BIOSIMILARS INITIATIVE

PHARMACY GUIDE

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BRITISH COLUMBIA PHARMACARE BIOSIMILARS INITIATIVE

PHARMACIST GUIDE

In This Guide

Across Canada, biologic drugs are a major contributor to healthcare costs increasing at an unsustainable rate. In 2017, Canada spent over $1.1 billion on Remicade® alone—more than on any other drug. With new drugs frequently entering the market (including new biologics and innovative therapies), the cost pressures for Canada's drug plans will only continue to increase.

One solution to this challenge is already available: biosimilar versions of originator biologic drugs offer significant cost savings. In B.C., Basaglar™ offers a 25% reduction in cost compared to Lantus®, a 28% reduction for etanercept biosimilars compared to Enbrel®, and a 50% reduction in cost for infliximab biosimilars compared to Remicade.

Despite these price differences, biosimilars have not yet captured much market share in Canada. At the end of 2017, Basaglar (approved in Canada since September 2015) accounts for only 2.6% of insulin glargine use. Etanercept biosimilars (approved in Canada since August 2016) account for only 3.1% of etanercept use. Infliximab biosimilars (approved in Canada since January 2014) account for only 4% of infliximab use in Canada.

Biosimilar uptake has been limited by many factors, including misconceptions about the safety and efficacy of biosimilars and reluctance to change the status quo.

B.C.'s previous strategy to encourage biosimilar uptake by listing those brands preferentially for treatment-naïve patients has been well-received; however, the impact of this strategy is limited by the small proportion of new starts.

With an ever-growing body of evidence and the support of stakeholders, PharmaCare is now positioned to enable the expansion of treatment options and the improvement of patient access by introducing the Biosimilars Initiative.

The Biosimilars Initiative changes coverage for specific biologic drugs. Patients and their prescribers have a period of 6 months to discuss switching from an originator brand to a biosimilar brand. Coverage and Special Authority (SA) approval is provided for both originator and biosimilar brands during switching. Patients unable to switch or who have an adverse response to the biosimilar(s) can seek exceptional SA coverage for the originator.

PharmaCare's strategy to ensure a successful switch includes:

- Involving various practitioners in patient identification, education and support
- Providing time to identify affected patients and guide them through the switching process
- Ensuring patient supports are in place for continuous care
- Having options for those unable to switch or experience challenges with switching
- Identifying areas of concern and providing information for both patients and practitioners
- Providing call-in information sessions and responsive contacts for healthcare practitioners
- Monitoring drug utilization, patient outcomes, and stakeholder feedback

The role of pharmacists in the switch process is critical. A pharmacist often interacts with a patient first, introduces the concept of biosimilar switching, sets the tone of discussion, serves as a source of information, and empowers the patient to expect and realize the best outcomes.

In accordance with Health Canada recommendations, the decision to switch to a biosimilar should be made by a well-informed patient and their prescriber. PharmaCare has created this guide to provide information for pharmacists supporting the biosimilar switch process.

(National statistics referenced in the section above are found in the Patented Medicine Prices Review Board *Meds Entry Watch 2017* report.)

What is changing?

PharmaCare is changing coverage of insulin glargine, etanercept, and infliximab products.

Coverage for the original biologic (originator) drugs will be discontinued for affected patients, and coverage will instead be provided for their biosimilars:

PHASE 1: May 27 to November 25, 2019			
Drug	**Originator**	**Biosimilars**	**Indications Affected**
insulin glargine	Lantus®	Basaglar™	Diabetes (Type 1 and 2)
etanercept	Enbrel®	Brenzys®	Ankylosing Spondylitis Rheumatoid Arthritis
		Erelzi™	Ankylosing Spondylitis Psoriatic Arthritis Rheumatoid Arthritis
infliximab	Remicade®	Inflectra® Renflexis®	Ankylosing Spondylitis Plaque Psoriasis Psoriatic Arthritis Rheumatoid Arthritis

PHASE 2: Summer 2019 to early 2020 (Dates to be confirmed)			
Drug	**Originator**	**Biosimilars**	**Indications Affected**
infliximab	Remicade®	Inflectra® Renflexis®	Crohn's Disease Ulcerative Colitis

The switching of Remicade patients has been designed in two phases to allow for stakeholder engagement and to ensure that switch support resources have capacity to address patient and prescriber needs.

