Health Reform Observer -
Observatoire des Réformes de Santé

Volume 11 | Issue 2 | Article 4

Implementing a Medication Switching Policy: Analysis of the Saskatchewan Biosimilars Initiative

Kirsten Fox, *Saskatchewan Health Authority*

13 June 2024

A Provincial/Territorial Health Reform Analysis

Recommended Citation: Fox K. 2024. Implementing a Medication Switching Policy: Analysis of the Saskatchewan Biosimilars Initiative. *Health Reform Observer - Observatoire des Réformes de Santé* 11 (2): Article 4. https://doi.org/10.13162/hro-ors.v11i2.5711.

Abstract

Biologics are drugs that are uniquely created through advanced biotechnology. Biologics can be classified as either a reference biologic or a biosimilar. Reference biologics are innovator drugs whereas biosimilars are structurally similar, but not identical, to the reference biologic. Biologic drugs, especially reference biologics, are expensive and their use is steadily increasing across Canada. In response to increasing medication costs associated with the use of biologic drugs, the Saskatchewan Ministry of Health implemented the Saskatchewan Biosimilars Initiative on 20 October 2022. The Saskatchewan Biosimilars Initiative is a medication-switching policy that requires patients using a reference biologic to transition to an available biosimilar. This policy is intended to increase the uptake of biosimilars, which cost up to 50% less than the reference biologic. Similar switching policies that have been implemented internationally have produced significant cost savings to public health insurance programs. Currently, no economic data from the Saskatchewan Ministry of Health or the Drug Plan and Extended Benefits Branch is available to assess policy effectiveness.

Les produits biologiques sont des médicaments créés de manière unique grâce à une biotechnologie avancée. Les produits biologiques peuvent être classés en tant que produits biologiques de référence ou biosimilaires. Les produits biologiques de référence sont des médicaments innovants, tandis que les biosimilaires sont structurellement similaires, mais pas identiques, au produit biologique de référence. Les médicaments biologiques, en particulier les médicaments biologiques de référence, sont coûteux et leur utilisation est en constante augmentation au Canada. En réponse à l'augmentation des dépenses associées à l'utilisation des médicaments biologiques, le ministère de la santé de la Saskatchewan a mis en place l'initiative des biosimilaires de la Saskatchewan le 20 octobre 2022. La Saskatchewan Biosimilars Initiative est une politique de substitution non médicale qui exige que les patients utilisant un médicament biologique de référence pour lequel existe un biosimilaire passent à ce biosimilaire. Cette politique vise à accroître l'utilisation des biosimilaires, qui coûtent jusqu'à 50 % de moins que le produit biologique de référence. Des politiques similaires de transition non médicale mises en œuvre à l'échelle internationale ont permis aux programmes publics d'assurance maladie de réaliser des économies considérables. À l'heure actuelle, le ministère de la santé de la Saskatchewan ou la Drug Plan and Extended Benefits Branch ne disposent d'aucune donnée économique permettant d'évaluer l'efficacité de la politique.

Key Messages

- Biologic drugs are expensive and subsequently accounted for 29.4% of total Canadian public drug program spending in 2022.
- Biosimilars cost 15% to 50% less than the reference biologic drugs.
- Switching policies that transition patients from a reference biologic drug to a biosimilar have been implemented in Europe, the United States, and in other Canadian jurisdictions as a means of increasing uptake of biosimilars to produce cost savings for public insurance programs and patients enrolled in cost-sharing.
- The Saskatchewan Biosimilars Initiative is a non-medical switching policy implemented on 20 October 2022.

Messages-clés

- *Les médicaments biologiques sont coûteux et représentaient 29,4 % des dépenses totales du programme public canadien de médicaments en 2022.*
- *Les biosimilaires coûtent de 15 % à 50 % de moins que les médicaments biologiques de référence.*
- *Des politiques de transition permettant aux patients de passer d'un médicament biologique de référence à un biosimilaire ont été mises en œuvre en Europe, aux États-Unis et dans d'autres juridictions canadiennes afin d'accroître l'utilisation des biosimilaires et de réaliser des économies pour les programmes d'assurance publique et les patients inscrits.*
- *La Saskatchewan Biosimilars Initiative est une politique de substitution non médicale mise en œuvre le 20 octobre 2022.*

1 BRIEF DESCRIPTION OF THE HEALTH POLICY REFORM

Biologics are high-cost medications with growing utilization domestically and internationally, with total sales equalling $11.2 billion in Canada in 2021 (Government of Canada 2023). Biosimilars, an alternative to reference biologic drugs, are less expensive and thus serve as a potential means of reducing drug costs for public insurance programs. Therefore, medication-switching policies that substitute a reference biologic drug to an available biosimilar have been implemented as a means of increasing biosimilar uptake to reduce public insurance drug costs (Patented Medicine Prices Review Board 2023).

