CADTH

Proposed Alignment of CADTH Drug Reimbursement Review Processes

June 2020

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ABBREVIATIONS

CAPCA	Canadian Association of Provincial Cancer Agencies
CDEC	CADTH Canadian Drug Expert Committee
CDR	CADTH Common Drug Review
CPEC	CADTH Canadian Plasma Protein Product Expert Committee
DIN	Drug Identification Number
FWG	Formulary Working Group
INESSS	Institut national d'excellence en santé et en services sociaux
NOC	Notice of Compliance
NOC/c	Notice of Compliance with Conditions
PAG	Provincial Advisory Group
pCODR	pan-Canadian Oncology Drug Review
pCPA	pan-Canadian Pharmaceutical Alliance
pERC	pan-Canadian Oncology Drug Review Expert Review Committee
PPP	Interim Plasma Protein Product Review
R2D2	Regulatory Review of Drugs and Devices

1. INTRODUCTION

1.1 Consultation

CADTH is inviting stakeholder feedback on a revised procedure for its drug reimbursement review processes (i.e., pan-Canadian Oncology Drug Review [pCODR], Common Drug Review [CDR], and Interim Plasma Protein Product Review [PPP]). This work has been undertaken to improve and align CADTH's procedures, submission requirements, and internal processes.

1.2 Principles for Establishing the Aligned Process

The proposed procedures have been established by adapting the best practices from each of the individual drug review processes, based on the following considerations:

- transparency for all stakeholders
- efficiency for CADTH and other stakeholders who participate the process
- timeliness to ensure that CADTH recommendations are available to stakeholders and decision-makers in a timely manner
- sustainability of CADTH's drug review programs
- equity for stakeholders who participate in the drug review process.

1.3 How to Participate

To provide comments on the proposal, please use the Survey Monkey feedback template.

Feedback must be received by CADTH by **5:00 p.m. EDT on August 10, 2020**. For feedback to be considered, you must identify yourself to CADTH. Only one response per organization will be considered. If you have any questions about the feedback process, please email CADTH.

Following the consultation period, CADTH will carefully assess all stakeholder feedback before announcing the final details of the new drug reimbursement review process. This may involve disclosing some or all comments or materials, or summaries of them, to CADTH's advisory bodies and the participating jurisdictions.

We thank you in advance for your interest in CADTH's drug reimbursement review process.

2. ADMINSTRATIVE PROCESSES

2.1 Communications for Drug Reimbursement Reviews

2.1.1 CADTH Communications

CADTH is proposing that it consolidate communications for its drug review programs into a single email newsletter that would be issued once per week. CADTH currently issues communications as required for the existing oncology and non-oncology drug review processes (i.e., notice of pending submission, call for stakeholder input, initial recommendation issued, and final recommendation issued). The consolidation of all of these communications into a single weekly update offers efficiencies for CADTH, greater predictability for stakeholders, and limits the amount of emails from CADTH that subscribers receive. The timeframes for stakeholders to respond to calls for input or feedback will not be reduced as a result of this change.

Table 1: Consolidation of CADTH Communications

Existing communications	New consolidated newsletter
Individual communications for each drug review: • Notice of pending submission (oncology) • Calls for stakeholder input (all reviews) • Notice of initial recommendation (oncology) • Notice of final recommendation (all reviews) **CADTH Pharmaceutical Reviews Update** • Procedural updates and clarifications • Consultation opportunities • Program news	**Single email issued each Tuesday:** • Calls for stakeholder input • Notice of draft recommendation • Notice of final recommendation • Procedural updates and clarifications • Consultation opportunities • Important program news

2.1.2 Stakeholder Inquiries

CADTH is similarly streamlining its processes for stakeholder inquiries and will be discontinuing the previous program-specific email addresses (e.g., pCODRinfo@cadth.ca will be discontinued and all inquiries will be directed to requests@cadth.ca). This change offers internal efficiencies for CADTH and ensures that all requests are appropriately tracked and triaged.

Stakeholders are reminded to use requests@cadth.ca for all program inquiries. Inquiries should not be addressed directly to the program director or other CADTH staff as this can disrupt the routine tracking and triaging of inquiries (and these types of disruptions can result in a lengthier time for obtaining a response).

2.1.3 Collaborative Workspaces

CADTH will be introducing a single collaborative space portal for all drug reimbursement reviews. This will consolidate the existing portals for the CDR, pCODR, and chimeric antigen receptor (CAR) T-cell applications, and eliminate the need for stakeholders to register separately for each type of application. Work is currently ongoing to consolidate these portals and stakeholders will be notified once the revisions are ready for implementation.

2.1.4 Webpages for Drug Reimbursement Reviews

CADTH will be consolidating all of the existing webpages for the individual drug programs. This will include the following changes:

- A common drug table will replace the existing individual summary tables for the CDR/PPP and pCODR programs. This consolidation will create efficiencies for CADTH by reducing the number of webpages to maintain and update, and for stakeholders by providing a single source for all CADTH drug reviews. For example, a subset of cancer drugs that pre-dated the establishment of the pCODR process are currently located on the CDR/PPP webpages.
- All submission templates will be aligned and consolidated on a single webpage. This offers efficiencies for CADTH and will simplify the application process for sponsors and consultants.

2.2 CADTH Reports and Recommendations

The following sections provide an overview of the key revisions that are proposed for improving and aligning the templates used to present CADTH's clinical reports, pharmacoeconomic reports, and expert review committee recommendations. It is important for stakeholders to note that CADTH is proposing revised confidentiality guidelines for the drug reimbursement review processes. These guidelines would be applied when determining what information may be subject to redaction prior to posting reports and recommendations on the CADTH website. The proposed revisions are summarized in Section 2.3.

2.2.1 CADTH Report Templates

CADTH previously launched an aligned pharmacoeconomic review template for all drug reimbursement reviews. At this time, no changes are being proposed to this template. In the existing CDR and PPP processes, CADTH currently posts the complete pharmacoeconomic review (with confidential information redacted at the sponsor's request); however, only an executive summary of the pharmacoeconomic review has been posted for drugs reviewed through the pCODR process. To enhance transparency for oncology drug reviews, CADTH will be posting the complete pharmacoeconomic review under the aligned process.

CADTH will be aligning the clinical review templates for all drug reimbursement reviews. The template will generally reflect the format and content of the existing template used in the CDR process, but will now also include a section that reflects input from the participating drug programs (as is used in the existing template for the pCODR process). These revisions will offer efficiencies for CADTH and improve the transparency of the drug reimbursement reviews. CADTH will continue to post the clinical reports for all drug reviews.

2.2.2 CADTH Recommendation Templates

CADTH will be aligning the format and content of the expert review committee recommendation documents. Following a consultation in 2018, CADTH implemented a revised format for presenting reimbursement conditions in CADTH Canadian Drug Expert Committee (CDEC) recommendations in order to provide greater clarity and consistency for stakeholders. This

format and structure will now be incorporated into the common recommendations for all CADTH drug reviews.

CADTH is proposing the inclusion of an expanded implementation guidance section within recommendations. This will build upon the format that is currently used in recommendations for oncology drugs (i.e., a clearly stated list of implementation issues identified throughout the review with guidance and advise from the expert review committees provided for each issue). Similar to the approach used for non-oncology submissions, this information will no longer be located in the appendix of the document and will be featured more prominently as a key deliverable for CADTH's expert review committees.

2.3 Handling of Confidential Information

2.3.1 Confidentiality Guidelines

CADTH is proposing revised confidentiality guidelines for the drug reimbursement review processes to enhance transparency, ensure clarity regarding definitions of confidential information, and streamline the processes for redaction. In July 2019, CADTH engaged in stakeholder consultations related to proposed revisions to the processes for handling confidential information (see *Proposal to Enhance Transparency of CADTH's Review Reports and Recommendations* for details). Since that time, CADTH has reviewed stakeholder feedback and engaged in further discussion with pharmaceutical industry representatives. Complete details regarding the proposed confidentiality guidelines are provided in Appendix 1.

In summary, CADTH is proposing that the following information not be considered confidential following the completion of CADTH's review and would be disclosable in CADTH reports and recommendations, irrespective of whether the information is already within the public domain:

- submitted prices for the drug under review, companion diagnostics, and comparators
- outputs of pharmacoeconomic evaluations, including, but not limited to, incremental cost-effectiveness ratios, incremental cost-utility ratios, or cost comparisons
- methodology of the economic model, including, but not limited to, the design, model inputs, and assumptions
- methods, results, appraisal, or interpretation of indirect treatment comparisons
- all clinical data filed by the sponsor, including ad-hoc or post-hoc analyses, irrespective of publication status or publication plans
- CADTH's critical appraisal and interpretation of any clinical and economic evidence included in the review, including indirect treatment
- CADTH's reanalyses of any pharmacoeconomic information, including, but not limited to, outputs of economic models and budget impact analyses
- descriptions of the design and methods of the budget impact analysis results
- summary statements about the budget impact analysis results
- information that will address sequencing of therapies.

The following types of information could be considered confidential and redacted at the sponsor's request:

- the sponsor's market research data, drug market share forecasts (from the sponsor's internal data), assumptions on competitor market share projections, and budget impact analysis numerical results
- information relating to the implementation plans provided by a sponsor on how the drug product may be delivered in the health care system (e.g., proposed launch date or facilities that may be built)
- information that meet with Health Canada's definition for confidential business information:
    - clinical information that was not used by the sponsor in the drug submission, supplement, or medical device application to support the proposed conditions of use or the purpose for which the drug or medical device is recommended
    - clinical information that describes the tests, methods, or assays used.

