# Pan-Canadian Oncology Biosimilars Initiative

## Action Plan

### March 2019

pCPA pan-Canadian Pharmaceutical Alliance

APP Alliance pancanadienne pharmaceutique

Ontario Cancer Care Ontario

# I. Abbreviations & Common Terms

**Biologic Medication (or Biologic)** – is a complex protein molecule created inside living cells with biotechnology. Biologics are used to treat diseases and medical conditions including cancer.

**Biosimilar** – is a drug demonstrated to be highly similar to a biologic drug that was already authorized for sale (known as the reference biologic drug). Biosimilars are approved based on a thorough comparison to a reference drug and may enter the market after the expiry of reference drug patents and data protection.

**Equivalence –** is the absence of a significant difference in the rate and extent to which the active ingredient in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of action when administered at the same dose under similar conditions in an appropriately designed study.

**Generalizability (or Extrapolation)** – is often used to refer to the authorization of a biosimilar for indications where clinical studies were not done.

**Jurisdiction** – refers to public drug plans from British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Québec, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland & Labrador, Yukon Territory, Northwest Territories, Nunavut, and Federal Drug Plans.

**OECD –** Organization for Economic Cooperation and Development is a forum of 36 member countries that helps governments foster prosperity and fight poverty through economic growth and financial stability.

**pCPA –** Established in August 2010, the pan-Canadian Pharmaceutical Alliance (pCPA) conducts joint provincial/territorial/federal negotiations for brand name and generic drugs in Canada to achieve greater value for publicly funded drug programs and patients through the use of the combined negotiating power of participating jurisdictions. The pCPA member jurisdictions include public drug plan and/or cancer agency participation from: British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Québec, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland & Labrador, Yukon, Northwest Territories, Nunavut, Non-Insured Health Benefits (NIHB), Correctional Services of Canada (CSC) and Veterans Affairs Canada (VAC).

**Reference Biologic** – is the original biologic product to which a biosimilar refers to in its application for marketing approval.

**Switching** – generally refers to a one-time change from a reference biologic drug to a biosimilar but can also refer to a change from a biosimilar to a reference biologic or another biosimilar.

# II. Introduction

The pan-Canadian Oncology Biosimilars Action Plan provides a high-level map for the implementation of therapeutic oncology biosimilar medications (biosimilars) in Canada. It has been informed by proceedings at the pan-Canadian Oncology Biosimilars Summit which was hosted by the pan-Canadian Pharmaceutical Alliance (pCPA) and Cancer Care Ontario (CCO). The summit took place in Toronto on November 16, 2018 and brought together patients, patient advocacy organizations, clinicians, healthcare administrators and government officials from nine provinces to discuss the opportunities and challenges of introducing therapeutic oncology biosimilars in Canada. This plan builds on the Summit and outlines the vision, goals, strategic objectives and implementation steps that will support the adoption of therapeutic oncology biosimilars in Canada.

Biologic medications (biologics) are complex protein molecules created inside living cells. Biologics have become mainstays in the treatment of many types of cancer, including breast, gastrointestinal, lung, ovarian and other cancers. Patents protect innovative biologics for a limited amount of time. In Canada, patents for some biologics are expiring and highly similar medications, known as biosimilars, are being developed. A biosimilar that is approved by Health Canada is not necessarily identical to its reference biologic, but based on guidelines and approval standards for the pharmacokinetics, pharmacodynamics, safety and clinical efficacy of biologics[1,2,3] the two are highly similar.

In 2016, biologics were the largest driver of drug spending growth, accounting for 15.9% of Canadian drug sales, or over $3.6 billion[4]. The expected arrival of therapeutic oncology biosimilars in Canada offers the potential to bring significant savings to provincial cancer expenditures, as biosimilars in other therapeutic areas are priced up to 47% lower than their reference biologic product[4].