For affected patients with existing Special Authority (SA) approval for insulin glargine, etanercept, or infliximab to maintain their coverage, prescribers must write a new prescription for a biosimilar option. The patient's existing SA remains in effect until the next renewal date (if applicable).

New SA requests and renewals for insulin glargine, etanercept, and infliximab will be granted for biosimilar brands only.

When do these changes take effect?

Patients using Lantus who wish to maintain PharmaCare coverage must switch to Basaglar before November 26, 2019.

Rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis patients using Enbrel who wish to maintain PharmaCare coverage must switch to either Brenzys or Erelzi before November 26, 2019.

Rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis patients using Remicade who wish to maintain PharmaCare coverage must switch to either Inflectra or Renflexis before November 26, 2019.

All originator and biosimilar brands will be covered during the transition period, May 27, 2019 to November 25, 2019, to provide time for patients to discuss switching with their prescriber and get a new prescription. Coverage of Lantus, Enbrel, and Remicade for Phase 1-affected patients will no longer be in place as of November 26, 2019.

Phase 2, affecting patients using Remicade for Crohn's disease or ulcerative colitis, will begin later in the summer of 2019. Additional information will be provided to support Phase 2.

Who will be affected?

INSULIN GLARGINE (LANTUS)
Patients will be affected by this change if they:
- use Lantus, and
- receive PharmaCare coverage for their medication under any PharmaCare plan, excluding Plan W (First Nations Health Benefits)

Patients who are covered under Plan W (First Nations Health Benefits) and take Lantus are encouraged to switch to Basaglar; however, their Lantus coverage will not end on November 25, 2019. Plan W beneficiaries will be affected by etanercept and infliximab switching.

ETANERCEPT (ENBREL)
Patients will be affected by this change if they:
- have rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and
- use Enbrel, and
- receive PharmaCare coverage for their medication under any PharmaCare plan

At this time, coverage for patients using Enbrel for plaque psoriasis will not be affected.

INFLIXIMAB (REMICADE)
Patients will be affected by this change if they:
- have rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, or plaque psoriasis, and
- use Remicade, and
- receive PharmaCare coverage for their medication under any PharmaCare plan

Coverage for patients using Remicade for Crohn's disease or ulcerative colitis will change during Phase 2 of the Biosimilars Initiative.

Why is coverage changing?

To enable expansion of the PharmaCare formulary and B.C. health services, PharmaCare develops evidence-informed strategies to better optimize how our public resources are used. Biologic drugs represent a huge portion of the annual PharmaCare budget, and biosimilars represent a correspondingly large, but unrealized, opportunity to find value that can be applied to new treatments and services.

In B.C., the biologic drugs being switched (Lantus, Enbrel, and Remicade) represent some of the largest provincial drug expenditures. In 2018, PharmaCare spent $125 million on just these three originator drugs.

Despite being listed preferentially for new starts, the biosimilars for these drugs have captured only a fraction of the market: Basaglar represented only 1.7% of 2018 insulin glargine PharmaCare expenditures, Brenzys and Erelzi only 6.8%, and Inflectra and Renflexis only 5.9%.

PharmaCare is always reviewing new drugs, new indications, and existing coverage and criteria; the provincial formulary must evolve and adapt to the current market, clinical requirements, best practices, and the needs of B.C. residents and practitioners.

Will patients need new Special Authority approval?

Patients with existing SA for insulin glargine, etanercept, or infliximab do not require a new SA for the biosimilar version of their medication. The existing SA remains in effect until the next scheduled renewal date (if applicable).

If a patient's SA expires during the transition period, it will be renewed for biosimilar brands only.

Patients with a clinical requirement that prevents switching can have their prescriber submit a new SA request for exceptional coverage of the originator biologic. Exceptional requests will be reviewed by Special Authority on a case-by-case basis.