The Saskatchewan Biosimilars Initiative (SBI) is a medication-switching policy implemented by the Government of Saskatchewan Ministry of Health Drug Plan and Extended Benefits Branch (Government of Saskatchewan 2024a). To maintain drug coverage, this policy requires that patients on a reference biologic drug switch to a biosimilar product, if available (Drug Plan and Extended Benefits Branch 2022a). The SBI was announced on 20 October 2022 and required patients to transition to a biosimilar by 30 April 2023 (Drug Plan and Extended Benefits Branch 2022b). The SBI was successfully implemented, experiencing only temporary pauses of the policy for certain biologics due to a lack of biosimilar supply availability in Canada.

1.1 Explicit goals

The SBI's explicitly stated goal is increased uptake of biosimilar drugs. Because biosimilars cost less than reference biologics, the increased uptake of biosimilars was intended to take advantage of potentially significant cost savings for the Saskatchewan Drug Plan (Drug Plan and Extended Benefits Branch 2022a).

1.2 Intrinsic goals

The SBI aligns with the Drug Plan and Extended Benefits Branch objective of reducing costs associated with drug materials to ensure the viability of the Drug Plan (Drug Plan and Extended Benefits Branch 2022c). This objective is intentionally implemented to provide Saskatchewan residents with "better value." Better value of the health system for patients is also an overall objective of the Ministry of Health, characterized by programs that "achieve best value for money, improve transparency and accountability, and strategically invest in facilities, equipment, and information structure" (Government of Saskatchewan 2023).

2 HISTORY AND CONTEXT

Biologics are drugs that are produced with living cells and tissues, often with the use of advanced biotechnology (Health Canada 2022a). Biologic drugs, such as insulin, vaccines,

and antibodies, are frequently used to treat a myriad of medical conditions, including anemia, diabetes, cancer, and inflammatory bowel disease (Health Canada 2022a). Compared to chemically synthesized drugs, biologics are more difficult to consistently manufacture, resulting in additional regulatory oversight by Health Canada's Biologic and Radiopharmaceutical Drugs Directorate (BRDD) (Health Canada 2022b). The BRDD reviews biologic drugs to ensure compliance with the requirements for market authorization for sale in Canada (Health Canada 2022b). Innovator biologic drugs authorized for sale are referred to as the "reference biologic drug" when subsequent entry biologics (SEBS) called "biosimilars" are later introduced to the Canadian market (Health Canada 2022c).

Biosimilars are biologic drugs that are structurally similar to a reference biologic drug already authorized for sale in Canada by the BRDD (Health Canada 2022c). Biosimilars are approved for sale by Health Canada after demonstrating comparable quality, efficacy, and safety to the reference biologic drug (Health Canada 2022c). Approved biosimilars are authorized for use for the same indication(s) as the reference biologic drug and therefore, per Health Canada, patients can safely switch between the reference biologic drug and biosimilars if indicated to treat the same medical condition (Health Canada 2022c). Biologics are expensive medications, accounting for $4.4 billion, or 29.4%, of total public drug program spending in 2022 (Canadian Institute for Health Information [CIHI] 2022). Therefore, a significant benefit of biosimilars is the reduced cost compared to the reference biologic drug. Biosimilars cost 15% to 50% less than the reference biologic drug (Government of British Columbia 2021).

Switching between reference biologic drugs and biosimilars is supported by literature and multiple bodies, both national and international. Several systematic reviews have demonstrated that switching between biologic drugs produces no differences in efficacy, safety, or immunogenicity (Barbier et al. 2020; de Oliveira Ascef et al. 2023). Switching between reference biologic drugs and biosimilars for various indications has been safely occurring in Europe since 2006 (Vogler et al. 2021). Subsequently, the European Medicines Agency and the Heads of Medicines Agencies produced a joint statement in support of the interchangeability of biosimilar medicines (European Medicines Agency and Heads of Medicines Agencies 2023). In Canada, switching between biologic drugs is supported by bodies such as the Arthritis Society of Canada and the Canadian Digestive Health Foundation (Arthritis Society of Canada 2020; Canadian Digestive Health Foundation 2021).

Switching between biologic drugs is not without concern. Patients report apprehension related to switching between biologic drugs, fearing destabilization of medical conditions (Chew et al. 2022). Accordingly, physicians are concerned that switching may negatively affect patients' mental health (McClean et al. 2022). Pharmacovigilance concerns also exist due to a general lack of long-term evidence, particularly with multiple switches between biologic drugs (Allocati et al. 2022; Lasala et al. 2023).