A variety of approaches have been used to promote uptake of biosimilars worldwide, with different degrees of price reduction and market uptake observed. Compared to many Organization for Economic Co-operation and Development (OECD) countries, Canada is significantly behind in terms of adopting biosimilars (e.g., the adoption rate for biosimilar infliximab was 1% in Canada in 2016[5] vs. 82% in Norway and 90% in Denmark in 2015[6]). This suggests that payer policies need to be carefully considered to optimize use and drive overall savings. Canadian provincial cancer systems differ in their policy, reimbursement and delivery environments in ways that may affect approaches to implementing therapeutic oncology

[1] Health Canada. (2016, December 2). *Guidance Document: Information and Submission Requirements for Biosimilar Biologic Drugs*. Retrieved from 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.html
[2] Health Canada. (2017, August 3). *Fact Sheet: Biosimilars*. Retrieved from https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html
[3] ICH Expert Working Group. (2004). *ICH Harmonised Tripartite Guideline: Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process Q5E*.
[4] Patented Medicine Prices Review Board. (2018, February 5). *Potential Savings from Biosimilars in Canada*. Retrieved from http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1304
[5] Patented Medicines Prices Review Board. (2017, April). *Potential Savings from Biosimilars in Canada*. Retrieved from https://www.cadth.ca/sites/default/files/symp-2017/presentations/april24-2017/Concurrent-Session-B4-Gary-Warwick.pdf
[6] OECD. (2017). *Health at a Glance 2017: OECD Indicators*. Paris: OECD Publishing. Retrieved from http://dx.doi.org/10.1787/health_glance-2017-en

biosimilars. However, harmonized decision-making across jurisdictions should positively impact the emerging biosimilars market in Canada.

The pCPA's recently published "Biologics Policy Directions & pCPA Negotiations" document aims to develop and pilot a clear and consistent pan-Canadian approach that encourages appropriate use of biologics (both innovators and biosimilars) in support of a common pCPA mandate to enhance patient access to clinically relevant and cost-effective drug treatment options. The document applies to all biosimilars, non-oncology and oncology, and its objectives are to:

- Encourage a harmonized approach to policies and review processes for biologics across all key stakeholders in Canada.
- Achieve the reduction of costs and to maximize access to effective treatments for Canadians.
- Increase awareness and confidence in the use of biosimilars through clinical evidence, education, and support for prescribers and patients.
- Promote appropriate uptake of biosimilars to enhance patient care and support drug plan sustainability.
- Facilitate post-market evaluation and monitoring of biologics in support of optimal use.

The pCPA and CCO have partnered to lead a pan-Canadian strategy with the goal of ensuring appropriate implementation and cost-effective use of therapeutic oncology biosimilars across the country. The development a cancer-specific strategy provides an opportunity to drive the acceptance and use of therapeutic oncology biosimilars while considering the different environments in which biologics are used to treat cancer. To move this work forward, the pCPA and CCO have assembled an Oncology Biosimilars Initiative Team to develop an implementation strategy. This Action Plan provides an overview of the anticipated pre-implementation steps to ensure the successful adoption of oncology biosimilars. At this time, there are three therapeutic oncology biosimilars that are expected on the Canadian market over the next few years: bevacizumab (Reference product: Avastin), trastuzumab (Reference product: Herceptin) and rituximab (Reference product: Rituxan).

# III. Vision

Stakeholders across Canada have implemented an oncology biosimilars strategy that improves outcomes for patients, is evidence-informed, ensures appropriate quality and safety measures are in place, and facilitates access to innovative cancer treatments.

# IV. Goals

Stakeholder Engagement

- Collaborate with stakeholders so they participate in the development of a pan-Canadian oncology biosimilars strategy.

Quality & Safety

- Ensure that oncology biosimilars are safely implemented and that clinical and patient considerations are taken into account.

Evidence-informed Policy Approach

- Engage pan-Canadian partners to discuss pricing, implementation and usage strategies that are informed by the best practices[7].

Sustainability & Value for Money

- Improve system sustainability and performance by facilitating the uptake of oncology biosimilars and ensuring stakeholders are benefiting from the transition.

# V. Strategic Objectives

1. **Engage stakeholders throughout the project to validate and inform ongoing work.** *Important considerations:* Stakeholders should be engaged throughout the planning and implementation process. Stakeholder working groups will be created to provide advice and guidance for the implementation of oncology biosimilars.

2. **Adopt best practices and standardized approaches to prescribing, storing, preparing, labelling, dispensing, and administering oncology biosimilars. This requires addressing technical[8] and logistical[9] challenges of implementation.** *Important considerations:* A system-wide change management plan with clear communication strategies should be developed to promote consistency across jurisdictions.

[7] Best practices seen in other jurisdictions (UK/Europe) who publicly fund multiple therapeutic oncology biosimilars
[8] E.g. CPOE/EMR, smart pumps, pharmacy preparation and dispensing, and medication administration recording
[9] Logistical considerations should also consider advanced warning for funding, standardized change management processes, policies, and procedures in advance of going live.