What is the Biosimilar Patient Support Fee for Pharmacists?

The Biosimilar Patient Support Fee for Pharmacists is a $15 payment offered to pharmacies in recognition of the additional effort involved in identifying affected patients, and providing information.

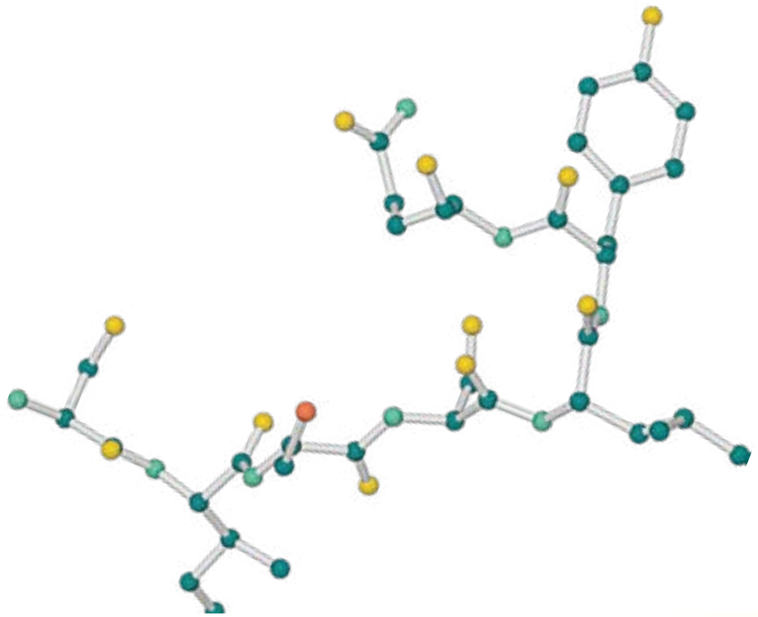
This fee is submitted as a PIN (66128196) in PharmaNet, to be paid monthly, in accordance with the usual monthly payment schedule.

Only one Biosimilar Patient Support Fee can be claimed for a PHN, even if the patient uses more than one of the biologics subject to switching. Fees will be paid for claims submitted during the transition period, May 27–November 25, 2019, for eligible patients (that is, patients who have active SA for the drug and are using the originator brand for one of the affected indications).

How can pharmacies support biosimilars switching?

If, when you interact directly with a patient (by dispensing a prescription or performing a medication review), you notice that their medication record indicates that they are currently using Lantus or Enbrel or Remicade:

1. Confirm that the patient will be affected. This may require a conversation to confirm the indication that they use the drug for and/or checking whether they have active coverage. Patients are affected if:
   - They use Lantus.
     or
     They use Enbrel for rheumatoid arthritis, ankylosing spondylitis, or psoriatic arthritis.
     or
     They use Remicade for rheumatoid arthritis, ankylosing spondylitis, plaque psoriasis, or psoriatic arthritis.
   - They have active Special Authority for that drug.
   - They have not already been provided switch support by another pharmacy or pharmacist (i.e. the Patient Support Fee for Pharmacists PIN has not already been claimed for that patient).
2. Provide them the Ministry of Health Patient Information Sheet for their drug.
3. Tell the patient that they may be affected by biosimilar switching and that they will have to discuss biosimilar switching with their prescriber prior to November 26, 2019 in order to maintain PharmaCare coverage of their medication.
4. Submit a claim in PharmaNet for the Biosimilar Patient Support Fee for Pharmacists.



How can I support patients with questions and concerns?

Patient acceptance of biosimilars is, understandably, easier to achieve among treatment-naïve patients started on a biosimilar. Treatment-experienced, stable patients using an originator biologic may require more support.

The best response to any concern your patient may have is your expertise and experience as a healthcare practitioner, as well as the provision of additional information. Patients who feel they understand the change and why it's necessary, who trust their practitioners, and who understand that there is a support plan in place are more positive and achieve better outcomes.