Non-medical switching occurs when an individual stabilized on one medication switches to an alternative medication for a non-medical reason (Fleischmann et al. 2020). Governments may implement non-medical switching policies for economic reasons. With respect to

biologics, by switching patients from costly reference biologic drugs to less expensive biosimilars, significant cost savings could result for provincial and territorial public insurance programs (Crosby, Tadrous, and Gomes 2020). Subsequently, medication switching policies for biosimilars have been implemented throughout Canada, with Manitoba, Nunavut, and Yukon currently existing as the only jurisdictions without a policy (Gastrointestinal [GI] Society 2023).

In 2019, British Columbia was the first jurisdiction to implement a biosimilars switching policy (Dormuth, Fisher, and Carney 2020). To monitor for unintended effects on patient health and/or utilization of health care services, a rapid monitoring plan was implemented with the biosimilar switching policy (Dormuth, Fisher, and Carney 2020). Data from the rapid monitoring plan demonstrated that the biosimilar switching policy generally produced few unintended negative effects. However, a non-permanent increase in the utilization of health care services occurred, attributed to medical appointments related to medication switching. Additionally, there were dose escalations for some medications, attributed to multifactorial causes beyond the switching policy (Fisher et al. 2022; Fisher, Kim, and Dormuth 2022a; Fisher, Kim, and Dormuth 2022b; Fisher, Kim, and Dormuth 2023).

Switching polices also exist internationally. To take advantage of cost savings associated with the use of biosimilars, European countries have implemented a variety of policies, including medication switching (Vogler et al. 2021). For example, pricing and procurement mechanisms to reduce biologic drug costs include price link policies, tendering, or reference price systems (Vogler et al. 2021). Additionally, demand-side measures to increase uptake of biosimilars include prescribing requirements and substitution policies (Vogler et al. 2021). Utilization of biosimilars in the United States is inhibited by Medicare reimbursement policies that encourage prescription of high-cost biologics, such as innovator products (Rome and Sarpatwari 2021). Therefore, internationally trained physicians in Canada will require familiarization with jurisdictional prescribing policies of biologic drugs.

On 20 October 2022, the Saskatchewan Ministry of Health Drug Plan and Extended Benefits Branch launched the SBI, a medication switching policy that included ten biologic drugs (Drug Plan and Extended Benefits Branch 2022b). At the time, Saskatchewan was the seventh Canadian jurisdiction to implement a medication switching policy. Patients using a reference biologic drug for any indication were advised that the switch to a biosimilar must occur by 30 April 2023 to maintain ongoing medication coverage (Drug Plan and Extended Benefits Branch 2023a). Patients could request an exemption to the initiative if the use of a biosimilar drug was considered not medically possible and ongoing use of the reference biologic drug was indicated (Drug Plan and Extended Benefits Branch 2023b). Medications included in the SBI were adalimumab (Humira), etanercept (Enbrel), enoxaparin (Lovenox), filgrastim (Neupogen), glatiramer (Copaxone), infliximab (Remicade), insulin aspart (NovoRapid), insulin glargine (Lantus), insulin lispro (Humalog), and rituximab (Rituxan) (Drug Plan and Extended Benefits Branch 2022b).

The launch of the SBI had opposition from multiple groups. Patients using reference biologic drugs expressed concern that switching to a biosimilar would result in a resurgence

or destabilization of their medical condition (Patterson 2023). Both Diabetes Canada and Crohn's and Colitis Canada opposed the initiative, arguing that medication switching policies should not be implemented as they diminish shared decision-making between patients and prescribers (Crohn's and Colitis Canada 2019; Diabetes Canada 2022). Conversely, the SBI received support from Arthritis Research Canada's Scientific Director Emeritus Dr. John Esdaile, who highlighted the safety and efficacy of biosimilars compared to the reference biologic. Additionally, Dr. Esdaile commented that Saskatchewan should be able to implement a medication-switching policy following the success of a similar policy in British Columbia (Government of Saskatchewan 2022a). Similarly, Cheryl Koehn, the Founder and President of Arthritis Consumer Experts, provided support for the SBI as a means of ensuring the ongoing affordability of biologic drugs for individual patients and an opportunity to reinvest cost savings into the health care system to maintain and improve patient care (Joint Health Express 2022).

