CADTH's Proposed Reassessment Framework

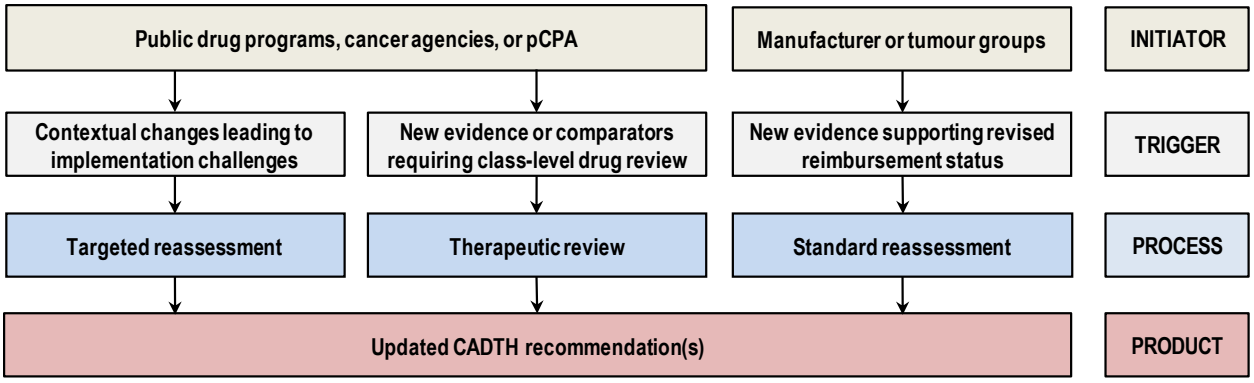
1. Proposal Objective

There is currently no standardized pan-Canadian process for monitoring and re-evaluating drugs in Canada once they have been funded. Establishing guidelines and processes for the reassessment of drugs is a key objective of CADTH's 2018-2021 Strategic Plan.

CADTH is seeking to leverage its current review processes to establish a framework that will facilitate the reassessment of drug products in Canada. As shown in Figure 1, CADTH believes that multiple approaches will be required to ensure that the reassessment of drugs is both effective and efficient. The proposed reassessment processes developed by CADTH will build upon the best practices of the existing pathways currently being used in the pharmaceutical review processes.

This document summarizes CADTH's proposed reassessment framework for the purposes of stakeholder consultation.

Figure 1: CADTH's Pharmaceutical Reassessment Processes



pCPA = pan-Canadian Pharmaceutical Alliance.

2. Potential Triggers for Reassessment

Reassessments could be carried out in response to a variety of potential triggers (Table 1), including:

- actions by regulatory and reimbursement authorities
- the availability of new evidence or new comparators leading to questions about the comparative clinical/cost-effectiveness
- changes in contextual factors resulting in implementation challenges.

While not in scope for the current reassessment framework, potential triggers that could be included in future iterations of the reassessment framework could be reassessments mandated as a condition tied to an outcomes-based reimbursement agreement.

Table 1: Potential Triggers for Reassessment

Trigger	Details
Regulatory activity	• Patent expiration/pending approval of generic formulations • Revised indications (e.g., changes that could alter coverage but wouldn't require a full submission) • Conversion from NOC/c to NOC (if specified as a concern in the initial review)
Reimbursement activity	• Expiration of reimbursement agreement • Required component of funding arrangement • Utilization issues (e.g., perceived overuse) • Uncertain or potentially high budget impact • Manufacturer proposes changes to existing reimbursement criteria
Questions about clinical/cost-effectiveness	• Emergence of new comparators • Completion of longer-term clinical studies • Availability of new clinical data (e.g., new RCTs or RWE studies) • Uncertainty of the magnitude of benefit
Contextual changes	• Clinical practice considerations (new Canadian guidelines that do not align with CADTH recommendation; additional therapies entering the same space, which alters the treatment algorithm)

NOC = Notice of Compliance; NOC/c = notice of compliance with conditions; RCTs = randomized controlled trials; RWE = real-world evidence.