PharmaCare has created a brief patient information sheet for you to provide to patients to summarize the changes and direct them to more detailed resources available at **www.gov.bc.ca/biosimilars**. Included later in this guide is a biosimilars primer that may be useful in explaining biosimilars to your patients.

The most critical information usually required by patients is that biosimilars:

- are safe and effective
- will work like their current medication
- have no additional risk of adverse reactions or immunological response
- do not require significant changes to their routines or dosing
- are accompanied by patient support programs that will help them with benefits coordination, scheduling, access, etc.
- are available at infusion centres near them, though it may be a different infusion centre than they currently attend (applies only to infliximab)
- are well-understood, that switching from an originator has been extensively studied, and that switch programs have been successful around the world

It is important to recognize this is a switch process (not a substitution policy), where patient and practitioner education, collaborative decision making, and exception options for those who need them are key.

Healthcare practitioners are essential in empowering patients with information, demonstrating that there is a support system in place, and setting them up for success.

What evidence supports biosimilar adoption and switching?

The safety, efficacy, immunogenicity, and therapeutic similarity of biosimilars is evidenced by a large body of clinical evidence, extensive post-market pharmacovigilance, as well as the results of biosimilar programs in other jurisdictions.

Additional reading is available online at **w**ww.gov.bc.ca/biosimilars/pharmacists.

The Ministry will be carefully monitoring drug utilization, patient outcomes, and the response from patients and healthcare practitioners during and after the biosimilar initiative in B.C.

What is the nocebo effect and how can I help prevent it?

The greatest hurdle for successful switching to a biosimilar is the potential for the nocebo effect, where a patient's negative expectations both psychologically and physiologically affect the outcomes of and adherence to their treatment.

Patients' pre-existing beliefs, previous healthcare experiences, and mindset can have a very real effect on symptoms and their sense of wellbeing.

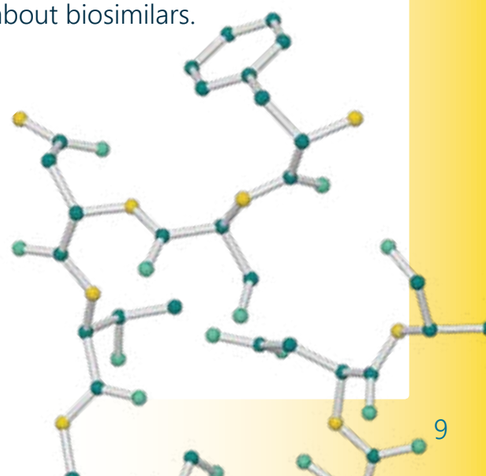
Many factors contribute to a patient's likelihood of experiencing the nocebo effect:

- Patient factors, such as other mental health comorbidities (especially anxiety, depression, or cognitive impairment), language barriers, a history of negative interactions with the healthcare system, or the use of online media as a source of medical information (where negative responses are highly over-represented, and bias or misrepresentation go unchecked).
- Practitioner factors, such as language choices, manner, non-verbal communication, or unbalanced focus on potential adverse reactions.
- Health care setting factors, such as the physical environment, comfort, ease of access, and interactions with other staff and patients.
- Drug factors, such as an appearance or smell, administration route or routine, change in delivery device, labelling, and price.

A variety of strategies can be effective in preventing the nocebo effect:

- Empower people with information and an active role in the switch process.
- Be attentive and empathetic, so patients feel safe asking questions or expressing concerns.
- Balance the presentation of desired effects and adverse effects.
- Promote a neutral or positive outlook instead of reiterating fears.
- Acknowledge the nocebo effect itself.
- Speak face-to-face, when possible.
- Discuss a plan for follow-up, acknowledging that there are options, no matter the outcome.

As the front line of healthcare in B.C. and often a patient's first source of information, pharmacists have a unique power to affect patient mindsets about biosimilars.



Where can I find more resources for my patients?

A library of patient resources is available online at www.gov.bc.ca/biosimilars. Here they can find detailed information about:

- the Biosimilars Initiative
- how they may be affected
- biologic and biosimilar drugs
- answers to frequently asked questions
- other resources and reading (including materials developed by patient groups)

If you require additional printed patient information sheets, please contact us at **Biosimilars.Initiative@gov.bc.ca**.