2.3.2 Redaction Processes

CADTH's existing processes for identifying and handling confidential information are different for oncology and non-oncology reviews. CADTH is proposing that the identification of confidential information occur in a manner that is similar to the current process for non-oncology drug reviews and using the revised confidentiality guidelines that are described in Appendix 1. This process will ensure that sponsors, CADTH, and other stakeholders have a clear understanding of how confidential information is defined at the outset of the review. In addition, CADTH will ensure that all drug reviews are based on the information that is most relevant for Canadian decision-makers. These determinations will be made solely by CADTH and will no longer involve negotiation with sponsors regarding the inclusion of data in CADTH reports (as is currently the process with oncology drugs). Overall, these revisions will make CADTH's review process more efficient, transparent, and predictable for stakeholders.

The CADTH clinical and pharmacoeconomic review reports will be distributed to the sponsor and drug programs at the time the draft recommendation is issued and will be posted on the CADTH website in accordance with the process and timelines that are currently applied for non-oncology drugs (see section 7.3.2 of the *Procedures for the CADTH Common Drug Review and Interim Plasma Protein Product Review*). This change is being made in order to accommodate increased transparency in the oncology review process through publication of the complete pharmacoeconomic review report. This will require additional time for sponsors to review the final reports and identify any confidential business information that CADTH will not be permitted to disclose in accordance with the confidentiality guidelines.

2.4 Application Fees

2.4.1 Fee Schedule

The structure and application of CADTH's fee schedule currently includes schedule A, B, C, and E fees. As part of CADTH's cost-recovery initiatives, a schedule D fee is currently applied for reconsideration requests in the process for non-oncology drugs. This will be applied to all drug reimbursement reviews going forward to help ensure the sustainability of CADTH's programs (i.e., all sponsor-initiated requests for reconsideration that are classified as major or minor

revisions would be subject to a schedule D application fee under the proposed process). Please see Section 8.6 for additional proposals regarding revisions to the reconsideration process for drug reimbursement recommendations.

2.4.2 Milestones for Invoicing and Performance Metrics

As noted in Section 6.1, CADTH is proposing that sponsors have the opportunity to review and comment on the draft reports. As such, CADTH is proposing that milestone 2 in the fee schedule be aligned with the existing non-oncology drug review process (i.e., draft reports sent to the sponsor).

There are no changes being proposed for the overall performance of 180 calendar days. CADTH partially aligned the terminology in the *Fee Schedule for CADTH Pharmaceutical Reviews* in January 2020 (see *CADTH Pharmaceutical Reviews Update — Issue 12* for details). Following this change, the term "accepted for review" was used for all drug reimbursement reviews (replacing "deemed complete" for pCODR submissions and resubmissions) when describing the starting point for calculating the 180-calendar day performance metric. As shown in Table 2, CADTH is proposing a minor revision to the description of the end point of the performance metric to align with the revised recommendation process describe in Section 8.5.

Table 2: Alignment of Timelines for Application Fees

Timelines	Current processes		Proposed process
	Oncology	Non-oncology	
Milestones for invoicing application fees	**Milestone 1:** Initiation of review by CADTH **Milestone 2:** Checkpoint meeting with sponsor is held	**Milestone 1:** Initiation of review by CADTH **Milestone 2**: Draft reports sent to sponsor for review and comment	**Milestone 1:** Initiation of review by CADTH **Milestone 2:** Draft reports sent to sponsor for review and comment
Timelines for determining performance metrics	**Start:** Date the file is accepted for review by CADTH **End:** Date the initial recommendation is issued	**Start:** Date the file is accepted for review by CADTH **End:** Date the embargoed recommendation is issued	**Start:** Date the file is accepted for review by CADTH **End:** Date the draft recommendation is issued to the sponsor and drug programs

2.5 Procedural Review

CADTH will be implementing a revised procedural review process for the drug reimbursement review processes (please refer to Appendix 2 for complete details). In addition to aligning the drug review processes, this revised procedural process provides stakeholders with greater clarity on the application and assessment processes for a request for procedural review. The grounds for a procedural review relate only to whether or not CADTH failed to act in accordance with its procedures in conducting the drug reimbursement review and issuing the final

recommendation. It is not an opportunity to reopen issues that CADTH's expert committee has decided on or to circumvent existing feedback mechanisms.

The revision is intended to introduce efficiencies for both CADTH and sponsors, particularly for non-oncology drugs, where the existing procedural review process is addressed through the reconsideration process (i.e., reconsideration on the grounds that CADTH and/or the expert review committee failed to act fairly and in accordance with its procedures in conducting the review). This can lead to confusion for stakeholders who mistakenly apply for reconsideration on procedural grounds when they intended to file on evidentiary grounds.

The following is a summary of the key proposed procedural review process steps:

- A party (e.g., sponsor, patient group, or clinician group) that participated in the process relating to the final recommendation in question will be eligible to make a request for a procedural review on the grounds that CADTH did not followed its own processes in issuing the final recommendation. If more than one eligible party makes a request and it is accepted for the same final recommendation in question, CADTH will conduct the requests jointly for the purpose of the procedural review proceeding.
- The eligible party(ies) must use the prescribed form and file the request within 20 business days of the final recommendation in question being posted on the CADTH website.
- If the request is accepted in accordance with the proposed terms and conditions set out Appendix 2, CADTH will convene a panel to conduct a procedural review.
- An eligible party(ies) will have an opportunity to make a brief presentation and respond to questions from the panel. Up to two representatives knowledgeable about the issue at hand will be invited; however, no legal representation will be permitted at the meeting.
- The panel will make the determination if the process was properly followed. The panel may issue one of two possible outcomes:
    - No change required because there was no deviation in the process.
    - Steps in the review process for the specific recommendation at issue must be revisited and/or re-deliberated. A re-deliberation may result in the expert committee final recommendation being upheld or being revised.
- There is no possibility of making any further procedural review requests against the decision of the panel, and no additional procedural review requests may be filed against the recommendation in question.
- The duration of the procedural review process may vary, depending on the complexity and nature of the request. While efforts will be made to issue a decision in the shortest possible time period, it may take up to a maximum of 60 business days to issue a decision from the date of receipt of the request.
- High-level details about the submitted procedural review request, including the name of the party(ies), the decision, and the reason for that decision from the panel, will be publicly posted on the CADTH website.

3. ELIGIBILITY FOR DRUG REIMBURSEMENT REVIEW PROGRAMS

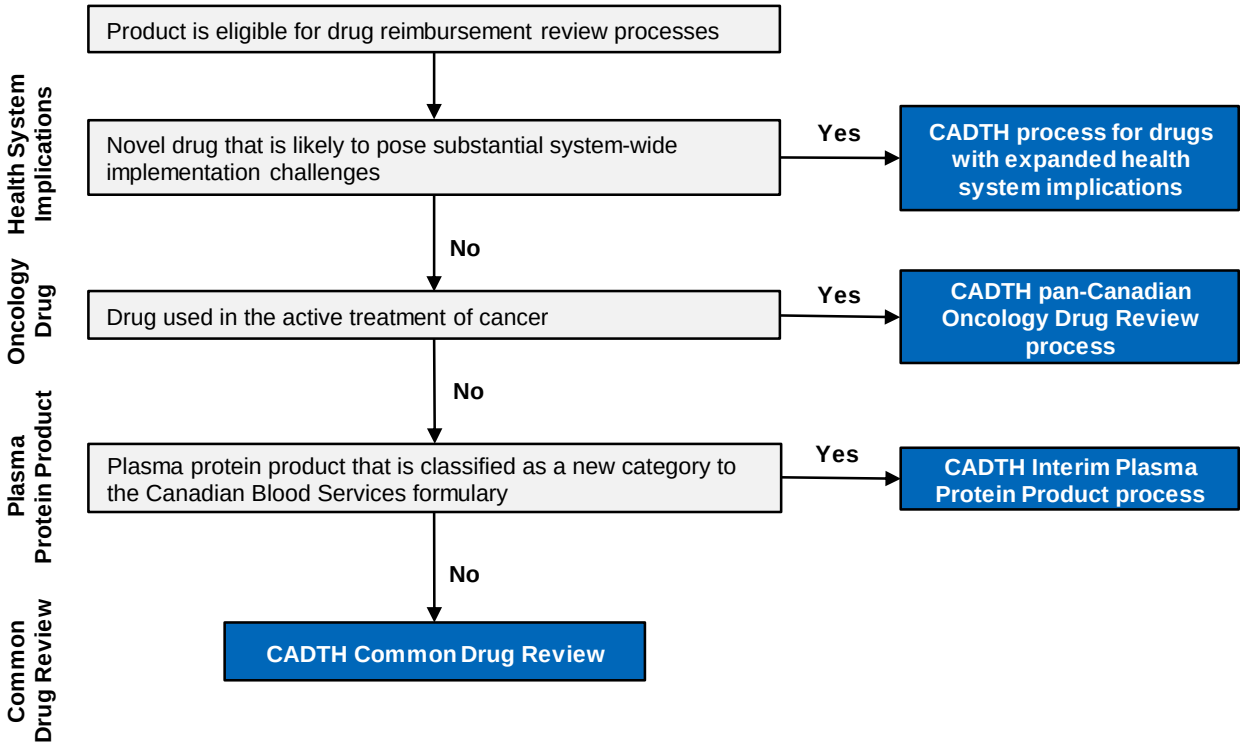
3.1 Drug Review Programs

The objectives of CADTH's drug reimbursement review processes are to reduce duplication across jurisdictions, maximize the use of limited resources, and enhance the consistency of drug reviews. CADTH undertakes reviews of drugs and issues reimbursement recommendations and/or review reports to all federal, provincial, and territorial drug programs and cancer agencies that participate in CADTH's review processes and those of Canadian Blood Services (hereafter referred to as drug programs).

