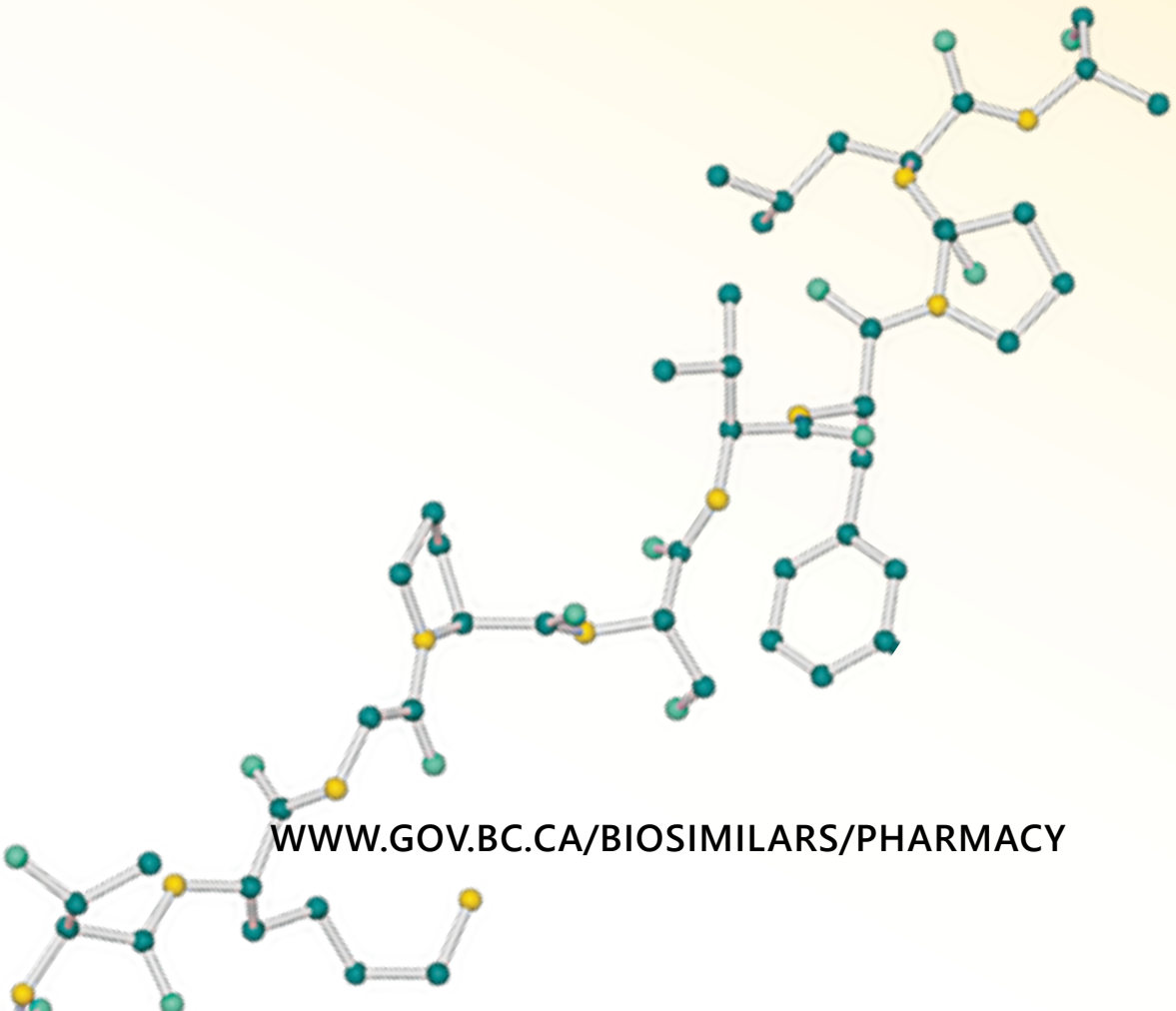
BIOSIMILARS INITIATIVE

PHARMACY GUIDE RITUXIMAB



WWW.GOV.BC.CA/BIOSIMILARS/PHARMACY

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 2016, Canada spent $241 million on Rituxan® alone—making it one of the top 10 highest biologic expenditures in the country. 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., Truxima®, Riximyo® and Ruxience™ (rituximab biosimilars) offer a 30-37% reduction in cost compared to Rituxan® (rituximab originator), for which expenditures in B.C. were $19.8 million in 2019.

Despite these price differences, biosimilars have not yet captured much market share 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. With an ever-growing body of evidence and the support of many stakeholders, PharmaCare introduced the Biosimilars Initiative in May 2019. The Initiative enables the expansion of treatment options and the improvement of patient access to safe care.