Will this be the only biosimilar switch?

In Phase 1 of the Biosimilars Iniative, the focus is on switching all Lantus (insulin glargine) users, patients using Remicade (infliximab) for rheumatological or dermatological indications, and those using Enbrel (etanercept) for rheumatological indications.

Phase 2 of the Biosimilars Initative will focus on switching patients using Remicade for GI indications.

It is likely that further switches to biosimilars will occur for other indications and drugs. All switches will be planned in consultation with the affected prescribers and stakeholders.

What if I have questions or need more information?

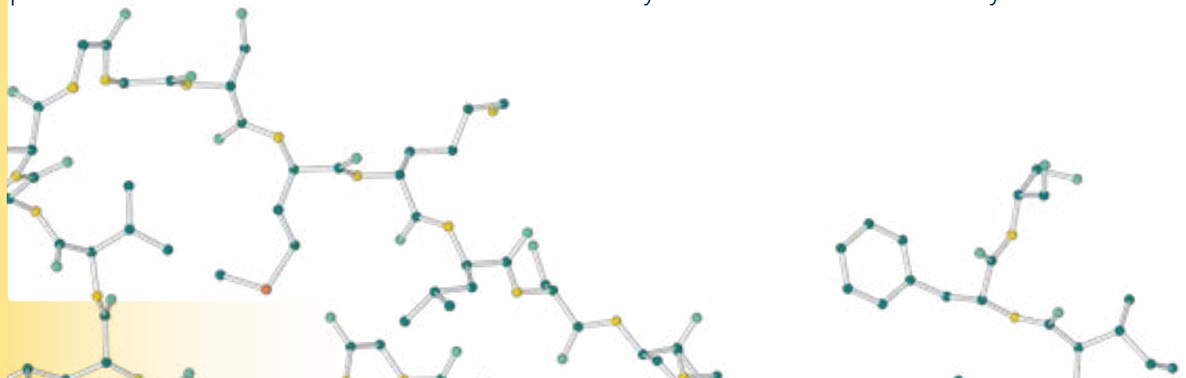
PharmaCare is committed to working with healthcare practitioners throughout the biosimilars initiative. Call-in information sessions, hosted by members of the PharmaCare team and specialist guests, will be scheduled throughout the transition period.

More detailed information is available at www.gov.bc.ca/biosimilars/pharmacists.

An up-to-date schedule of information sessions will be available at the link above.

The PharmaCare team is also available at **Biosimilars.Initiative@gov.bc.ca** for your questions and feedback.

For those with additional interest in biosimilars, the British Columbia Pharmacy Association provides two online learning modules about biosimilars. This training is available to B.C. pharmacists at no cost. The modules are not funded by or affiiliated with the Ministry of Health.



What patient support programs are available for biosimilars?

Biosimilar manufacturers are committed to minimizing the impact of this initiative, especially regarding patient support program processes and services, as well as access to infusion centres. Prescribers are generally responsible for initiating the patient enrollment process in a patient support program (PSP).

PSP agents will not be aware of Special Authority expiry dates, nor will they have information regarding coordination of benefits. Pharmacies will likely need to reprint prescription receipts with SA coding for patients to provide to PSPs for this purpose.

INFLECTRA

The Inflectra Patient Assistance Program provides support services, including coordination with private payers and infusion centres, for patients taking Inflectra.

Phone: 1-844-466-6627 | Fax: 1-844-295-0219 | Email: inflectrasupport@innomar-strategies.com
Hours: Monday to Friday, 5:00 a.m. to 5:00 p.m. PST

B.C. Inflectra Navigators

- Marlena Giordano: District Manager, B.C. and Ontario
  mgiordano@innomar-strategies.com, 1-416-452-3464
- Kelly Blumeschein: Inflectra Navigator, Kelowna and Kamloops
  kblumenschein@innomar-strategies.com, 1-250-300-1313
- Rekha Singh: Inflectra Navigator, Vancouver and Lower Mainland
  resingh@innomar-strategies.com, 1-604-347-8815
- Jennifer Bayntun: Inflectra Navigator, Vancouver
  jbayntun@innomar-strategies.com, 1-604-340-3795
- Jennifer Paronen: Inflectra Navigator, Vancouver Island
  jparonen@innomar-strategies.com, 1-250-418-5549