Eligible products are reviewed through one of the following drug review processes (Figure 1):

- Novel products that are likely to pose substantial system-wide implementation challenges may be reviewed through the CADTH process for drugs with expanded health system implications.
- Drugs used in the active treatment of cancer are reviewed through the pCODR process.
- Plasma protein products are reviewed through the interim PPP process.
- All other eligible products are reviewed through the CDR process.

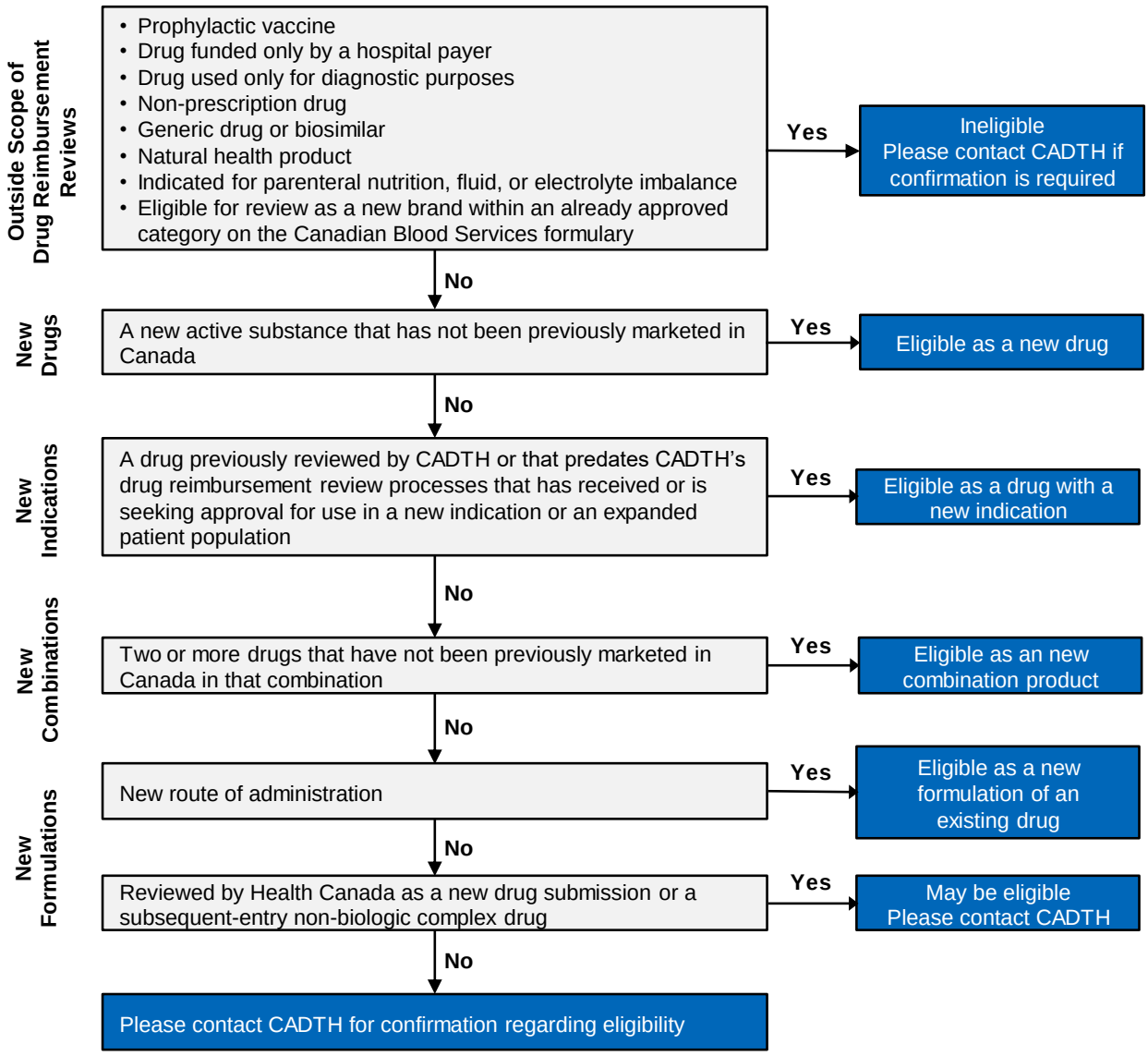
Figure 1: CADTH's Drug Reimbursement Review Programs



3.2 Submission Eligibility

In consultation with the participating drug programs, CADTH has aligned the eligibility criteria for the drug reimbursement review processes (see Figure 2 for a summary). The key revision to note is the alignment of criteria regarding the eligibility of selected new formulations of existing drugs. These are routinely reviewed for non-oncology drugs and CADTH has heard from the participating jurisdictions that reviews and recommendations would be valuable for certain new formulations of oncology drugs. It was noted that this could reduce duplication of efforts across the public payers and provide support for those programs that have limited resources to process these files on their own.

Figure 2: Eligibility for CADTH's Current Drug Reimbursement Review Programs

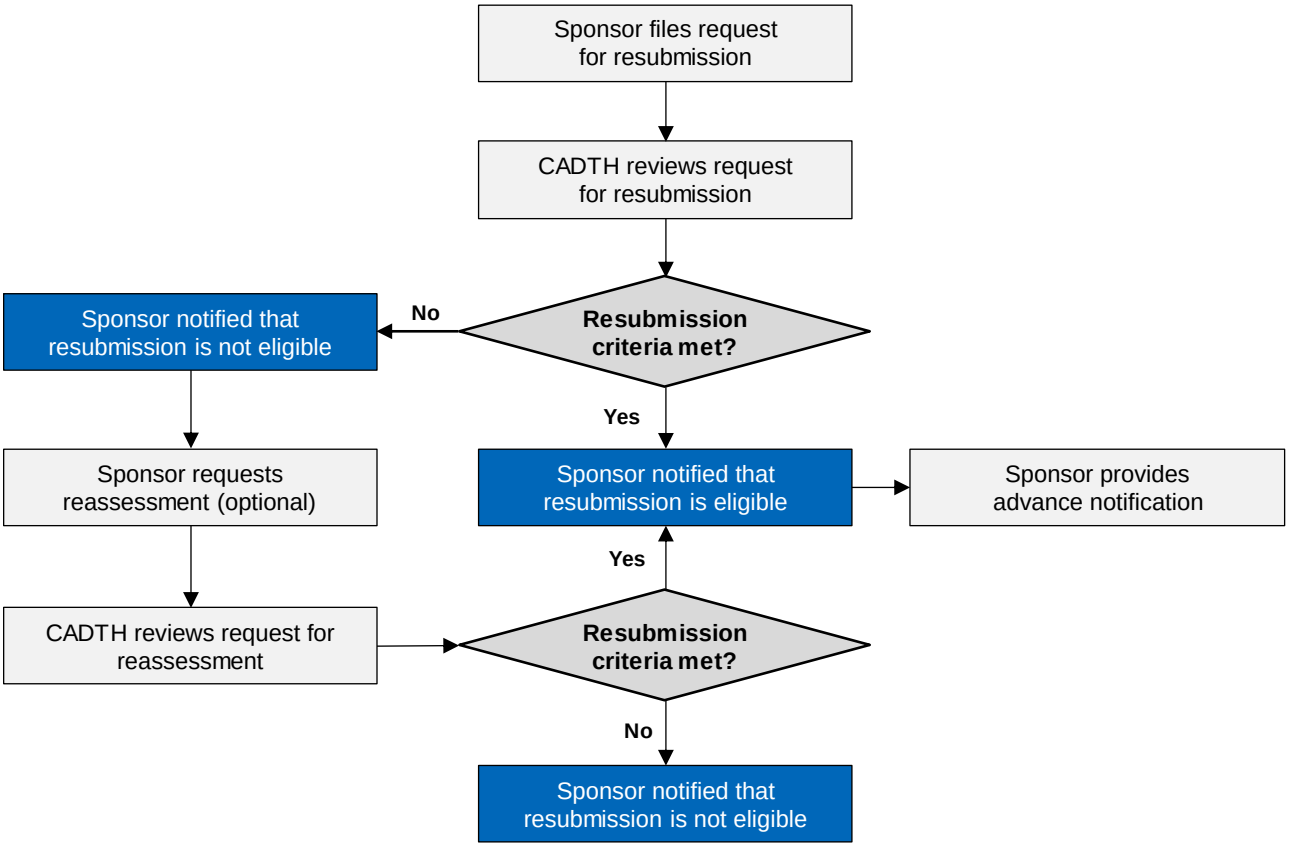


3.3 Resubmission Eligibility

In January 2020, CADTH implemented revisions to the oncology drug review process to align the resubmission eligibility processes (see *CADTH Pharmaceutical Reviews Update — Issue 12* for details). This revision stated that submissions that are withdrawn and re-filed in the pCODR process will no longer be classified as resubmissions. These changes align with procedural revisions introduced by CADTH for non-oncology drugs in 2014, and simplify the process and terminology by ensuring that resubmissions only apply in situations where CADTH has completed a review and issued a final recommendation for the drug and indication under review.