3. Type of Reassessments Conducted

Table provides a summary of the different types of reassessments that will be conducted by CADTH. CADTH will conduct reassessments using the most efficient process that can effectively evaluate the questions raised in the request for reassessment.

- A **standard reassessment process** will be used to address questions related to comparative clinical benefit and/or cost-effectiveness of a single drug. This new reassessment process would replace the existing resubmission process for drugs that are currently reimbursed by the public drug plans.

- A **targeted reassessment process** will be used to address questions related to changes in contextual factors that may affect the ability of the participating jurisdictions to implement existing Canadian Drug Expert Committee (CDEC) or pan-Canadian Oncology Drug Review (pCODR)

Expert Review Committee (pERC) recommendations. Contextual information can include items such as regulatory actions, changes in clinical practice, or other forms of information that have introduced implementation questions or challenges for the jurisdictions. This new process would replace and build upon CADTH's existing request for advice process.

- The existing **therapeutic review process** will be used for questions regarding the comparative safety, clinical effectiveness, and cost-effectiveness of multiple drugs.

Table 2: Overview of CADTH's Reassessment Process

CADTH Process	Basis for Reassessment	CADTH Output	Eligible Requestors	Typical Timelines
Standard Reassessment	• Uncertainty regarding safety, clinical effectiveness, and cost-effectiveness of a single drug	• Updated CDEC/pERC recommendation • Clinical and economic review reports • Patient group input	• Manufacturers • Tumour groups • Participating drug plans and cancer agencies	• ≤180 calendar days
Targeted Reassessment	• Changes in contextual information that may affect the ability to implement existing CDEC or pERC recommendations	• Updated CDEC/pERC recommendation • Reassessment review report(s) • Patient group input	• Participating drug plans and cancer agencies • pCPA	• 90 to 150 calendar days
Therapeutic Review	• Uncertainty regarding the comparative safety, clinical effectiveness, and/or cost-effectiveness of multiple drugs	• Therapeutic review recommendations • Updated CDEC recommendations (if required) • Patient group input • Clinical and economic review reports	• Participating drug plans and cancer agencies • pCPA	• 12 months

CDEC = Canadian Drug Expert Committee; pCPA = pan-Canadian Pharmaceutical Alliance; pERC = pan-Canadian Oncology Drug Review Expert Review Committee.

4. Eligibility for Reassessment

4.1 Product Eligibility

Any drug that is currently reimbursed in the Canadian public health care system could be eligible for a reassessment through one of CADTH's processes.

4.2 Eligibility for a Standard Reassessment

- The standard reassessment process is used when there is uncertainty regarding the comparative safety, clinical effectiveness, and/or cost-effectiveness of a single drug.

- The standard reassessment process requires the manufacturer or tumour groups to file new clinical and/or economic information with CADTH.

- Manufacturers can initiate the standard reassessment process in a proactive or reactive manner.
    - **Proactive reassessments** can be initiated by manufacturers that are interested in pursuing revisions to any of the conditions associated with a previous CDEC or pERC recommendation, provided they have new evidence that can support the revisions.
    - **Reactive reassessments** can be initiated by manufacturers that have received a formal request for reassessment from CADTH on behalf of the participating jurisdictions.
- Similar to CADTH's resubmission process, applicants that wish to proactively have a drug considered through the standard reassessment process will be required to submit an application form and copies of one or more new studies that support the requested revisions to the reimbursement criteria for the drug.
- CADTH will assess the information provided by the applicant using the same approach that is currently used for resubmissions and will confirm eligibility with the manufacturer.
- After receiving confirmation from CADTH that the proposed reassessment is eligible for review through the CDR or pCODR processes, applicants would be required to provide CADTH with advance notification for the pending reassessment in accordance with CDR and pCODR procedures.