3 THE POLICY-MAKING PROCESS

3.1 Institutions

Multiple components of the Saskatchewan government are involved with the coverage of medications through the provincial health insurance program. The Saskatchewan Ministry of Health supports several health-related programs and services for Saskatchewan residents (Government of Saskatchewan 2024b). Under the Ministry of Health, the Drug Plan and Extended Benefits Branch oversees the provision of coverage for medical and community services for Saskatchewan residents (Government of Saskatchewan 2024c). Medication coverage is provided to eligible patients by the Saskatchewan Drug Plan, the publicly funded provincial drug program (Drug Plan and Extended Benefits Branch 2023d).

The Saskatchewan Drug Plan provides coverage for medications listed on the Saskatchewan Formulary. Medications are added to the Formulary by the Minister of Health, who is advised by the Drug Advisory Committee of Saskatchewan (Drug Plan and Extended Benefits Branch 2024a). Additionally, certain medications are only covered by the Saskatchewan Drug Plan through the Exception Drug Status (EDS) program. Medications included within the EDS Program require confirmation of patient eligibility and approval by the Minister of Health before coverage is provided (Drug Plan and Extended Benefits Branch 2024a). Approval is granted to patients that meet the medication-specific EDS criteria for use.

The Saskatchewan Ministry of Health's Drug Plan and Extended Benefits Branch, with consideration of the Saskatchewan Drug Plan, Saskatchewan Formulary, and EDS program, implemented the SBI. The biologic drugs included in the initiative were all listed within the EDS program prior to its implementation (Drug Plan and Extended Benefits Branch 2024b). Per the SBI, to maintain coverage for a biologic drug through the EDS program, patients must obtain a prescription for a biosimilar product by 30 April 2023 or apply for an exemption to use a reference biologic (Drug Plan and Extended Benefits Branch 2022b).

3.2 Interests

The mission of the Drug Plan and Extended Benefits Branch can be summarized as the promotion of citizen-centred service through rational and appropriate use of medications and extended benefits; the pursuit of value strategies such as low-cost policies, product listing agreements, standing offer contracts, and generic and drug pricing policies; and the provision of information to stakeholders and the public regarding policies, benefit assessments, and program utilization (Drug Plan and Extended Benefits Branch 2024c). The implementation of the SBI, as a means of producing cost savings while maintaining rational medication use, aligns with this mission.

In particular, the Saskatchewan Ministry of Health was interested in the potential for cost savings resulting from the implementation of the policy. Paul Merriman, the Health Minister at the time of the SBI's implementation, announced that the policy would contribute to the overall sustainability of the Saskatchewan Drug Plan's coverage of essential medications. Merriman stated that cost savings from the implementation of the SBI would be reinvested into the province's drug plan to support access to other drugs and extended benefits (Government of Saskatchewan 2022a). The Saskatchewan Ministry of Health's interest in identifying cost-saving strategies may have been influenced by growing expenses, totalling $457.1 million above projected in the 2021-2022 fiscal year (Government of Saskatchewan 2022b). Among other causes, the increased expenditures were attributed to prescription drug plan utilization pressures (Government of Saskatchewan 2022b).

3.3 Ideas

The literature has repeatedly demonstrated the potential cost savings associated with the use of biosimilars and medication-switching policies. A 2019 study that retrospectively analyzed Canadian drug store and hospital purchasing data of infliximab, insulin glargine, and filgrastim found that the current utilization of biosimilars saved $46 million in drug costs, but exclusive use of biosimilars could have saved up to $1 billion (Mansell et al. 2019). Similarly, an Ontario-based study estimated that non-medical switching of etanercept, infliximab, and adalimumab would save $645.9 million over three years (Gomes et al. 2021).

At the time the SBI was announced, the use of medication-switching policies were already implemented in Europe, the United States, and six other Canadian jurisdictions. Medication-switching policies were in existence in Europe by 2016 and real-world evidence suggests these policies increase drug access by improving affordability without significantly reducing medication safety or efficacy (Noce and Ernst 2018). As a result of biosimilar-switching policies in Europe, a 2020 report found that drug budgets were reduced by 5% since 2014 (Troein, Newton, and Scott 2020). In the United States, a 2021 report from the Association of Accessible Medicines found that cost savings resulting from biosimilar usage totalled $8 billion in 2020, with projected savings of $133 billion by 2025 (Association of

Accessible Medicines 2021). Prior to the implementation of medication-switching policies across Canadian jurisdictions, the usage of the biosimilars infliximab, etanercept, insulin glargine, and filgrastim saved Canadians an estimated $93.9 million in 2018 (Patented Medicine Prices Review Board 2020). Recent data suggests that generic- and biosimilar-switching policies reduced drug costs by $171 million in 2021-2022 (Patented Medicine Prices Review Board 2023).