Eligibility requirements for resubmissions were aligned in February 2018 when the evidentiary requirements were adjusted for oncology drug reviews to align with those used for non-oncology drugs. This revision allowed resubmissions to be filed based on new evidence that was collected from study designs other than a randomized controlled trial (see *pCODR Update — Issue 63* for details). Application and screening processes for submissions are currently aligned (Figure 3) and no revisions are being proposed at this time.

Figure 3: Assessing the Eligibility of Resubmissions



3.4 Reassessment Eligibility

As part of the 2018-2021 Strategic Plan, CADTH initiated stakeholder consultation on a reassessment framework (see *CADTH Pharmaceutical Review Reassessment Framework* for details). As part of the initiative to align and modernize its drug review processes, CADTH will be implementing the proposed reassessment framework.

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. Reassessments could be carried out in response to a variety of potential triggers, including:

- actions by regulatory and reimbursement authorities
- the availability of new evidence or new comparators leading to questions about the comparative clinical or cost-effectiveness
- changes in contextual factors that result in implementation challenges (e.g., new Canadian clinical practice guidelines).

3.4.1 Standard Reassessments

The standard reassessment process would be applied when there is uncertainty regarding the comparative safety, clinical effectiveness, and/or cost-effectiveness of a single drug or drug regimen. The standard reassessment process will require the sponsor to file new clinical and/or economic information with CADTH. Sponsors can initiate the standard reassessment process in a proactive or reactive manner. Proactive reassessments can be initiated by sponsors that are interested in pursuing revisions to any of the conditions associated with a previous CADTH recommendation, provided they have new evidence that can support the revisions. Reactive reassessments can be initiated by sponsors that have received a formal request for reassessment from CADTH on behalf of the drug programs.

Similar to CADTH's resubmission process, sponsors 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 existing 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 sponsor. After receiving confirmation from CADTH that the proposed reassessment is eligible for review, sponsors would be required to provide CADTH with advance notification for the pending reassessment (in accordance with procedures specified in Section 4.2).

3.4.2 Targeted Reassessments (Formerly Request for Advice)

CADTH will typically apply the targeted reassessment process when jurisdictions or the pan-Canadian Pharmaceutical Alliance (pCPA) raise issues with changes in contextual information that affect their ability to implement existing CADTH recommendations. All targeted reassessments will be related to a drug that has previously been reviewed through one of CADTH's drug reimbursement review processes and for which a final recommendation has been issued. To initiate the targeted reassessment process, CADTH must receive a formal request from the drug programs or the pCPA that provides a clear description of the issues that

are of interest to the drug programs. Drug manufacturers and tumour groups are not permitted to initiate the targeted reassessment process.

3.5 Market Authorization Status

3.5.1 Timing of Filing Submissions

As part of Health Canada's Regulatory Review of Drugs and Devices (R2D2) aligned reviews initiative, CADTH and Institut national d'excellence en santé et en services sociaux (INESSS) both introduced revised and aligned eligibility criteria for filing submissions prior to market authorization in March 2018 (see *Common Drug Review Update — Issue 134*). Since that time, any submission may be filed with CADTH up to 180 calendar days in advance of the anticipated date of approval from Health Canada. There are no further changes with respect to the timing of pre-Notice of Compliance (NOC) filings being proposed at this time.

3.5.2 Health Canada Information Sharing

The *Aligned Reviews Between Health Canada and Health Technology Assessment Organizations* process was launched in June 2018 as part of Health Canada's Regulatory Review of Drugs and Devices (R2D2) initiative. This is a joint initiative between Health Canada, CADTH, and INESSS that established a process to facilitate information sharing between Health Canada and the health technology assessment agencies (CADTH and INESSS).

Health Canada, CADTH, and INESSS have continuously monitored participation rates by sponsors and the operational impact of the aligned review process. Participation rates have been sufficient to determine that the information-sharing process is beneficial for the health technology assessment review processes in Canada. However, CADTH is currently forced to operate two parallel pre-NOC submission processes to accommodate the voluntary nature of the information-sharing process (i.e., one process with information sharing and one without information sharing). This creates operational inefficiencies for CADTH and limits the ability of the agency to maximize the benefits of interacting with Health Canada and leverage opportunities to build upon the interpretation and appraisal conducted by Health Canada reviewers. As such, CADTH, INESSS, and Health Canada are seeking stakeholder feedback on an important procedural revision that would make participation in the information-sharing process mandatory for all submissions filed on a pre-NOC basis. Please see the following documents for complete details:

- *Proposed Enhancements to the Health Canada, CADTH, and INESSS Aligned Review Processes*
- *Améliorations proposées au processus d'examen harmonisé de Santé Canada, l'ACMTS et l'INESSS*

3.5.3 Placement on Expert Review Committee Agenda

CADTH's existing processes differ with respect to placement on the expert review committee agenda while market authorization is pending. For non-oncology drugs, CADTH will place a drug on the expert review committee agenda and allow a recommendation to be drafted prior to approval by Health Canada. The recommendation is not issued by CADTH until the drug has been approved by Health Canada and CADTH has reviewed the final approved indications and

recommended dosage regimens. In the event there are important changes, the drug will be placed on the agenda for a subsequent deliberation by the committee. In contrast, oncology drug reviews are not placed on the expert review committee agenda until market authorization has been issued and all documentation must be filed with CADTH at least six days prior to the target committee meeting.

CADTH is proposing that the process for non-oncology drugs be adopted for all drug reimbursement reviews; however, this would be contingent upon information sharing with Health Canada becoming a mandatory component of the pre-NOC submission process (as described in the consultation described in Section 3.5.2). Provided CADTH is fully aware of the regulatory status of the drug under review, it can establish a process that would permit the shortest possible review timelines. Information sharing is critical to ensuring that CADTH's pre-NOC submission process can proceed in the most efficient manner, and CADTH encourages all stakeholders to review the proposed revisions in the joint consultation.

3.5.4 Submissions for Unapproved Indications

CADTH currently accepts submissions for selected oncology drugs for new indications that are not approved or undergoing review by Health Canada. CADTH considers a review by Health Canada to be a critical component of ensuring that new indications are investigated in a robust and consistent manner in Canada. However, at the request of stakeholders, CADTH will continue to allow submissions for unapproved indications for oncology drugs. It is important to note that this process will not be expanded to include non-oncology indications at this time (i.e., this will not be aligned in the revised process) as CADTH has not been asked to expand the scope of its non-oncology drug review processes at this time.

There are no changes proposed to the eligibility criteria for oncology drug reviews for unapproved indications:

- where the drug is currently marketed in Canada;
- the Drug Information Number (DIN) holder confirms that a submission to Health Canada is not pending for the indication of interest;
- the DIN holder confirms that a submission to Health Canada has not been made in the past for the indication of interest and received an Notice of Deficiency (NOD) or Notice of Non-Compliance (NON);
- there is sufficient clinical evidence for the new indication to support a submission to CADTH; and,
- the drug has the potential to address an unmet therapeutic need.

3.5.5 Terminology

CADTH aligned the terminology with respect to market authorization status at the time of filing in January 2020 (*CADTH Pharmaceutical Reviews Update — Issue 12* for details). Submissions filed before market authorization by Health Canada are referred to as pre-NOC submissions and those filed after market authorization are referred to as post-NOC submissions. This revision simplified the procedural documentation for oncology drugs by eliminating the distinction between NOC or Notice of Compliance with Conditions (NOC/c) in the description of submission types. There are no further changes being proposed at this time.

3.6 Sponsor Eligibility

CADTH has aligned processes and terminology with respect to pharmaceutical industry sponsors (i.e., these are typically the DIN holders, but could be another manufacturer, supplier, distributor, or other entity that has been recruited by the DIN holder). CADTH's processes are similarly aligned with respect to applications filed by the participating drug programs (i.e., these will be accepted provided the required documentation are filed with CADTH).

There are important differences between the oncology and non-oncology drug review processes with respect to applications that are filed by clinician groups. Historically, provincially recognized clinician-based tumour groups have been permitted to file applications with CADTH only for the pCODR program. CADTH will continue to receive these applications, provided they meet the CADTH submission requirements that ensure that CADTH is able to complete a review and recommendation (i.e., they include the required documentation and economic model). This will not be expanded beyond oncology drugs at this time (i.e., will not be aligned in the revised process).

3.7 Declining to File a Submission With CADTH

Following stakeholder consultation in August 2018 (see *Addressing Non-Submissions by Manufacturers* for details), CADTH introduced aligned procedures for declining to file a submission for an eligible product (i.e., non-submissions) in response to a formal enquiry by the participating drug programs. As this process is currently aligned, effective, and efficient, it has proposed revisions at this time.

3.8 Type of Review Conducted by CADTH

CADTH aims to conduct its reviews in the most efficient manner and uses various review types depending on the type and complexity of the drug reimbursement review at hand. The proposed review types are summarized in Table 3 and described in detail in the sections that follow.

Table 3: Proposed CADTH Review Types

CADTH Process	Eligibility	Typical timelines	Application fee
Standard review	• New drugs, drugs with new indications, and selected new combination products	≤180 calendar days	Schedule A or B
Tailored review[a]	• New combination products or new formulations of existing drugs that CADTH has designated as tailored reviews • Subsequent-entry non-biologic complex drugs		Schedule C
Cell and gene therapy review[a]	• New cell and gene therapies and new indications for cell and gene therapies		Schedule E
Resubmission[a]	• Drugs that are not reimbursed and have previously been reviewed by CADTH and for which a final recommendation has been issued		Schedule B
Standard reassessment[a]	• Drugs that are currently reimbursed and there is uncertainty regarding safety, effectiveness, and cost-effectiveness • Sponsors seeking revisions to existing reimbursement criteria on the basis of new clinical or economic evidence		

Targeted reassessment	• Changes in contextual information that may affect the ability to implement existing CADTH recommendations	90 to 150 calendar days	Not applicable
Therapeutic review	• Uncertainty regarding the comparative safety, clinical effectiveness, and/or cost-effectiveness of multiple drugs	12 months	Not applicable

[a] Eligibility must be confirmed prior to filing the application.