4.3 Eligibility for a Targeted Reassessment

- CADTH will typically apply the targeted reassessment process when jurisdictions or the pCPA raise issues regarding changes in contextual information that affect their ability to implement existing CDEC or pERC recommendations.
- To initiate the targeted reassessment process, CADTH must receive a formal request from the participating jurisdictions or pCPA that provides a clear description of the issues that are of interest to the jurisdictions.

4.4 Eligibility for a Therapeutic Review

- The topic selection process for a therapeutic review is described in detail in the *CADTH Therapeutic Review Framework and Process.*

5 Pre-Submission Procedures

5.1 Pre-submission Meetings

- Standard reassessments will be eligible for a pre-submission meeting with CADTH, provided the eligibility has been assessed and confirmed by CADTH.

5.2 Advance Notification

- CADTH will apply the existing advance notification procedures that are used in the CDR and pCODR processes.

6 Stakeholder Engagement

6.1 Patient Engagement

- The call for patient input will be posted 20 business days in advance of the anticipated filing date (as provided in the advance notification form) for a standard reassessment and on the same day the request is received by CADTH for a targeted reassessment. All other aspects of the patient input processes will be conducted in accordance with existing CDR and pCODR procedures.

- Patient engagement opportunities during a therapeutic review are described in detail in the *CADTH Therapeutic Review Framework and Process*.

6.2 Clinician Engagement

- Clinician engagement for reassessments will occur in accordance with CADTH's existing procedures for the CDR and pCODR processes.

6.3 Drug Plan Engagement

- Drug plan engagement for reassessments will occur in accordance with CADTH's existing procedures for the CDR and pCODR processes.

7 Initiating Reassessments

- Standard and targeted reassessments will be screened and initiated in accordance with the existing procedures for resubmissions and requests for advice, respectively, as described in the *Procedure and Submission Guidelines for the CADTH Common Drug Review* and *pCODR Procedures*.

- Therapeutic reviews will continue to be initiated in accordance with the *CADTH Therapeutic Review Framework and Process*.

8 Reassessment Review Procedures

8.1 Standard Reassessment Process

- Standard reassessments will typically be conducted in accordance with CADTH's existing CDR and pCODR processes for standard reviews and resubmissions based on new clinical and economic information.

- CADTH will prepare clinical and economic review reports in accordance the current descriptions in the *Procedure and Submission Guidelines for the CADTH Common Drug Review* and *pCODR Procedures*. This will involve opportunities for manufacturer comment in the CDR process and a checkpoint meeting in the pCODR process.

8.2 Targeted Reassessment Process

- Targeted reassessments will typically be conducted in accordance with CADTH's existing CDR and pCODR processes for requests for advice.
- CADTH will prepare a reassessment report in accordance with the current description in the *Procedure and Submission Guidelines for the CADTH Common Drug Review* and *pCODR Procedures*. This will involve opportunities for manufacturer comment in the CDR process.

8.3 Therapeutic Review Process

- As stated in the *CADTH Therapeutic Review Framework and Process* and the *Procedure and Submission Guidelines for the CADTH Common Drug Review*, one of the outputs from a CADTH therapeutic review may be revised CDEC or CEDAC recommendations for drugs that have previously been reviewed through the CDR process.
- The processes used by CADTH to conduct reassessments through the therapeutic review process are detailed in the aforementioned documents.

9 Recommendation Process

- The output of CADTH's standard and targeted reassessment process would be a revised or updated recommendation from CDEC or pERC. In the case of a CADTH therapeutic review, one of the outputs may be revised recommendations for drugs that have previously been reviewed through the CDR or pCODR processes.
- When issuing reassessment recommendations, CADTH's expert review committees will apply the existing recommendation framework that is described in the *Procedure and Submission Guidelines for the CADTH Common Drug Review* and *pCODR Procedures*.
- The recommendation document would include standardized disclaimers, indicating that the new recommendation supersedes the previous recommendation that was issued at the conclusion of the initial CADTH review of the drug.
- The outcome of the standard and targeted reassessment processes will be an updated CDEC or pERC recommendation document, regardless of whether or not the expert review committee concludes that the existing recommendation should be upheld or revised as a result of the reassessment.