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

Phases One and Two of the Initiative switched three biologics that were among the largest drug expenditures in B.C.: infliximab, etanercept, and insulin glargine. Biosimilar uptake in these phases was very positive, with PharmaNet data seeing 73% and 78% of total patients switched successfully in Phase One and Phase Two respectively. Those that are unaccounted for may have switched to a different biologic not included in the Initiative or may have ceased treatment entirely for various reasons.

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 responsive contacts for healthcare practitioners;
- Facilitating changes that optimize patient care in affected therapeutic areas (e.g., adding fecal calprotectin testing for GI patients, reducing SA criteria, etc.); and
- 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 to support your discussions with affected patients.

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

What is changing?

As in the first two phases of the Biosimilars Initiative, PharmaCare continues to change the coverage of certain biologic drugs, including rituximab.

Coverage for the originator biologic drug (Rituxan) will be discontinued for PharmaCare-covered patients being treated for indications including those listed below.

RITUXIMAB SWITCH PERIOD: August 20, 2020 to February 18, 2021			
Drug	**Originator**	**Biosimilar***	**Indications Include**
rituximab	Rituxan®	Truxima™ Riximyo™** Ruxience™	rheumatoid arthritis relapsing-remitting multiple sclerosis microscopic polyangiitis granulomatosis with polyangiitis

*Additional rituximab biosimilar brands may be approved and listed at www.gov.bc.ca/biosimilars/pharmacists

**At this time, Riximyo is not indicated for microscopic polyangiitis or granulomatosis with polyangiitis.

For affected patients with existing Special Authority (SA) approval for rituximab 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 rituximab will be granted for approved biosimilar brands only.

When do these changes take effect?

PharmaCare-covered patients using Rituxan who wish to maintain PharmaCare coverage must switch to a rituximab biosimilar by February 18, 2021.

All brands of rituximab, both originator and biosimilar, will be covered during the rituximab switch period (August 20, 2020 to February 18, 2021) to provide time for patients to discuss the switch with their prescriber and get a new prescription. Rituxan will no longer be covered for affected patients as of February 19, 2021.

Who will be affected?

Your patients will be affected by the biosimilars switch beginning August 20, 2020 if they:

- use Rituxan; and
- receive PharmaCare coverage (i.e., have existing SA for rituximab).

"Health Canada has not observed unexpected post-authorization safety signals for biosimilars marketed in Canada. The efficacy and safety profiles of biosimilars authorized in Canada remain in line with those of their reference biologic drugs."

Health Canada Fact Sheet: Biosimilars

How many biosimilar switches will there be?

In Phase One of the Biosimilars Initiative, the focus was on switching all Lantus patients, patients using Remicade for rheumatological or dermatological indications, and those using Enbrel for rheumatological indications.

Phase Two of the Biosimilars Initiative focused on switching patients using Remicade for GI indications.

The current switch period (August 20, 2020 – February 18, 2021) aims to switch over those taking Rituxan.

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.

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 successfully switched by Pharmacare in 2019 (Lantus, Enbrel, and Remicade) represented some of the province's largest drug expenditures. In 2018, PharmaCare spent $125 million on just these three originator drugs.

Despite being listed preferentially for new starts, the biosimilar versions of these drugs had captured only a fraction of the market before the Biosimilars Initiative. In 2018, Basaglar™ represented only 1.7% of 2018 insulin glargine PharmaCare expenditures, Brenzys® and Erelzi® only 6.8%, and Inflectra® and Renflexis® only 5.9%. As of June 1, 2020, 73% of Phase One patients and 78% of Phase Two patients have switched to the biosimilar version of their medication.

Building on the success of previous phases, PharmaCare has identified rituximab as another valuable cost-saving opportunity for the Initiative. Data shows that B.C. spent over $19.8 million on originator rituximab (Rituxan) in 2019. Now that three biosimilar options have been approved for use in Canada, the moment presents itself to effect the same opportunity to improve access to medications for patients. In B.C., rituximab biosimilar is priced at approximately 30-37% less than the originator brand.

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. As such, more phases may be added to the Initiative as biologic patents expire and other biosimilars are approved for safe and effective use in Canada.

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 www.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 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 (**66128266**) 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. Fees will be paid for claims submitted during the transition period, August 20, 2020 – February 18, 2021, for eligible patients (that is, patients who have active SA for the drug and are using the originator brand.

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 Rituxan:

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 have active Special Authority for Rituxan.
2. Provide them the Ministry of Health Patient Information Sheet for Rituxan.
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 February 19, 2021 in order to maintain PharmaCare coverage of their medication.
4. Submit a claim in PharmaNet for the Biosimilar Patient Support Fee for Pharmacists. Ensure the patient has not already been provided switch support by another pharmacy or pharmacist.

Will patients need new Special Authority approval?

Patients with an existing SA for rituximab 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 switch period, it will be renewed for approved 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.

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

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; and
- 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.

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

The greatest hurdle for the 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.

