reference biologic. [12]
  
• The money saved by using biosimilars can be put back into the cancer system to help pay for, and improve access to, new treatments.

Have any other jurisdictions successfully implemented biosimilars?
• Biosimilars have been in use for more than 10 years in Europe.
  
• As of January 2019, Europe has approved almost 60 different biosimilars.
  
• Europe has had more than 700 million patient treatment days and has not detected any signals that the products were less safe or efficacious than the reference biologic.
  
• The National Health Service has achieved almost 100% uptake of rituximab biosimilar. [13]

When are oncology biosimilars expected to enter the market?
• The first therapeutic oncology biosimilars are expected to enter the Canadian market in 2019.

What cancer drugs will have biosimilars?
• In 2019 to 2020, Canada is expecting biosimilars of bevacizumab (Avastin), trastuzumab (Herceptin) and rituximab (Rituxan).
References


