CADTH

CADTH's Proposed Revisions to the Biosimilar Review Process for its Common Drug Review and pan-Canadian Oncology Drug Review Programs

1. Proposal Objectives

CADTH is proposing revisions to the submission process for biosimilars through its Common Drug Review (CDR) and the pan-Canadian Oncology Drug Review (pCODR) programs that would reduce duplication of work, optimize resources, and ensure that all participating jurisdictions benefit from a single approach to evidence review that would facilitate decision-making and keep with CADTH's value of excellence. The proposed process would enable CADTH to support the review of biosimilars by providing a centralized coordinating role working in collaboration with Health Canada, the pan-Canadian Pharmaceutical Alliance, and the participating federal, provincial and territorial public drug plans (with the exception of Quebec) and provincial cancer agencies to support improved access for patients for these products.

2. Background

Biologic drugs come from living organisms or from their cells, and are often made using biotechnology. They are used to treat diseases and medical conditions including anemia, diabetes, inflammatory bowel disease, psoriasis, rheumatoid arthritis, hormone deficiency, and some forms of cancer. A biosimilar biologic drug, or biosimilar, is a drug demonstrated to be highly similar to a biologic drug (known as the reference biologic drug) that was already authorized for sale by regulatory bodies (i.e., Health Canada). Biosimilars are approved based on a thorough comparison to a reference drug and may enter the market after the expiry of reference biologic drug patents and data protection.[1-3]

The regulators in Canada and in international jurisdictions follow similar scientific principles in the authorization of biosimilars. Regulators require extensive comparative data to assess the quality of the biosimilar, including comparative structural and functional studies. The amount of residual uncertainty in the similarity of the biosimilar to the reference product determines the amount of non-clinical and clinical comparative data required.

For a biosimilar review, Health Canada evaluates the information provided by the manufacturer of the biosimilar to confirm that the biosimilar and the reference biologic drug are similar and that there are no clinically meaningful differences in safety and efficacy between the biosimilar and reference drug. The regulatory approval of a biosimilar drug relies in part on prior information regarding safety, efficacy, and effectiveness that is deemed relevant due to the demonstration of similarity to the reference biologic drug and which influences the amount and type of original data required.[4]

Health Canada may authorize a biosimilar for use in more than one indication because of the rigorous demonstration of similarity between the biosimilar and the reference biologic drug. Since a biosimilar is very similar in structure and function to a reference biologic drug with well-established safety and efficacy, in many cases clinical studies do not need to be repeated for each indication.[4]

CADTH examined the different review processes in a select number of international jurisdictions to help inform on how biosimilar reviews could be carried out in Canada. Information gathered from international jurisdictions including the UK, Scotland, and Australia reveals that the process for reviewing biosimilars through health technology assessment appears to vary among the jurisdictions; however, each of the aforementioned jurisdictions have taken a streamlined approach to biosimilar reviews.

In reflecting the international approach on the assessment of biosimilars and given that the health technology assessment recommendations rely on the totality of comparative evidence between the biosimilar and its reference biologic product that has been rigorously reviewed by Health Canada, CADTH is proposing to revise the review process for biosimilars.

3. Highlights of Proposed Changes

Overview of Proposed Revisions to the Biosimilar Review Process

In developing a more streamlined approach, it is proposed that the submitter would complete the designated sections of the proposed *Biosimilar Summary Dossier Template* outlining the details of the reimbursement request along with key clinical and economic information. CADTH review teams would provide commentaries and analyses on designated sections of the template and work closely with Health Canada to include a summary of the market authorization of the biosimilar under review. It is proposed that the Biosimilar Summary Dossier will not be brought forward to CADTH's Canadian Drug Expert Committee (CDEC) or pCODR Expert Review Committee (pERC). However, CADTH reserves the right to request a full submission in limited cases.

To ensure timely reviews, submitters are encouraged to file to CADTH shortly after making a submission to Health Canada if submitters are looking to pursue public reimbursement of the biosimilar. A submitter making a submission for a biosimilar drug will be required to complete and file the proposed *Biosimilar Summary Dossier Template* along with their submission package, which will be reviewed by CDR and pCODR clinical and economic reviewers to become the publicly available Biosimilar Summary Dossier. The proposed *Biosimilar Summary Dossier Template* is an abbreviated version of the current biosimilar submission template, and the proposed submission requirements are fewer than the current requirements. To ensure that the CADTH drug review processes are transparent and accountable, CADTH considers it essential that any information provided in the template to support the biosimilar submission is fully disclosable.