Stakeholders need to consider the impact on pharmacy and clinical operations, the system's capacity for this change, and the resources required to manage workload and safety issues.

3. **Develop comprehensive education programs for health professionals and patients.**
   *Important considerations:* Educational resources should be tailored to the target audience, focused on safety and efficacy, and rolled out before biosimilars implementation. It should be accessible, language appropriate and provided in various modalities. Patient advocacy organizations and clinicians were identified as trusted sources of information for patients. Furthermore, patients want to be assured that they will be monitored and that a long-term monitoring strategy will be in place.

4. **Support the overall intent of creating a viable market for oncology biosimilars by developing reimbursement strategies that promote implementation across Canada.**
   *Important considerations:* The market should allow for multiple biosimilars which may or may not include the reference biologic medication. It was felt that a guaranteed market share for manufacturers will incentivize them to enter and stay on the market. This allows jurisdictions to ensure a viable supply chain in case of drug shortages, supply interruptions or unexpected toxicities.

5. **Develop clear guidance on clinical scenarios such as initiating, switching and generalizability.**
   *Important considerations:* There should be the option to switch a patient to other biosimilar alternatives or the reference biologic medication in case of adverse reactions. Clinician education is important; patients are more at ease if their prescriber is knowledgeable and confident about a biosimilar treatment plan.

6. **Reinvest savings from oncology biosimilars back into the cancer system[10], with the objective of optimizing health outcomes.**
   *Important considerations:* The savings offered by biosimilars should be reinvested into the cancer system (e.g., cancer drugs, staffing resources, technologies, cancer prevention strategies). Performance metrics should be developed to quantify and evaluate the system improvements achieved from biosimilar savings (e.g., incremental new therapies funded and patients treated). Cost savings could also be invested to directly support Strategic Objective 7, real-world evidence (RWE). The creation of a prioritization framework should help determine how to reallocate savings.

[10] Cancer system is defined to include drugs, resources (e.g. staff), technologies (e.g. PET), cancer prevention strategies

7. **Develop an evaluation and monitoring plan that includes the collection and generation of real-world evidence (RWE).**
   *Important considerations:* Real-world data should be collected to assess utilization, safety, and effectiveness of therapeutic oncology biosimilars. Consideration should be given to collecting baseline data on the biologic innovator product prior to the introduction of its biosimilar to most effectively compare the biosimilar and biologic innovator products. Additionally, patient-reported outcomes (related to switching, sequencing, downstream impact etc.) and the net value of biosimilar adoption (cost savings vs. cost of adoption) should be assessed.

# VI. Implementation

## PRE-LAUNCH

**1. Horizon Scanning [2018, on-going]**
Watch market for new biosimilars to ensure that jurisdictions have sufficient time to complete pre-implementation steps before adopting a new biosimilar. Invite biosimilar manufacturers to share expected product launch dates. As noted above, bevacizumab and trastuzumab biosimilars are expected to be launched in late 2019, and rituximab is expected in early 2020.

**2. Stakeholder Engagement [January 2019, on-going]**
Engage stakeholders within the following priority areas as described in the strategic objectives:

- Education
- Clinical Operations
- Clinical Guidance
- Reimbursement
- Evaluation
- Reinvestment

Engage cancer agency and ministry of health (MOH) leaders to help identify participants for two working groups: Education and Clinical Operations. These working groups will be interdisciplinary and will seek representation from all jurisdictions.

For the remaining priority areas: Clinical Guidance, Reimbursement, Evaluation and Reinvestment, existing pan-Canadian committees and cancer agency leaders from across the country will be engaged to provide advice and guidance on implementation decisions specific to these areas.

Patients and patient advocates will be engaged through representation on the Education Working Group and existing pan-Canadian expert committees. Other relevant stakeholder groups such as manufacturers, group purchasing organizations, and clinician professional associations will be engaged through other engagement mechanisms which will be defined more clearly as implementation carries forward.

### 3. Education Working Group [February 2019, on-going]

The Education Working Group will provide input, share advice, and vet biosimilar educational resources that will be develop specifically for clinicians (medical oncologists, pharmacists, and nurses) and patients. These resources will be designed to meet their needs and address educational gaps. The working group will seek opportunities to collaborate with patient advocacy organizations and clinical champions to co-create these resources. The major deliverables for this working group include:

- Providing input and vetting educational resources in various modalities including print, online and peer-to-peer teaching (in-person).
- Endorsing standardized content and language for all educational resources to prevent patients receiving contradictory information from different sources. Also, information must align with messaging from relevant patient advocacy organizations.