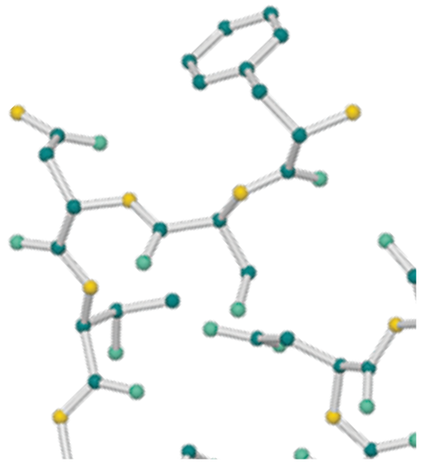
Many factors contribute to a patient's likelihood of experiencing the nocebo effect:

- Patient factors, such as 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 frontline 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.



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 enrolment 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.

TRUXIMA®

The Truxima® Teva Support Solutions® – Patient Support Program provides support services, including educational materials for patients, reimbursement services, financial assistance and medical updates to prescribers.

Phone: 1 877 714-2469 | Fax: 1 833 981-2254 | Email: tss.info@truximacanada.com
Hours: Monday to Friday, 8AM to 8PM EST

RIXIMYO®

The XPOSE® Patient Support Program by Sandoz® - an experienced full service PSP, provides support services to physicians / nurses and their patients through one point of contact; including securing coverage and providing the financial assistance patients require with their out-of-pocket expenses. The XPOSE® Patient Support Program by Sandoz® also offers infusion/education services. The Program will be working with a variety of infusions centers to provide patient accessibility.

Phone: 1 888 449-7673| Fax: 1 844 449-7673 | Email: xpose@sandozprogramsupport.ca

RUXIENCE™

Register to the PfizerFlex Patient Support Program or get more information at:

Phone: 1 855 935-3539 (FLEX) | Fax: 1 833 958-3539 (FLEX) | Email: ruxience@pfizerflex.com
Hours: Monday to Friday, 8AM to 8PM EST

What if I have questions or need more information?

PharmaCare is committed to working with healthcare practitioners throughout the Biosimilars Initiative.

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

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.

BIOSIMILAR BASICS

A PRIMER FOR PATIENT DISCUSSIONS

What is a biologic drug?

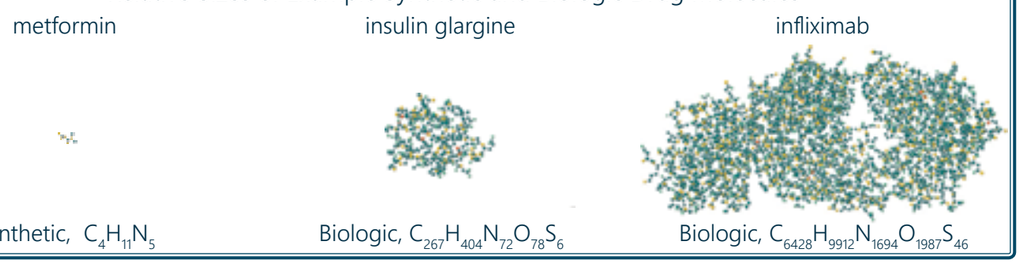
Most drugs (like aspirin, metformin, antibiotics, etc.) are considered synthetic drugs, where certain chemicals can be combined in a lab using a set recipe. The result is a consistent drug product composed of relatively small molecules that can be easily tested to ensure everything is identical in composition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

As 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*

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 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 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

"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 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."

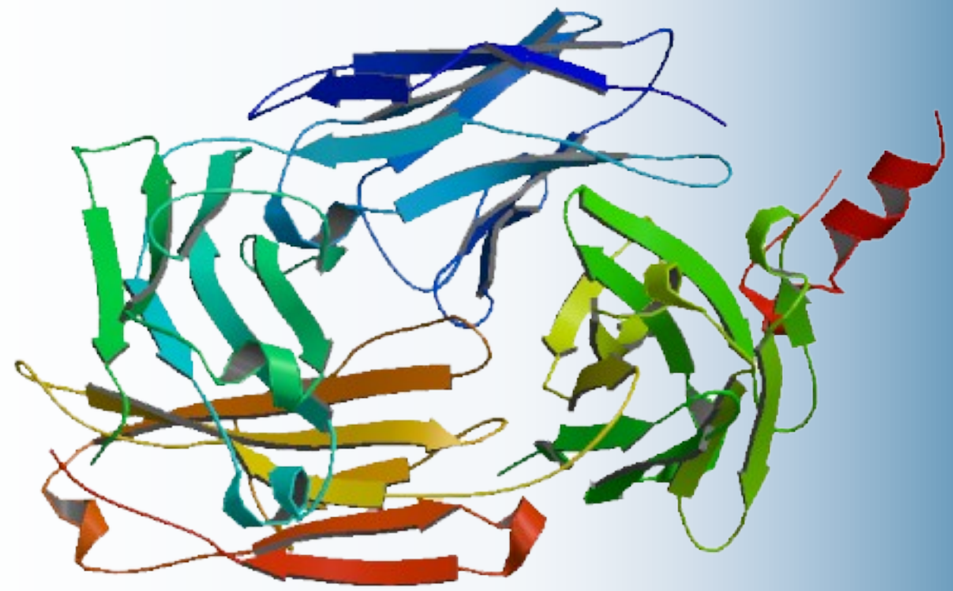
U.S. Food and Drug Administration
Prescribing Biosimilar Products

"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."