4 IMPLEMENTATION AND EVALUATION

The SBI was launched on 20 October 2022 and was applied to ten medications: adalimumab (Humira), etanercept (Enbrel), enoxaparin (Lovenox), filgrastim (Neupogen), glatiramer (Copaxone), infliximab (Remicade), insulin aspart (NovoRapid), insulin glargine (Lantus), insulin lispro (Humalog), and rituximab (Rituxan) (Drug Plan and Extended Benefits Branch 2022b). Patients on reference biologic drugs were sent letters advising that a switch to a biosimilar was required to maintain medication coverage through the Saskatchewan Drug Plan EDS program. The medication switch needed to occur by 30 April 2023 (Drug Plan and Extended Benefits Branch 2022b).

Portions of the SBI were amended on 12 December 2022 due to the restricted availability of insulin products (Drug Plan and Extended Benefits Branch 2022d). Specifically, the transition for insulin lispro (Humalog) was paused until an adequate supply of the biosimilar product, Admelog, was available. Additionally, medication coverage would be maintained for patients utilizing the reference biologic version of insulin aspart (NovoRapid) with an insulin pump, because the biosimilar drugs were still undergoing insulin pump certification. Lastly, patients using insulin glargine (Lantus) and insulin aspart (NovoRapid) in vials would continue to receive medication coverage until a biosimilar product in vial format was available on the Saskatchewan Formulary (Drug Plan and Extended Benefits Branch 2022d). The availability of insulin lispro (Admelog) improved, therefore on 25 September 2023 it was announced that patients must switch to the biosimilar by 31 March 2024 (Saskatchewan Drug Plan and Extended Benefits Branch 2023c).

Currently, no evaluation of the SBI has been announced or completed. When the initiative was implemented, biologic drugs accounted for 35.7% of Saskatchewan's drug budget. The initiative was estimated to save the Government of Saskatchewan $20 million by May 2024 (Boulton 2022). Prior to the implementation of the SBI, the Government of Saskatchewan Ministry of Health Annual Report for 2021 to 2022 indicated that the Saskatchewan Drug Plan had $383.5 million in expenses (Government of Saskatchewan 2022b). Given that patients were not required to switch to a biosimilar until 30 April 2023, updated financial information will be available in the Ministry of Health Annual Report for 2023 to 2024. To align with their mission, it would also be beneficial for the Drug Plan and Extended Benefits Branch to provide and publish information to stakeholders regarding the effectiveness of the implementation of the SBI.

5 CONCLUSION

Biologics are expensive medications, accounting for nearly 30% of total public drug program spending in Canada in 2022. Biosimilars undergo significant regulatory oversight by Health Canada to ensure comparable safety and efficacy with the reference biologic drug (Health Canada 2022c). As a result, it is considered safe for patients to switch between different biologics approved for the same indication. However, limited long-term data on biosimilars and medication switching warrants post-marketing surveillance. The establishment of a national registry would be beneficial, such as distributed data networks used by the Canadian Network for Observational Drug Effect Studies (Canadian Network for Observational Drug Effect Studies 2024).

Medication-switching policies, where a patient transitions from a reference biologic product to a biosimilar, have been implemented in Europe, the United States, and several Canadian jurisdictions to increase uptake of biosimilars to improve potential cost savings. The SBI is an example of a medication-switching policy and was implemented in Saskatchewan on 20 October 2022. Because patients were not required to switch until 30 April 2023, financial reporting that evaluates the effectiveness of the SBI are not currently available. This information could be presented in the Government of Saskatchewan Ministry of Health 2023 to 2024 Annual Report or as information published by the Saskatchewan Drug Plan and Extended Benefits Branch.

6 STRENGTHS, WEAKNESSES, OPPORTUNITIES, THREATS

Table 1 summarizes the strengths, weaknesses, opportunities, and threats.

Table 1: SWOT Analysis

Strengths	Weaknesses
• The initiative facilitates significant increased uptake of biosimilars. • Patients may apply for exemption to the policy if biosimilars are inappropriate to use or are contraindicated. • The policy increases knowledge regarding the availability and the equivalent efficacy and safety of biosimilars compared to reference biologic drugs.	• The policy requires patients to obtain a prescription for a biosimilar which may result in increased use of primary health care services. • Medication switching reduces patient autonomy as to medication selection. • Long-term Canadian data on the actual cost savings of biosimilars is not yet available. • Need to monitor biosimilars for safety and efficacy of medication switching.
Opportunities	**Threats**
• Implementing therapeutic drug monitoring may mitigate nocebo effect. • The inclusion of additional biosimilars in the policy could produce increased cost savings. • Cost savings can be reinvested in other areas of the province's drug plan. • The province could collaborate with professional bodies, such as the College of Pharmacy Professionals, to allow pharmacists to switch to a biosimilar without requiring a prescription from a physician. • The province could collaborate nationally and internationally with other Ministries of Health to conduct surveillance and cost-effectiveness analyses of biosimilar medication switching policies.	• Nocebo effect may result in patients applying for exemption to the policy to remain on the reference biologic drug. • Poor biosimilar product availability or drug shortages may prevent successful implementation of the policy. • Stakeholder (e.g., patients, physicians, manufacturers of reference biologic drugs) may demonstrate resistance to medication switching policies.