### 4. Clinical Operations Working Group [February-August, 2019]

The Clinical Operations Working Group will evaluate the service impact and anticipated challenges of implementing biosimilars in the oncology clinic. This working group work will support the transitioning of cancer systems to the routine use of biosimilars, addressing key pharmacy operational issues. The major deliverables for this working group include:

- Providing guidance for developing a system-wide change management plan that mitigates risk and promotes consistency across jurisdictions. The plan will address pharmacy-led operations including prescribing, storing, preparing, labelling, dispensing, administering, and unexpected side-effect monitoring/reporting.
- Championing the work at the local level within respective jurisdictions.
- Discussing solutions to ensure that the brand of the administered biologic can be traced to the individual patient. This will ensure that any outcomes can be attributed to the correct biologic product and will help inform Evaluation (9).

### 5. Clinical Guidance [January-March, 2019]

Engage existing expert committees to discuss and advise on the following clinical scenarios:

- Initiating
- Switching
- Generalizability

Advice from these committees will help inform decisions at the jurisdictional level regarding the scenarios listed above. While there are differences in the organization and delivery of cancer services across Canada, consistent policies and approaches will be sought. This priority area will inform work in other priority areas, particularly Education (3), Clinical Operations (4) and Reimbursement (6).

### 6. Reimbursement [April-July, 2019]

As public reimbursement models differ across jurisdictions, cancer agency leaders and ministry of health representatives will be engaged to promote reimbursement strategies that support the vision and goals outlined here. Reimbursement strategies will be informed by decisions made for Clinical Guidance (5), pricing and market share.

Pricing

The pCPA will negotiate pricing for therapeutic oncology biosimilars to enhance patient access and support drug plan sustainability. Considering the varied pricing approaches used by hospitals and cancer agencies, pCPA is committed to a clear, consistent negotiation process and has established guidelines for how biologics and biosimilars will be negotiated. These guidelines were informed by pCPA's First Principles, a set of principles to support a national approach towards negotiations:

- Commitment to a national pCPA negotiation process
- Decisions informed by evidence
- Foster a competitive biologics market supporting long term cost reductions and sustainability
- Lower transparent pricing
- Pursuit of optimal value from all industry stakeholders

The Action plan will support pCPA negotiations through:

- Clinician and patient education to increase awareness and comfort with the use of biosimilars (Education)
- Mobilizing clinical experts to discuss and advise on approaches to initiating, switching, generalizability etc. across jurisdictions (Clinical Guidance)
- Engaging pan-Canadian stakeholders to develop guidance on clinical operations and reimbursement strategies to implement biosimilars. Guidance will be informed by best practices with the aim of supporting consistency across jurisdictions (Clinical Operations & Reimbursement).

With regards to economic considerations, the pCPA will serve as a platform for discussion and decision on market share for biosimilars and/or reference biologics in Canada.

### 7. Status Updates [January 2019, on-going]

Deliver status reports to identified advisory committees and stakeholder groups to keep them informed.

## LAUNCH

### 8. Biosimilars Implementation [currently anticipated for Q3, 2019]

Bevacizumab and trastuzumab biosimilars are expected to be launched in Q3, 2019. The exact date of a biosimilar being publicly funded and delivered in a hospital or cancer centre will depend on multiple variables including pricing, reimbursement decisions, product availability, clinical decisions and clinical-operation readiness. This Action Plan aims to address and coordinate these variables to facilitate the effective implementation of bevacizumab and trastuzumab biosimilars. Approximate timelines will become clearer as implementation deliverables are carried out.

## POST-LAUNCH

### 9. Evaluation

The rate of uptake, utilization and budget impact for publicly funded biosimilars will be assessed periodically to track usage and financial outcomes. Depending on the availability of resources, evaluation could include a data collection infrastructure which could examine outcomes meaningful to stakeholders (e.g., patient-reported outcomes) and develop real-world evidence to assess benefit. Ideally, an evaluative infrastructure would involve collaboration between jurisdictions and would answer questions that would be relevant to all jurisdictions

### 10. Reinvestment

The reinvestment of cost savings from the use of biosimilars is at the discretion of each jurisdiction and they will ultimately decide how funds are used to optimize health outcomes. However, stakeholders consulted to date have strongly supported reinvestment in the cancer system as a priority.

# VII. Biosimilars Implementation Timeline