3.8.1 Submissions

CADTH reviews new submissions through of the following three review types:

- A **standard review** consists of CADTH conducting a systematic review of clinical evidence provided by the sponsor along with studies identified through its independent, systematic literature search, and an appraisal of the sponsor-provided pharmacoeconomic evaluation.
- A **tailored review** consists of CADTH conducting an appraisal of the clinical evidence and pharmacoeconomic evaluation filed by the sponsor using a CADTH-provided review template. CADTH currently conducts tailored reviews for a subset of non-oncology drugs and is proposing to expand this process to oncology drugs with similar characteristics.
- A **cell and gene therapy review** is conducted in a manner similar to a standard review, but involves additional review and consideration of potential implementation issues and ethical challenges.

The output of CADTH's review of a submission will be a recommendation advising the drug programs on whether or not the drug under review should be reimbursed and under what conditions reimbursement should be considered.

3.8.2 Resubmissions

A **resubmission** is conducted when new evidence is available for a drug that has previously been reviewed by CADTH for the indication of interest and for which a final recommendation has been issued. Resubmissions are typically limited to drugs that were not recommended for reimbursement by a CADTH expert review committee and are not currently reimbursed by the participating drug programs for the indication of interest. The output of CADTH's review of a resubmission will be an updated recommendation that will be supersede the document for the initial submission and any other prior resubmissions for the drug under review.

3.8.3 Reassessments

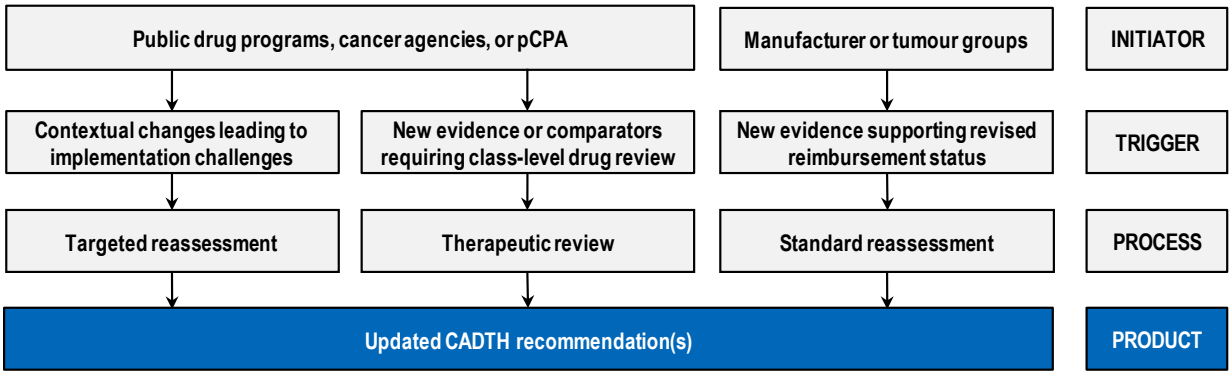
Following the consultation in July 2019, CADTH will be implementing the *Proposed Reassessment Framework* as part of the initiative to improve and align its drug review processes. As shown in Figure 4, CADTH believes that multiple approaches are required to ensure that the reassessment of drugs is both effective and efficient. The proposed reassessment processes developed by CADTH have built upon the best practices of the review pathways that have previously been used in the pharmaceutical review processes.

- A **standard reassessment** is conducted to address questions related to the comparative clinical benefit and/or cost-effectiveness of a single drug that is currently reimbursed by the

participating drug programs for the indication(s) of interest. The output of CADTH's review will be an updated recommendation that will supersede the document for the initial submission and any other prior resubmissions for the drug under review.

- A **targeted reassessment** is conducted to address changes in contextual factors that may affect the ability of the participating jurisdictions to implement existing recommendations from CADTH. Contextual information can include regulatory actions, changes in clinical practice, or other forms of information that have introduced implementation questions or challenges for the jurisdictions. This form of reassessment was formerly referred to as a Request for Advice in CADTH's drug review processes. The output of CADTH's review will be an updated recommendation document that will supersede the document for the initial submission and any other prior resubmissions for the drug under review.
- A **therapeutic review** is conducted when there are questions regarding the comparative safety, clinical effectiveness, and cost-effectiveness of multiple drugs.

Figure 4: CADTH Reassessment Processes



pCPA = pan-Canadian Pharmaceutical Alliance.

4. PRE-SUBMISSION PHASE

4.1 Pre-submission Meetings

Pre-submission meetings are offered to facilitate the efficient preparation and filing of applications with CADTH. The goal of the meeting is to assist the sponsor in improving the quality, relevance, and clarity of the information filed for review. These meetings are not meant to be consultative in nature, outside of clarifying procedural questions. This is because at the time of a pre-submission meeting, CADTH has not reviewed the application in detail and therefore is not in a position to provide final advice to the sponsor. Any information and advice provided by CADTH at the pre-submission meeting will continue to be non-binding.

4.1.1 Frequency and Timing of Meetings

As with the existing CDR, pCODR, and PPP processes, sponsors will continue to be permitted to engage with CADTH at a pre-submission meeting for each pending application. These meetings may occur anytime within 12 months of the anticipated filing date and must occur prior to the application being received by CADTH. In the current pCODR process, sponsors are

limited to one in-person pre-submission meeting within a six-month period. This restriction will be removed in the aligned review process and sponsors are welcome to request in-person meetings for any pending applications (please note that CADTH office sites are currently closed due to COVID-19 and all pre-submission meetings are currently being held via teleconference or webinar). Pre-submission meetings will be scheduled for a maximum of one hour and sponsors are limited to one meeting per drug submission or resubmission.

4.1.2 Attendance

Sponsors may bring consultants and/or clinical experts as representatives. Representatives from the drug programs, pCPA, Canadian Blood Services, Canadian Association of Provincial Cancer Agencies (CAPCA), and INESSS may attend pre-submission meetings at their discretion.

4.1.3 Meeting Requests and Preparation

Pre-submission meeting requests are currently filed using a dedicated form for non-oncology drugs or embedded in the advance notification form for oncology drugs. Under the aligned process, CADTH will adopt the pre-submission meeting request process that is currently used for non-oncology submissions to accommodate the revisions to the advance notification process described in Section 4.2.

4.2 Advance Notification Procedure

4.2.1 Timing

Sponsors will be required to provide CADTH with a minimum of 30 business days of advance notice for anticipated submissions, resubmissions, and reassessments. The advance notification period of 120 calendar days for oncology drugs is being reduced to accommodate novel expedited review pathways in the regulatory environment (e.g., project ORBIS) and to improve the accuracy of advance notification information (e.g., pending dates, proposed indications, and the sponsor's requested reimbursement conditions). The 30-business day notification period will be counted from the date CADTH receives all of the required documentation.

4.2.2 Required Documents

CADTH will continue to require that sponsors use a standardized template to provide key information regarding the pending application. In addition, sponsors will be required to provide an additional document that details the proposed place in therapy for the drug under review. The proposed place in therapy will be required for all drug submissions and resubmissions with the exception of those filed under CADTH's tailored review process (where the place in therapy for a product is well-established).

4.2.3 Filing Process

Pre-submission documentation must be filed using CADTH Collaborative Workspaces. CADTH will no longer be accepting documents via email (as is current practice for non-oncology submissions). CADTH will discontinue the advance notification web forms that are currently

used for oncology drugs and will adopt a standardized template that can be downloaded, completed, and filed by sponsors. These advance notification forms were pilot tested to seek efficiencies in the advance notification process and may be re-introduced at a later date.

5. APPLICATION AND SCREENING PHASE

5.1 Filing Applications

As described in Section 2.1.3, CADTH will be introducing a common collaborative space portal for all drug reimbursement reviews. This will consolidate the existing portals for CDR, pCODR, and CAR T-cell applications, and avoid the need for stakeholders to register separately for each type of application.

5.2 Screening Applications

CADTH's processes for receipt and screening applications are currently aligned for all drug reimbursement reviews and no changes are being proposed at this time. Applications will continue to be processed in the order they are received and in accordance with the published submission requirements. The screening period will continue to be 10 business days and the date of receipt by CADTH will be considered day zero for the purposes of calculating timelines. Once the file has been accepted for review by CADTH, the key milestones for the review will be posted on the CADTH website.

5.3 Submission Requirements

5.3.1 Proposed Requirements

Table 4 provides a summary of the proposed documentation that would be required for submissions for standard, tailored, and cell and gene therapy reviews.