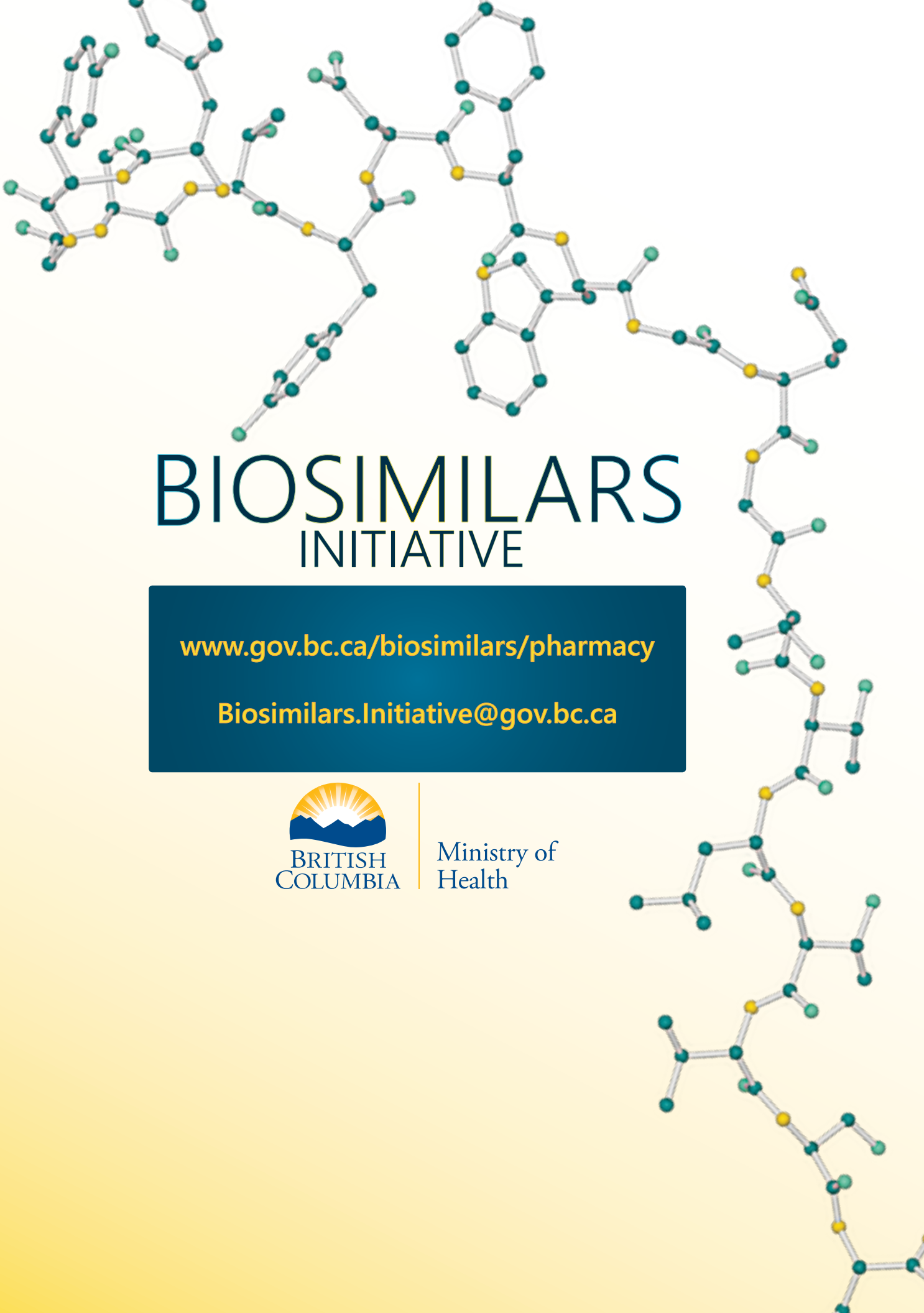
Canadian Agency for Drugs and Technology in Health
Biosimilars—Regulatory, Health Technology Assessment, Reimbursement Trends, and Market Outlook

"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



Protein structure of rituximab (DrugBank.ca, 2020)



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