7 REFERENCES

Arthritis Society of Canada. 2020. Biologics and biosimilars. https://arthritis.ca/living-well/2020/biologics-and-biosimilars.

Association of Accessible Medicines. 2021. The US generic and biosimilar medicines savings report. https://accessiblemeds.org/sites/default/files/2021-10/AAM-2021-US-Generic-Biosimilar-Medicines-Savings-Report-web.pdf.

Barbier L, Ebbers HC, Declerck P, Simoens S, Vulto AG, Huys I. 2020. The efficacy, safety, and immunogenicity of switching between reference biopharmaceuticals and biosimilars: a systematic review. *Clinical Pharmacology & Therapeutics* 108(4): 734-755. https://doi.org/10.1002/cpt.1836.

Boulton S. 2022. Saskatchewan launching biosimilar initiative to lower drug costs. *DiscoverEstevan*. https://discoverestevan.com/articles/saskatchewan-launching--biosimilar-initiative-to-lower-drug-costs.

Canadian Digestive Health Foundation. 2021. Transition pathway brochure for IBD patients. https://cdhf.ca/wp-content/uploads/2022/08/CDHF-EnglishBiosimilarTransitionPathwayBrochure.pdf.

Canadian Network for Observational Drug Effect Studies. 2024. Common data model: overview. https://www.cnodes.ca/cdm-overview/.

Chew C, Aguiar M, Bansback N, Law MR, Harrison M. 2022. Patient perspectives on the British Columbia Biosimilars Initiative: a qualitative descriptive study. *Rheumatol Int* 42(10): 1831-1842. https://doi.org/10.1007/s00296-021-04874-8.

CIHI (Canadian Institute for Health Information). 2022. Prescribed drug spending in Canada, 2022. https://www.cihi.ca/en/prescribed-drug-spending-in-canada-2022#:~:text=Biologics%20accounted%20for%20%244.4%20billion,Columbia%20to%204%25%20in%20Saskatchewan.

Crohn's and Colitis Canada. 2019. Biosimilars in Canada. https://crohnsandcolitis.ca/Crohns_and_Colitis/documents/2019-Factsheet-Biosimilars-REVISED-122020.pdf.

Crosby M, Tadrous M, Gomes T. 2020. Potential cost implications of mandatory non-medical switching policies for biologics for rheumatic conditions and inflammatory bowel disease in Canada. *Clinical Pharmacology & Therapeutics* 109(3): 739-745. https://doi.org/10.1002/cpt.2042.

de Oliveira Ascef B, Almeida MO, de Medeiros-Ribeiro AC, de Andrade DCO, de Oliveira Junior HA, de Soárez PC. 2023. Therapeutic equivalence of biosimilar and reference biologic drugs in rheumatoid arthritis: a systematic review and meta-analysis. *JAMA Network Open* 2023;6(5): e2315872. https://doi.org/10.1001/jamanetworkopen.2023.15872.

Diabetes Canada. 2022. Saskatchewan new drug policy requires switching from biologic drug to a biosimilar insulin. https://www.diabetes.ca/media-room/news/saskatchewan-new-drug-policy-requires-switching-from-biologic-drug-to-a-biosimilar-insulin.

Dormuth CR, Fisher A, Carney G. 2020. A rapid monitoring plan following a shift in coverage from brand name to biosimilar drugs for rheumatoid arthritis in British Columbia. *Pharmacoepidemiology and Drug Safety* 2020;20: 796-802. https://www.doi.org/10.1002/pds.4957.

Drug Plan and Extended Benefits Branch. 2022a. Saskatchewan Biosimilars Initiative. https://www.saskatchewan.ca/residents/health/prescription-drug-plans-and-health-coverage/extended-benefits-and-drug-plan/biosimilars#transitioning-to-a-biosimilar.

Drug Plan and Extended Benefits Branch. 2022b. Letter to health care providers - Saskatchewan Biosimilars Initiative announcement. https://publications.saskatchewan.ca/api/v1/products/119429/formats/137600/download.