RENFLEXIS AND BRENZYS

The Merck Harmony® Patient Support Program provides support services, including coordination with private payers (for patients taking Renflexis or Brenzys) and infusion centres, for patients taking Renflexis. To enroll a patient, contact the Merck Harmony central number, and you will be directed to an assigned coordinator

Phone: 1-866-556-5663 | Fax: 1-866-240-4076 | Email: info@merckharmony.ca
Hours: Monday to Friday, 8:00 a.m. to 8:00 p.m. PST | Saturday and Sunday 12:00 p.m. to 5:00 p.m. PST

B.C. Merck Harmony Coordinators

- Bobbie Uppal: bobbie.uppal@merckharmony.ca, 1-289-295-0709
- Kirk Chen: kirk.chen@merckharmony.ca, 1-289-295-0710
- Beth-Anne Holbrook: bethanne.holbrook@merckharmony.ca, 1-289-295-0711
- Meghan Keenan: Meghan.keenan@merckharmony.ca, 1-289-295-0702

For additional information, contact the Merck Harmony B.C. Patient Support Program Managers

- Rose Wilbee, 1-604-999-1164
- Baloo Dosanjh, 1-604-999-1173

ERELZI

The Erelzi XPOSE® program provides support services, including self-injection training, for patients taking Erelzi. To enroll in the program, both prescriber and patient must sign a completed enrollment form.

Phone: 1-844-279-7673 | Fax: 1-866-872-5771
Hours: Monday to Friday, 5:00 a.m. to 5:00 p.m. PST

BIOSIMILAR BASICS

A PRIMER FOR PATIENT DISCUSSIONS

What is a biologic drug?

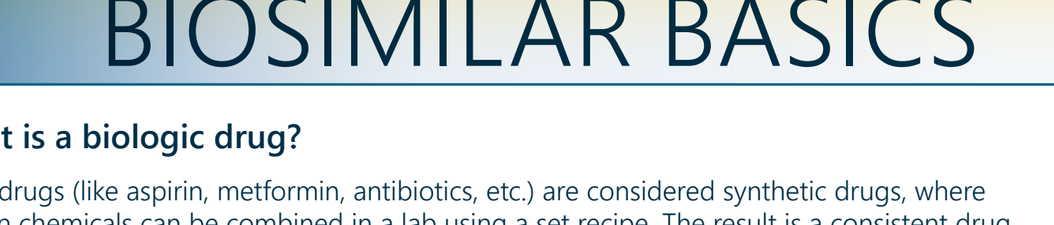
Most drugs (like aspirin, metformin, antibiotics, etc.) are considered synthetic drugs, where certain chemicals can be combined in a lab using a set recipe. The result is a consistent drug product composed of relatively small molecules that can be easily tested to ensure everything is identical in composition and potency across different batches and different manufacturers.

Biologic drugs were first introduced in the 1980s, as advancements allowed scientists to manipulate other organisms' cells and better identify complex compounds and feedback systems involved in human metabolism and disease processes.

Biologic drugs are produced by engineering a living cell line (like bacteria, yeast, or mammal cells, etc.) to produce a specific protein compound that is then collected and purified for human use. These protein compounds are very large and complex compared to synthetic drugs.

Biologic drugs have created new fields of research and disease treatment, providing more and better options for cancer treatment and the management of chronic diseases like rheumatoid arthritis, Crohn's disease, and diabetes.

Relative Sizes of Example Synthetic and Biologic Drug Molecules



What is a biosimilar drug?

Like with synthetic drugs, when a unique biologic drug is no longer protected by patents, other manufacturers can produce that protein compound themselves under a different brand name. These new versions of a biologic drug are called biosimilars.