Table 4: Proposed Requirements for CADTH Drug Reimbursement Reviews

Section	Specific items and criteria	CADTH review type		
		Standard	Tailored	Cell and gene
General information	Application overview template	Required	Required	Required
	Signed cover letter	Required	Required	Required
	Executive summary template	Required	Required	Required
	Proposed place in therapy template	Required	Not required	Required
	Product monograph	Required	Required	Required
	Declaration letter template	Required	Required	Required
Submission template	Tailored review submission template	Not applicable	Required	Not applicable
Health Canada documentation	NOC or NOC/c and Letter of Undertaking, or a placeholder	Required	Required	Required
	Table of Clarimails or Clarifaxes	Required	Required	Required

Section	Specific items and criteria	CADTH review type		
		Standard	Tailored	Cell and gene
Efficacy, effectiveness, and safety information	Common Technical Document sections 2.5, 2.7.1, 2.7.3, 2.7.4, and 5.2, or a statement indicating any section(s) that are not available	Required	Required	Required
	Clinical study reports for pivotal and key clinical studies	Required	Required	Required
	Reference list and copies of key clinical studies and errata	Required	Required	Required
	Table of studies	Required	Required	Required
	Reference list and copies of editorial articles	Required	Not required	Required
	Reference list and copies of new data	Required	Not required	Required
	Reference list and articles for validity of outcome measure	Required	Not required	Required
	Indirect comparison with full technical report	May be required	Not required	May be required
Economic information	Pharmacoeconomic evaluation for the full indicated population	Required	Not required	Required
	Unlocked and fully executable economic model	Required	Not required	Required
	Economic model supporting documentation	Required	Not required	Required
Budget impact analysis	Aggregate pan-Canadian budget impact report	Required	Required	Required
	Aggregate pan-Canadian budget impact model	Required	Required	Required
	Supporting documentation used in budget impact analysis	Required	Required	Required
Epidemiologic information	Disease prevalence and incidence data	Required	Required	Required
	Number of patients accessing a new drug	May be required	May be required	May be required
Pricing and distribution	Price per smallest dispensable unit to four decimal places	Required	Required	Required
	Method of distribution	Required	Required	Required
Reimbursement status	Template with reimbursement status of all relevant comparators	Required	Required	Required
Companion diagnostics	Reference list and articles that highlight the clinical utility	If applicable	If applicable	If applicable
	Disclosable price	If applicable	If applicable	If applicable
Implementation plan	Implementation plan template	Not required	Not required	Required
Pre-NOC letter	Letter for sending NOC or NOC/c to CADTH	Required	Required	Required

NOC = Notice of Compliance; NOC/c = Notice of Compliance with Conditions.

For those familiar with the existing submission requirements for non-oncology drugs, the following is a summary of the revisions to the requirements:

- CADTH is discontinuing all category 2 requirements for non-oncology drug submissions. Sponsors should ensure that an individual jurisdictional-specific budget impact analysis is provided to all participating drug programs that require such documentation.
- Required documentation for plasma protein products has been harmonized with the standard review requirements for other non-oncology drugs.
- Previous revisions to the requirements for non-oncology submissions were undertaken in March 2020 to adopt the best practices from the oncology drug review process (e.g., requirement for a pan-Canadian budget impact analysis).

For those familiar with the existing submission requirements for oncology drugs, the following is summary of the revisions to the requirements:

- CONSORT diagrams will no longer be required as separate documents; this information is to be included with the existing study documentation (e.g., clinical study reports, common technical documents, and/or manuscripts).
- A copy of the Health Canada Screening Acceptance Letter will no longer be required by CADTH for submissions filed on a pre-NOC basis.
- Copies of Clarifaxes will no longer be required at the time a submission is filed; however, these must be made available to CADTH upon request.
- Separate documentation with the study protocol for pivotal studies and studies that address key clinical issues is no longer required; this information should be included within the clinical study reports.
- Separate documentation with the statistical analysis plan pivotal studies and studies that address key clinical issues is no longer required; this information should be included within the clinical study reports.
- An updated advance notification form (previously referred to as the Pre-Submission Information Requirements Form) will no longer be required at the time the application is filed with CADTH.
- The sponsor will now be required to provide an executive summary using a standardized CADTH template.

5.3.2 Proposed Revisions to Pharmacoeconomic Requirements

CADTH's position is that a cost-utility analysis is the preferred form of pharmacoeconomic evaluation for all drug reimbursement reviews (with the exception of those filed for review through the tailored review process). However, in the interest of aligning with other health technology assessment agencies and to seek efficiencies within CADTH's drug review processes, stakeholder feedback is being sought regarding a proposal to accept cost-minimization analyses for the pharmacoeconomic evaluation for a subset of drugs. Specifically, CADTH is proposing that a cost-minimization analysis could be acceptable in the following circumstances:

- the drug represents an additional drug in a therapeutic class in which there is already a reimbursed drug for the same indication
- the drug under review demonstrates comparable clinical effects (i.e., efficacy and harms) compared to the most appropriate comparator(s)[1], based on:
    - one or more clinical studies that directly compared the drug under review to relevant comparator(s); or
    - one or more indirect comparisons that allow for the comparison of the drug under review to relevant comparator(s); and
- the drug under review is anticipated to result in equivalent or lesser costs to the health system.

5.4 Templates for Required Documents

CADTH made interim changes in February 2020 to simplify the application process for oncology drugs by making the templates for category 1 requirements available on the CADTH website (as many were previously only accessible through the Collaborative Spaces portal) and by launching the first set of aligned submission templates (see *CADTH Pharmaceutical Reviews Update — Issue 13*). CADTH will be implementing the next phase of this consolidation by launching aligned versions of all of the remaining templates. As described in Section 2.1.4, all of these templates will now be available on a single webpage. The previously described revisions offer considerable efficiencies for CADTH and will further simplify the application process for sponsors and consultants.

5.5 Review Initiation

CADTH's drug review reimbursement review processes are currently aligned with respect to review initiation and there are no changes being propose at this time. All applications will continue to be initiated on a first-come, first-served basis, as determined by the date they are accepted for review. All drug reviews will be initiated within one to 10 business days of acceptance for review. Initiation dates and other key milestones will be confirmed once the application has been accepted for review.

6. STAKEHOLDER ENGAGEMENT

6.1 Industry Engagement

6.1.1 Pre-submission Meetings

As described in Section 4.1, CADTH will adopt the pre-submission meeting process that is currently used for non-oncology drugs. This involves removing existing restrictions on the number of pre-submissions within a six-month period and opening attendance to

[1] The most appropriate comparators are typically drugs that are currently reimbursed by the participating drug programs and are the mostly likely to be replaced by the drug under review.

representatives from the participating drug programs and other agencies (e.g., pCPA and CAPCA). To further improve the pre-submission meeting preparation process, CADTH has revised the agenda template to provide more detailed guidance to sponsors on the suggested structure of the meeting, as well as more detailed instructions to assist the sponsor in planning and conducting the pre-submission meeting. CADTH is interested in feedback from sponsors and consultants on the proposed revisions, as well as any other suggestions they may have to improve the overall pre-submission meeting process.

6.1.2 Sponsor Review of Draft CADTH Reports

CADTH is proposing that sponsors will have the opportunity to review and comment on draft clinical and pharmacoeconomic reports prior to deliberation by the expert review committee. CADTH believes that the review and commentary from sponsors strengthens the review process and promotes transparency. This is currently part of the review process for non-oncology drugs and will be adopted for all drug reimbursement reviews. As in the existing non-oncology process, CADTH will provide responses to the commentary and revise the reports as required. Sponsors will be provided with the CADTH's responses eight days prior to the scheduled expert review committee meeting.

6.1.3 Checkpoint Meetings Discontinued

As communicated at the *CADTH Drug Portfolio Information Session* in November 2019, CADTH will no longer be offering checkpoint meetings with sponsors in lieu of the opportunity for sponsors to review and comment on the draft reports. Instead, CADTH has revised its process for the handling of confidential information (as described in Section 2.3) and put greater focus on providing rapid communication between CADTH and the sponsor to resolve any areas of uncertainty (e.g., immediate correspondence to address issues, similar to the Clarifaxes and Clarimails used by Health Canada).

6.2 Patient Engagement

Patient input includes patients' experiences and perspectives of living with a medical condition for which a drug under review is indicated, their experiences with currently available treatments for that medical condition, and the improved treatment outcomes they desire. Table 5 provides a summary of the key proposed changes to patient group involvement in the proposed drug reimbursement review processes.

Table 5: Key Milestones for Patient Group Engagement

	Current processes		Proposed aligned process
	Oncology	Non-oncology	
Timing of patient group input	**Start:** 20 business days prior to the anticipated date of filing **End:** 10 business days after the application has been filed **Total:** 30 business days	**Start:** 20 business days prior to the anticipated date of filing **End:** 15 business days after the application has been filed **Total:** 35 business days	**Start:** 20 business days prior to the anticipated date of filing **End:** 15 business days after the application has been filed **Total:** 35 business days
Filing patient group input	Uploaded to CADTH collaborative space (requires registration and login)	Uploaded to CADTH webpage (no registration or login required)	Uploaded to CADTH webpage (no registration or login required)
Patient group review of CADTH summary	Not applicable (patient groups are not currently provided with an opportunity to review the summary before it is incorporated in the report)	Patient groups can review and validate the summary of their input that has been written by CADTH	Patient groups can review and validate the summary of their input that has been written by CADTH
Posting complete patient group input	Not applicable (individual submissions are not posted on the CADTH website)	All patient group input submissions are posted on the CADTH website	All patient group input submissions will be posted on the CADTH website
Posting patient group input conflict of interest	All conflict of interest declarations from patient groups are posted without redaction (as of January 2, 2020)	All conflict of interest declarations from patient groups are posted without redaction	All patient group conflicts of interest will be posted without redaction
Commentary on recommendations	Patient groups can review and comment on initial recommendations	Not applicable (draft recommendations are issued under embargo)	Patient groups can review and comment on draft recommendations
Follow-up correspondence with CADTH	Verbal feedback from CADTH provided on request	Following completion of the review, patient groups receive a feedback letter from CADTH identifying aspects of the input that were especially helpful to CADTH staff and the expert committee	Following completion of the review, all groups that contribute input to a drug reimbursement review will receive a feedback letter

[a] Actual timelines for these steps may vary slightly depending on the work schedule for the review.
[b] This will include all conflict of interest declarations.