As part of the proposed template, CADTH will coordinate with Health Canada to complete *Section 3: Health Canada's Assessment of [Biosimilar] for Market Authorization* within the *Biosimilar Summary Dossier Template.* This coordination is to reduce the duplication of work and support the timely completion of this summary. In addition to this summary, it is proposed that CADTH CDR and pCODR reviewers will provide an appraisal of the clinical evidence provided by the submitter that assesses the clinical efficacy and safety of patients transitioning to the biosimilar from the reference product or other relevant drugs, as well as an appraisal of the economic submission. It is proposed that the Biosimilar Summary Dossier will be made publicly available on the CADTH website.

Below are the key conceptual elements of the proposed revised process for biosimilars:

Submission Requirements	In order to reduce duplication of efforts and resources, CADTH is proposing a modified submission package for biosimilars. It is proposed that a submitter would be required to file the following information: • Completed *Biosimilar Summary Dossier Template* (only certain sections would need to be completed by the submitter) • Other procedural requirements that are set out in the CDR and pCODR procedures will apply to a biosimilar submission; these include: ○ pre-submission notification requirements ○ signed cover letter confirming that all the required information has been provided ○ letter authorizing sharing of information ○ list of published and unpublished studies, including any non-randomized observational studies to support switching ○ copy of the Notice of Compliance (NOC) or NOC With Conditions (NOC/c), dated and signed by Health Canada ○ product monograph ○ drug benefit listing table.
Stakeholder Participation	Insights, perspectives, and experiences from stakeholders (submitter, patient groups, registered clinicians, Formulary Working Group and Provincial Advisory Group) are integral to the process. CADTH wants to ensure that stakeholders' perspectives and experiences with biosimilars are considered as part of this revised process, and have outlined the following options for comment: • continue with the use of the current template (i.e., for patient groups and registered clinicians) for each biosimilar review • respond to questions that address issues specific to the biosimilar under review • provide feedback on a draft CADTH Biosimilar Summary Dossier • contribute to a report on broader (or more general) expectations and concerns that could be used for biosimilar therapeutic class reviews rather than individual single biosimilar reviews.
CADTH Appraisal	It is proposed that CADTH would support the timely review of biosimilars by providing a centralized coordinating role, working in collaboration with Health Canada and other partners to reduce duplication of work. CADTH CDR and pCODR reviewers will provide an appraisal of the clinical evidence provided by the submitter that assesses the clinical efficacy and safety of patients transitioning to the biosimilar from the reference product or other relevant drugs, as well as an appraisal of the economic submission.
Transparency	As part of CADTH's commitment to transparency, the Biosimilar Summary

	Dossier will be posted on the CADTH website. In working closely with Health Canada to coordinate the information, it is anticipated that the review timelines for biosimilars will be reduced, and thereby, ensuring more timely access for patients.

Please submit your written comments via email at feedback@cadth.ca by using this **feedback template** by **September 15, 2017 at 5:00 p.m. ET**. All feedback submitted by the deadline will be carefully considered and used to inform the proposed changes to CADTH's CDR and pCODR processes for biosimilar reviews. We thank you in advance for your interest.

References

1. Fact sheet: biosimilars [Internet]. Ottawa: Health Canada; 2016 Nov. [cited 2017 Jul 28]. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html

2. Biosimilar drugs [Internet]. Ottawa: CADTH; 2017 Nov. [cited 2017 Jul 28]. Available from: https://cadth.ca/sites/default/files/pdf/biosimilar_drugs_professional_en.pdf

3. Biosimilar drugs: your questions answered [Internet]. Ottawa: CADTH; 2017 Nov. [cited 2017 Jul 28]. Available from: https://cadth.ca/sites/default/files/pdf/biosimilar_drugs_patient_en.pdf

4. Guidance document: information and submission requirements for biosimilar biologic drugs [Internet]. Ottawa: Health Canada; 2016 Nov. [cited 2017 Jul 28]. Available 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-1.html