Drug Plan and Extended Benefits Branch. 2022c. Annual report for 2021-2022. https://formulary.drugplan.ehealthsask.ca/Publns/2021-2022_Annual_Report.pdf.

Drug Plan and Extended Benefits Branch. 2022d. Saskatchewan formulary bulletin: Saskatchewan Biosimilars Initiative: insulin coverage updates. https://formulary.drugplan.ehealthsask.ca/Bulletins/Bulletin-0224-Dec-2022.pdf.

Drug Plan and Extended Benefits Branch. 2023a. Letter to health care providers - Saskatchewan Biosimilars Initiative update. https://publications.saskatchewan.ca/api/v1/products/119429/formats/138886/download.

Drug Plan and Extended Benefits Branch. 2023b. Saskatchewan Biosimilars Initiative exemption request form. https://publications.saskatchewan.ca/api/v1/products/120144/formats/139646/download.

Drug Plan and Extended Benefits Branch. 2023c. Letter to health care providers: Saskatchewan Biosimiliars Initiative Policy notice: Humalog® (insulin lispro). https://publications.saskatchewan.ca/api/v1/products/119429/formats/141604/download.

Drug Plan and Extended Benefits Branch. 2023d. Saskatchewan drug plan overview. https://formulary.drugplan.ehealthsask.ca/DrugPlanOverview.

Drug Plan and Extended Benefits Branch. 2024a. About the Saskatchewan formulary. https://formulary.drugplan.ehealthsask.ca/About.

Drug Plan and Extended Benefits Branch. 2024b. Appendix A: exceptional drug status program. https://formulary.drugplan.ehealthsask.ca/PDFs/APPENDIXA.pdf.

Drug Plan and Extended Benefits Branch. 2024c. Branch information. https://formulary.drugplan.ehealthsask.ca/BranchInformation.

European Medicines Agency and Heads of Medicines Agencies. 2023. Statement on the scientific rationale supporting interchangeability of biosimilar medicines in the EU. https://www.ema.europa.eu/en/documents/public-statement/statement-scientific-rationale-supporting-interchangeability-biosimilar-medicines-eu_en.pdf.

Fisher A, Kim JD, Carney G, Dormuth C. 2022. Rapid monitoring of health services use following a policy to switch patients from originator to biosimilar etanercept – a cohort study in British Columbia. *BMC Rheumatology* 6(5). https://doi.org/10.1186/s41927-021-00235-x.

Fisher A, Kim JD, Dormuth D. 2022a. The impact of mandatory nonmedical switching

from originator to biosimilar insulin glargine. *Clinical Therapeutics* 44(7): 957-970. https://doi.org/10.1016/j.clinthera.2022.05.003.

Fisher A, Kim JD, Dormuth D. 2022b. Mandatory nonmedical switching from originator to biosimilar infliximab in patients with inflammatory arthritis and psoriasis in British Columbia: a cohort study. *CMAJ Open* 10(1): E109-E118. https://doi.org/10.9778/cmajo.20200319.

Fisher A, Kim JD, Dormuth D. 2023. Monitoring a mandatory nonmedical switching policy from originator to biosimilar infliximab in patients with inflammatory bowel disease: a population-based cohort study. *Gastrointestinal Research and Practice* 2794220. https://doi.org/10.1155/2023/2794220.

Fleischmann R, Jairath V, Mysler E, Nicholls D, Declerck P. 2020. Nonmedical switching from originators to biosimilars: does the nocebo effect explain treatment failures and adverse events to rheumatology and gastroenterology? *Rheumatology and Therapy* 7(1): 35-64. https://doi.org/10.1007/s40744-019-00190-7.

GI (Gastrointestinal) Society. 2023. Provincial and territorial biologics policies. https://badgut.org/information-centre/a-z-digestive-topics/provincial-biologics-policies/.

Gomes T, McCormack D, Kitchen SA, Paterson JM, Mamdani MM, Proulx L, Bayliss L, Tadrous M. 2021. Projected impact of biosimilar substitution policies on drug use and cost in Ontario, Canada: a cross-sectional time series analysis. *CMAJ Open* 9(4): E1055-E1062. https://doi.org/10.9778/cmajo.20210091.

Government of British Columbia. 2021. BC's biosimilars program expands. https://news.gov.bc.ca/releases/2021HLTH0067-000653.

Government of Canada. 2023. Biosimilars in Canada: polices to promote switching and what it means for payers. https://www.canada.ca/en/patented-medicine-prices-review/services/npduis/analytical-studies/posters/biosimilars-policies-promote-switching.html.