6.2.1 Timing of Patient Group Input

CADTH is proposing that the call for patient input will continue to be issued 20 business days prior to the anticipated date for the submission to be received. The time period for patient input will be at least 35 business days. This is consistent with the process for non-oncology drug reviews and will be adopted for all drug reimbursement reviews.

6.2.2 Format for Patient Group Input

CADTH has previously aligned the template for patient group input for its drug review processes (see the Patient Input Template).

6.2.3 Filing Patient Group Input

CADTH will no longer require patient groups to register and file their input using Collaborative Workspaces. As Collaborative Workspaces is primarily a tool to facilitate the secure exchange of confidential documentation with drug sponsors, CADTH will not require patient groups to continue to use this tool (as is currently required for oncology drug reviews). In addition to facilitating the patient input process, this change also offers efficiencies for CADTH as the agency will no longer be required to manage collaborative space accounts and provide technical support for patient groups.

6.2.4 Posting Patient Group Input

CADTH currently posts a summary of patient group input in both the oncology and non-oncology drug reimbursement review processes. In the existing non-oncology drug review process, all patient group input submissions are posted on the CADTH website in their entirety (typically within several weeks after the closing date for the call for patient input). This process will be expanded to all drug reimbursement reviews; a revision that will enhance transparency in the oncology drug review process. In January 2020, CADTH aligned its processes for disclosing conflict of interest declarations from patient groups by no longer redacting that information from patient group input for drugs being reviewed through the pCODR process (see *CADTH Drug Portfolio Information Session* and *CADTH Pharmaceutical Reviews Update — Issue 12* for details).

6.2.5 Patient Group Review of CADTH Summary

All patient group input received in CADTH's drug reimbursement review processes is collated and summarized for inclusion in the clinical reports. In CADTH's non-oncology drug review process, the draft summary that is prepared by CADTH is distributed to the patient groups for confirmation of accuracy. CADTH is proposing to extend this process to all drug reimbursement reviews; a revision that will enhance transparency in the oncology drug review process and ensure accuracy of the summary. As in the current process for non-oncology drugs, patient groups would be provided up to five business days to review and provide comments on the summary document.

6.2.6 Commentary on Draft Recommendations

As described in Section 8.5, CADTH will post draft recommendations for stakeholder feedback, including from patient groups. This is the current process used for oncology drug reviews and will be expanded to all drug reviews. Feedback from patient groups will be sought using a standardized template.

6.2.7 Follow-Up Correspondence

Once final recommendations have been published, CADTH will provide a personal letter to each patient group that contributed input. This letter will highlight aspects from the input that the review teams and expert committee members found especially useful and will offer suggestions for future submissions. Since April 2014, CADTH has prepared over 420 individual feedback letters to patient groups that have contributed input. Groups have indicated that they appreciate the letters and find the feedback helpful in preparing future input to CADTH.

6.3 Clinician Engagement

6.3.1 Call for Input From Clinician Groups

A summary of the key milestones for clinician group engagement in CADTH's proposed drug review process is provided in Table 6.

Table 6: Key Milestones for Clinician Groups

	Current process (oncology only)	Proposed process
Eligibility	Physicians who treat cancer patients, oncology nurses, and oncology pharmacists. Of note, the input from an oncology pharmacist and oncology nurse must be part of a joint submission with a registered physician treating the cancer indication.	Groups or associations of health care professionals practicing in the therapeutic area for which the drug under review is indicated. Individual clinicians who wish to provide input are encouraged to work with a group that represents their profession to prepare a group submission.
Timing of clinician group input	**Start:** 20 business days prior to the anticipated date of filing **End:** 10 business days after the application has been filed **Total:** 30 business days	**Start:** 20 business days prior to the anticipated date of filing **End:** 15 business days after the application has been filed **Total:** 35 business days
Filing clinician group input	Uploaded to CADTH collaborative space (requires registration and login).	Uploaded to CADTH webpage (no registration or login required).
Clinician group review of CADTH summary	Not applicable (clinicians are not currently provided with an opportunity to review the summary before it is incorporated in the report).	Clinician groups will have five business to review and validate the summary of their input that has been written by CADTH.
Posting complete clinician input	Not applicable (individual submissions are not posted on the CADTH website).	All clinician group input submissions will be posted in their entirety 10 business days after the deadline.
Posting clinician conflict of interest	All conflict of interest declarations from clinicians are posted without redaction (as of January 2, 2020).	All clinician group conflict of interest will be posted without redaction.
Commentary on recommendations	Clinicians have 10 business days to review and comment on initial recommendations.	Clinicians will have 10 business days to review and comment on draft recommendations.

[a] Actual timelines for these steps may vary slightly depending on the work schedule for the review.
[b] This will include all conflict of interest declarations.

a) Eligibility for Clinician Input

CADTH is proposing that a call for clinician input be issued for all pending drug reviews. As previously communicated at the CADTH Drug Portfolio Information Session, CADTH is proposing a new clinician engagement strategy that would focus on input from groups and associations of health care professionals (e.g., tumour groups, guideline groups, or professional associations) as opposed to individual clinicians. This revision is being made based on open input from individual health care professionals who have worked within with the oncology drug review process. The revised process will encourage individuals to work with associations on submissions to improve quality, reduce duplication of effort, and reduce the overall administrative burden for all participants.

b) Timing of Clinician Group Input

CADTH is proposing that the call for clinician group input continue to be issued 20 business days prior to the anticipated date of receipt of the application, and that the time period for clinician group input be at least 35 business days. This is identical to the proposed process for patient group input and the two processes would run concurrently.

c) Format for Clinician Group Input

CADTH will now be seeking input from clinician groups using a standardized template (see Clinician Group Input Template) that can be downloaded from the CADTH website. For efficiencies, the template will no longer be customized for each drug review and will use standardized sections and questions that will be continuously monitored and updated as required (based on experience and feedback from clinician groups). There are no changes proposed to the existing conflict of interest declaration section of the clinician input template.

d) Filing Clinician Group Input

Similar to the previously noted process for patient group input (Section 6.2.3), CADTH will no longer require clinician groups to file their input using Collaborative Workspaces. This is based on feedback on and experience with the oncology drug review process.

e) Posting Clinician Group Input

CADTH currently posts a summary of the clinician input that is received for oncology drug reviews, but not the individual summaries in their entirety. CADTH is proposing that all clinician input submissions be posted (in the same manner as currently occurs for patient input in the non-oncology drug review process; see Section 6.2.4 for details). CADTH ceased redacting conflict of interest information from clinician input received for oncology drugs in January 2020 (see *CADTH Drug Portfolio Information Session* and *CADTH Pharmaceutical Reviews Update — Issue 12* for details). This policy of transparency and disclosure will be continued in the aligned drug reimbursement review process.

f) Commentary on Draft Recommendations

As described in Section 8.5, CADTH will be posting draft recommendations for stakeholder feedback, including from clinician groups. This is the current process used for oncology drug

reviews and will be expanded to all drug reviews. Feedback from clinician groups will be sought using a standardized template.

6.3.2 Clinical Experts on the Review Team

a) Role of Clinical Experts

Clinical experts are a critical part of the review team and are involved in all phases of the review process (e.g., providing guidance on the development of the review protocol; assisting in the critical appraisal of clinical evidence; interpreting the clinical relevance of the results; and providing guidance on the potential place in therapy). In addition, clinical experts are invited to attend expert committee meetings to address any issues raised by the committee and provide input to assist in resolving requests for reconsideration and clarifications.

Table 7: Key Functions of Clinical Experts

Phase	Role in current processes		Role in proposed process
	Oncology	Non-oncology	
Review phase	• Providing guidance on the development of the review protocol • Assisting in the critical appraisal of the clinical evidence • Advising on assumptions used in the pharmacoeconomic analysis to assist in critical appraisal and inform CADTH reanalyses • Interpreting the clinical relevance of the results • Drafting the interpretation section of the clinical report • Providing guidance on the potential place in therapy • Advising on implementation issues raised by jurisdictions • Advising on treatment sequencing within a particular indication	• Providing guidance on the development of the review protocol • Assisting in the critical appraisal of the clinical evidence • Advising on assumptions used in the pharmacoeconomic analysis to assist in critical appraisal and inform CADTH reanalyses • Interpreting the clinical relevance of the results • Reviewing and advising on the appraisal and interpretation sections of the clinical report • Providing guidance on the potential place in therapy	• Providing guidance on the development of the review protocol • Assisting in the critical appraisal of clinical evidence • Interpreting the clinical relevance of the results • Providing guidance on the potential place in therapy • Reviewing and advising on the appraisal and interpretation sections of the clinical report • Advising on assumptions used in the pharmacoeconomic analysis to assist in critical appraisal and inform CADTH reanalyses • Advising on implementation issues raised by jurisdictions

Recommendation phase	• Attending expert committee meetings to address any issues raised by the committee	• Attending expert committee meetings to address any issues raised by the committee • Providing input on requests for reconsideration and clarification	• Attending expert committee meetings to address any issues raised by the committee • Providing input on requests for reconsideration
Implementation phase	• Not applicable	• As part of an implementation advice panel, experts may advise on outstanding implementation issues and further develop and refine reimbursement conditions	• As part of an implementation advice panel, experts may advise on outstanding implementation issues and further develop and refine reimbursement conditions • Advising on treatment sequencing within a particular indication for oncology drugs

b) Review Teams Experts and Clinical Panels

All CADTH review teams include at least one clinical specialist with expertise in the diagnosis and management of the condition for which the drug is indicated. CADTH increases the number of clinical specialists involved in each review depending on the complexity of the drug under review. In addition to including multiple core clinical specialists in the review team, CADTH may establish clinical panels for selected drugs with higher levels of complexity. These panels will be used to characterize unmet therapeutic needs, assist in identifying and communicating situations where there are gaps in the evidence that could be addressed through the collection of additional data, promote the early identification of potential implementation challenges, gain further insight into the clinical management of patients living with a condition, and explore the potential place in therapy of the drug (e.g., potential reimbursement conditions).