Biosimilars are designed to be highly similar to the biologic originator, with no clinically meaningful differences in safety or efficacy. Because biologics are complex to manufacture, it is impossible to make identical copies between a biosimilar and biologic originator. Similarly, when an originator changes their manufacturing process, the subsequent product is also not identical to the original version made and would be considered a "biosimilar" of the original product.

Producing biosimilars builds on the work already done for the biologic originator, and therefore requires less investment into research and development. This means the biosimilar product can be offered at a lower cost, providing patients and the healthcare system better value for the same benefit.

> "Health Canada's rigorous standards for authorization mean that patients and health care providers can have the same confidence in the quality, safety and efficacy of a biosimilar as any other biologic drug."
>
> Health Canada
> *Fact Sheet: Biosimilars*
> 2017

How is a biosimilar drug proven to be as safe and effective as the originator?

Health Canada's rigorous requirements demand that a biosimilar demonstrate that there are no clinically meaningful differences in terms of physiochemical structure, quality, potency, pharmacokinetics, and immunogenicity. Clinical efficacy studies must demonstrate that the therapeutic effects of the biosimilar (both risk and benefit) are consistent.

After a drug is approved for sale, post-market analyses and studies can further demonstrate no meaningful differences in clinical efficacy between a biosimilar and the originator. These studies are common in the European Union, where biosimilars have been in use longer and have a higher adoption rate.

Are biosimilars interchangeable with their biologic originator?

As biosimilars cannot be proven to be identical to their biologic originator, they are not classified as interchangeable; that is, a pharmacist could not substitute one for the other at the pharmacy level without involvement of the prescribing physician.

Biosimilars and their originator biologics are proven to have no clinically meaningful differences in function or effect, meaning that switching from one to another is appropriate at the direction of the prescribing physician, in collaboration with the patient.

> "Health Canada considers a well-controlled switch from a reference biologic drug to a biosimilar in an approved indication to be acceptable, and recommends that a decision to switch a patient being treated with a reference biologic drug to a biosimilar, or between any biologics, be made by the treating physician in consultation with the patient and take into account any policies of the relevant jurisdiction."
>
> *Health Canada's 2017 Biosimilars Workshop: Summary Report*

What are the benefits of biosimilars?

Biosimilars offer major cost savings to the healthcare system, which allows for improved access to drug therapies for more people who need them. Biosimilars also contribute to a healthy and competitive drug market in Canada, supporting diversification of drug products and manufacturers, as well as driving both demand and capacity for newer, better drugs.

WHAT OFFICIALS ARE SAYING ABOUT BIOSIMILARS

"Policies and position statements on biosimilars are evolving to reflect increasing experience with and confidence in biosimilars as a treatment option."

Health Canada's 2017 Biosimilars Workshop: Summary Report

"By increasing treatment options, biosimilars can enhance competition in the market for biological products without reducing incentives to innovate."

U.S. Food and Drug Administration
Biosimilars Action Plan: Balancing Innovation and Competition
July 2018

"Policies regarding switching from a reference biologic drug to a biosimilar should consider the need for cost savings as well as patient and physician choice."

Health Canada's 2017 Biosimilars Workshop: Summary Report

"Patients and their physicians can expect that there will be no clinically meaningful differences between taking a reference product and a biosimilar when these products are used as intended."