Government of Saskatchewan. 2022a. Saskatchewan launches biosimilars initiative. https://www.saskatchewan.ca/government/news-and-media/2022/october/20/saskatchewan-launches-biosimilars-initiative#:~:text=The%20Ministry%20of%20Health%20is%20introducing%20a%20biosimilars,a%20reference%20drug%29%20no%20longer%20has%20patent%20protection.

Government of Saskatchewan. 2022b. Ministry of Health annual report for 2021-22. https://publications.saskatchewan.ca/api/v1/products/25499/formats/136195/download.

Government of Saskatchewan. 2023. Ministry of Health annual report for 2022-23. https://publications.saskatchewan.ca/api/v1/products/25499/formats/141173/download.

Government of Saskatchewan. 2024a. The Saskatchewan drug plan. https://www.saskatchewan.ca/residents/health/prescription-drug-plans-and-health-coverage/extended-benefits-and-drug-plan/saskatchewan-drug-plan.

Government of Saskatchewan. 2024b. Ministry of Health programs and services. https://www.saskatchewan.ca/health#programs-and-services.

Government of Saskatchewan. 2024c. Prescription drug plans and health coverage. https://www.saskatchewan.ca/residents/health/prescription-drug-plans-and-health-coverage.

Health Canada. 2022a. Regulatory roadmap for biologic (Schedule D) drugs in Canada. https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/regulatory-roadmap-for-biologic-drugs.html.

Health Canada. 2022b. Biologic and radiopharmaceutical drugs directorate. https://www.canada.ca/en/health-canada/corporate/about-health-canada/branches-agencies/health-products-food-branch/biologic-radiopharmaceutical-drugs-directorate.html.

Health Canada. 2022c. Guidance document: information and submission requirements for biosimilar biologic drugs. https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/information-submission-requirements-biosimilar-biologic-drugs-1.html.

Joint Health Express 2022. Saskatchewan launches biosimilars initiative for Saskatchewan drug plan. https://jointhealth.org/programs-jhexpress-view.cfm?id=2708&locale=en-CA.

Lasala R, Abrate P, Zovi A, Santoleri F. 2023. Safety and effectiveness of multiple switching between originators and biosimilars: literature review and status report on interchangeability. *Therapeutic Innovation & Regulatory Science* 57: 352-364. https://doi.org/10.1007/s43441-022-00473-2.

Mansell K, Bhimji H, Eurich D, Mansell H. 2019. Potential cost-savings from the use of biosimilars filgrastim, infliximab, and insulin glargine in Canada: a retrospective analysis. *BMC Health Services Research* 19: 827. https://doi.org/10.1186/s12913-019-4680-2.

McClean AR, Law MR, Harrison M, Bansback N, Gomes T, Tadrous M. 2022. Uptake of biosimilar drugs in Canada: analysis of provincial policies and usage data. *CMAJ* 194(15): E556-E560. https://doi.org/10.1503/cmaj.211478.

Noce AL and Ernst M. 2018. Switching from reference to biosimilar products: an overview of the European approach and real-world experience so far. *European Medical Journal* 3(3): 74-81. https://doi.org/10.33590/emj/10313082.

Patented Medicine Prices Review Board. 2020. Biologics in Canada part 2: biosimilar savings, 2018. https://www.canada.ca/content/dam/pmprb-cepmb/documents/reports-and-studies/chartbooks/biologics-part2-biosimilar-savings2018.pdf.

Patented Medicine Prices Review Board. 2023. Annual public drug plan expenditure report 2021-2022. https://www.canada.ca/content/dam/pmprb-cepmb/documents/npduis/analytical-studies/compassrx-9th-edition/NPDUIS-CompassRx9th-2021-2022_en.pdf.

Patterson D. 2023. Some patients concerned as change to medications in Sask. drug plan approaches. CBC News. https://www.cbc.ca/news/canada/saskatoon/biologic-pharmaceutical-drugs-medications-biosimilars-patients-1.6721293.

Rome, BN and Sarpatwari A. 2021. Promoting biosimilar competition by revising Medicare

reimbursement rules. *JAMA Network Open* 4(11): e2134463. https://doi.org/10.1001/jamanetworkopen.2021.34463.

Troein P, Newton M, Scott K. 2020. The impact of biosimilar competition in Europe. IQVIA white paper. https://health.ec.europa.eu/system/files/2021-01/biosimilar_competition_en_0.pdf.

Vogler S, Schneider P, Zuba M, Busse R, Panteli D. 2021. Policies to encourage the use of biosimilars in European countries and their potential impact on pharmaceutical expenditure. *Frontiers in Pharmacology* 12:625296. https://doi.org/10.3389/fphar.2021.625296.