10 Implementation of Reassessment Recommendations

- Following the issuance of an updated recommendation from CADTH, there are several potential outcomes that may arise from the reassessment process (Table 3).
- CADTH will seek to develop strategies to monitor the impact and uptake of any recommendations resulting from reassessments.

Table 3: Potential Implications of CADTH Reassessment

Category	Examples
No changes	• Confirmation of existing reimbursement conditions • Validation of assumptions that were used to estimate cost-effectiveness
Renegotiation	• Revised reimbursement conditions • Renegotiation of effective price(s)
Changing scope of use	• Narrowing the scope to a more restricted population • Expanding the scope to include additional subpopulations
Sequencing of drugs	• Establishing lines of therapy for drugs that are indicated for a particular condition • Preferential placement of certain drugs within a sequence
Disinvestment	• Delisting one or more products that are currently listed by the public drug programs

11 Submission Requirements for Reassessments

11.1 Standard Reassessment Process

- The proposed submission requirements for a standard reassessment are summarized in Table 4.
- Complete details regarding each of these requirements are available in the *Procedure and Submission Guidelines for the CADTH Common Drug Review* and *pan-Canadian Oncology Drug Review Submission Guidelines*.

Table 4: Submission Requirements for Standard Reassessments

Section	Specific Items and Criteria
General information	• Completed application overview template
	• Signed cover letter
	• Completed executive summary template for a reassessment
	• Product monograph
	• Completed declaration letter
New efficacy and/or safety information	• Reference list and copies of new clinical studies and errata
	• Updated table of studies
	• Reference list and copies of new editorial articles
	• Reference list and copies of articles for validity of outcome measures
Economic information	• Updated pharmacoeconomic evaluation addressing the following populations: ▪ population(s) addressed under the current reimbursement criteria ▪ population(s) addressed under proposed reimbursement criteria (if applicable)
	• Unlocked and fully executable economic model
Epidemiologic information	• Updated disease prevalence and incidence data
Pricing and distribution	• Submitted price per smallest dispensable unit to four decimal places
	• Method of distribution
Budget impact analyses	• Updated BIA reports for all jurisdictions
	• Updated BIA models for all jurisdictions
	• Reference list of all supporting documentation used and/or cited in BIAs
	• Copies of all supporting documentation used and/or cited in BIAs

BIA = budget impact analysis.

11.2 Targeted Reassessment Process

- CADTH must receive a formal request from the participating jurisdictions or pCPA that provides a clear description of the issues that are of interest to the jurisdictions. Copies of key documents informing the request for reassessment should be included.

- Manufacturers will be asked to provide the names and contact information for two individuals who can serve as the primary and secondary contacts for communicating with CADTH during a targeted reassessment of their product.

- Manufacturers will be invited to provide information to CADTH that they feel could provide relevant information for reassessment of their product.

11.3 Therapeutic Review Process

- Manufacturers will be asked to provide the names and contact information for two individuals who can serve as the primary and secondary contacts for communicating with CADTH during a therapeutic review involving one of more their products.

- Manufacturers and other stakeholders are invited to provide feedback at key stages of the therapeutic review process.

12 How to Submit Feedback

To provide feedback on the proposals, please use the feedback template. The completed template must be saved in one of the following formats:

- Microsoft Word document (.doc or.docx)
- unlocked PDF document that permits copying and pasting of text.

The completed templates must be uploaded sent to feedback@cadth.ca.

Feedback should be presented clearly and succinctly in 11-point font and must be received by CADTH by **5:00 p.m. EDT on Friday, September 13, 2019**. For feedback to be considered, you must identify yourself to CADTH. Only one response per organization will be considered. If more than one response is received, only the first will be considered.

If you have any questions about the feedback process, please email us at feedback@cadth.ca. We thank you in advance for your interest.