U.S. Food and Drug Administration
Prescribing Biosimilar Products
2019

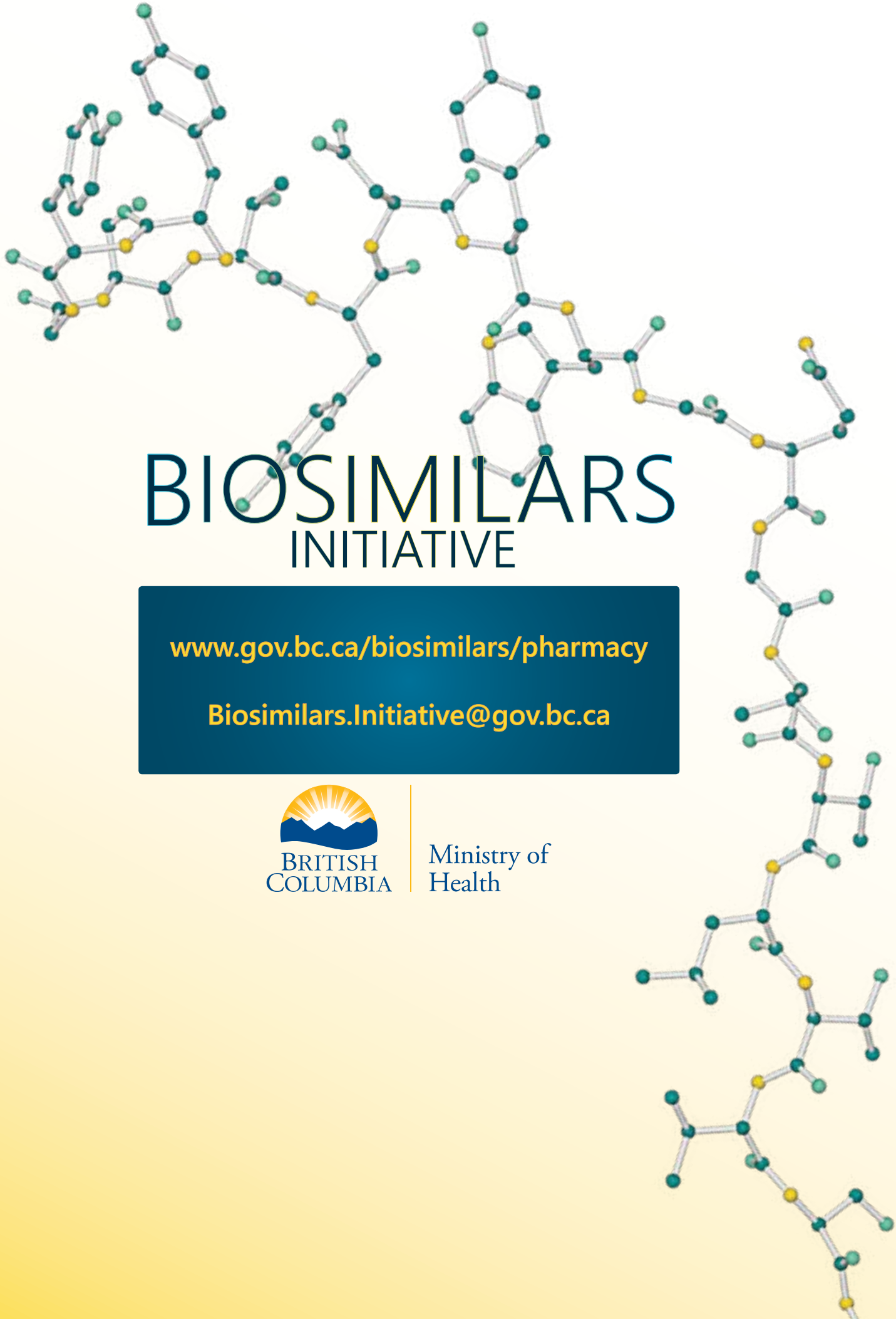
"In Europe, the availability of lower priced biosimilars has been reported to reduce the average list prices of reference products as well as prices of products within the whole therapeutic class."

Canadian Agency for Drugs and Technology in Health
Biosimilars—Regulatory, Health Technology Assessment, Reimbursement Trends, and Market Outlook
January 2018

"Over the past 10 years, the EU has approved the highest number of biosimilars worldwide, amassing considerable experience in their use and safety. The evidence acquired over 10 years of clinical experience shows that biosimilars approved through EMA can be used safely and effectively in all their approved indications as other biological medicines. Over the last 10 years, the EU monitoring system for safety concerns has not identified any relevant difference in the nature, severity or frequency of adverse effects between biosimilars and their reference medicines."

European Medicines Agency
Biosimilars in the EU: Information Guide for Healthcare Professionals
2017

complete infliximab protein structure and assembly



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www.gov.bc.ca/biosimilars/pharmacy

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