- Lower complexity drugs include all tailored reviews as well as standard reviews with the following characteristics: are follow-on products within established drug class, are reviewed through Health Canada's standard review pathway, and have a generally well-defined place in therapy. These reviews will typically include one to two clinical specialists as part of the review team and do not require convening a clinical panel.
- Higher complexity products include cell and gene therapies as well as standard reviews for products with the following characteristics: are often first-in-class, are reviewed through one of Health Canada's expedited review pathways (i.e., priority review or advance consideration under NOC/c policy), and have an undefined place in therapy. These reviews will typically include two to three clinical specialists as part of the review team and CADTH may convene a panel with additional clinical specialists.

The inclusion of a clinical panel in the review process will have no impact on the overall review timelines. The sponsor will be notified that the review will include a clinical panel at the time the submission or resubmission is accepted for review by CADTH.

c) CADTH and INESSS Joint Engagement

CADTH and INESSS will continue to jointly engage with clinical experts on selected drug products. Products selected for joint engagement with INESSS include those with the following characteristics: challenges in generating robust evidence due to the rarity of the condition, potential for challenging implementation issues, perceived ethical challenges for decision-makers, and high acquisition costs and/or substantial budget impact. There are no changes currently proposed for the processes for joint engagement between CADTH and INESSS. Please see Section 4.2.3 *Procedures for the CADTH Common Drug Review and Interim Plasma Protein Product Review* for details regarding this process.

d) Panel Composition

The panels will comprise clinical experts with experience in the diagnosis and management of the condition for which the drug under review is indicated. Whenever possible, CADTH will seek to obtain representation from across Canada. Potential experts will be identified by CADTH. The number of clinical specialists included on the panels may vary based on input from the drug programs and the complexity of the review. The identities of the clinical experts who participate in the panels will remain confidential.

The attendance at clinical panel meetings will be limited to the clinical experts, key expert committee members (i.e., chairs and lead discussants), and CADTH staff (i.e., review team members). If the drug is being reviewed through the CADTH and INESSS joint engagement process, staff from INESSS, as well as members of its expert committee, will also attend the clinical panel meetings.

e) Input From Clinical Panels

The clinical panels' activities will occur before the expert committee meeting to ensure that the committee has this information available to inform its deliberation and recommendation. The outcome of these panel meetings will be made available to the sponsor for review and commentary prior to the expert committee meeting. CADTH will aim to integrate the input of the clinical panel into the review report(s) before they are sent to the sponsor for review and commentary.

The reports will still be sent to the sponsor for comment in the event CADTH is unable to integrate the clinical panel's findings into the draft review report(s) at the time the distribution is scheduled to occur (e.g., due to challenges scheduling meetings with the clinical experts). In the event this occurs, the sponsor will receive the panel's findings for review and commentary in a separate distribution as soon as possible. CADTH will notify the sponsor if there are any anticipated delays regarding these steps in the process.

Any feedback from the sponsor regarding the input from the clinical panel will be reviewed and addressed by CADTH and the clinical experts (as required). The review report(s) will be revised as CADTH deems appropriate. The input from the clinical expert panel will be made available to the expert committee for its deliberations on the drug under review.

6.4 Drug Program Engagement

A summary of the key milestones for drug program engagement in the current and proposed drug review reimbursement processes is provided in Table 8.

Table 8: Key Milestones for Drug Program Engagement

	Current processes		Proposed process
	Oncology	Non-oncology	
Timing of drug program input	Drug programs currently provide input in the pre-submission phase (i.e., before the application has been filed by the sponsor).	Drug programs currently provide input late in the review phase (i.e., after the CADTH reports have been completed).	Drug programs will provide input early in the review phase (i.e., 10 to 15 business days after the file has been accepted for review by CADTH).
Documents provided to drug programs	Advance notification documentation.	Complete documentation provided by the sponsor and CADTH reports.	Advance notification documentation followed by the complete submission package filed by the sponsor.
Format for drug program input	CADTH creates a customized survey for each drug under review. All PAG members complete the survey in a blinded manner and the results are collated and finalized at a PAG meting.	CADTH provides a standardized template that is completed by the lead jurisdiction and finalized at an FWG meeting.	CADTH will provide a standardized template for completion by the lead jurisdiction. The initial draft will be discussed and finalized at the next scheduled PAG or FWG meeting.
Posting drug program input	PAG input is currently incorporated in the clinical guidance report and posted publicly.	FWG input is obtained after completion of the CADTH reports and is provided to the expert review committee before the meeting (it is not publicly posted).	Drug program input will be incorporated into the CADTH clinical report and posted publicly.
Role at expert committee meeting	At the pERC meeting, the lead jurisdiction presents a summary of the implementation issues that were identified by PAG.	At the request of the CDEC chair, the FWG chair (or other designated FWG member) may respond to questions from the expert committee.	Lead jurisdiction would present a summary of the implementation issues identified by the drug programs and respond to inquiries from the committee members.
Commentary on recommendations	PAG provides formal written feedback on all initial recommendations.	FWG discusses each recommendation, but formal written feedback is only required when the drug programs are filing a request for clarification.	Drug programs would provide formal written feedback on all draft recommendations.
Implementation phase	Not applicable.	Drug programs may request that an implementation advice panel be convened	Drug programs may request that an implementation advice panel be convened

CDEC = CADTH Canadian Drug Expert Committee; FWG = Formulary Working Group; PAG = Provincial Advisory Group; pERC = pan-Canadian Oncology Drug Review (pCODR) Expert Review Committee.

6.4.1 Format for Drug Program Input

CADTH is proposing that the engagement process with the drug programs be restructured to introduce efficiencies for both parties, including that new standardized templates be established for use by the drug programs in drafting their input. This is similar to the procedures used for non-oncology drug reviews and would replace the existing open-survey process that is used in the oncology review process. CADTH would assign a lead jurisdiction to prepare draft input, which would subsequently be reviewed and finalized at Provincial Advisory Group (PAG) and Formulary Working Group (FWG) meetings.

6.4.2 Timing of Drug Program Input

CADTH is proposing that the timing of drug program input be shifted to occur during the early stages of the review phase (i.e., shortly after CADTH has screened the documentation and accepted the application for review). This input is currently received in the pre-submission phase for oncology submissions and at the later stages of the review phase for non-oncology submissions (i.e., after CADTH has prepared draft clinical and economic review reports). This revision is being undertaken to ensure that all of the relevant information is available to the drug programs when advising CADTH on implementation issues (most notably the submitted price and budget impact analysis) and to allow their input to be drafted and finalized in time for inclusion in the draft CADTH reports at the time they are provided to sponsors for review and comment.

6.4.3 Inclusion of Drug Program Input in CADTH Reports

To offer the greatest possible transparency for stakeholders, CADTH is proposing that finalized drug program input be incorporated into the clinical reports for all drug reviews. This is consistent with the current oncology review process.

6.4.4 Presentation at Expert Review Committee Meeting

CADTH is proposing that the lead jurisdiction provide a brief overview of the input from the drug programs at the expert review committee meeting for all drug reviews. This is consistent with the current oncology drug review process.

7. REVIEW PROCEDURES

7.1 Standard Reviews

7.1.1 Clinical Review

CADTH will continue to conduct a systematic review for all drugs reviewed through the standard review process. CADTH sought consultation on the inclusion of a systematic literature review as a requirement for all submissions and resubmissions that are filed for review through the standard review processes (see *Proposal to Revise Category 1 Requirements* for details), and heard from stakeholders that revisions to the drug review processes should be phased in gradually, as a result of the numerous changes that are currently occurring within the Canadian

regulatory and health technology assessment processes. CADTH acknowledges this feedback and will not be mandating that sponsors file a systematic literature review at this time. However, CADTH remains interested in pursuing this procedural revision as it offers efficiencies and will promote alignment throughout Canadian and international health technology assessment requirements. Stakeholders will be notified and consulted on guidance documentation for filing a systematic literature review at a later date.

The clinical review processes for oncology and non-oncology drugs were generally similar. CADTH has reviewed its internal processes and developed a revised process that will build on the strengths of the existing processes. As noted in Section 6.4.3, drug program input will be incorporated into the clinical review report to improve transparency (as is currently done in the oncology drug review process).

7.1.2 Economic Review

CADTH has launched an aligned pharmacoeconomic review template for all drug reimbursement reviews. As described in Section 2.2.1, CADTH will begin posting the complete pharmacoeconomic review (with confidential information redacted at the sponsor's request) for all drug reimbursement reviews. This is consistent with the existing process for non-oncology drugs and will improved the transparency of the oncology drug review process (as only an executive summary is currently posted).

7.2 Cell and Gene Therapy Reviews

7.2.1 Clinical and Economic Review

The clinical and economic reviews for cell and gene therapies will continue to be completed in accordance with the procedures applied for standard reviews

7.2.2 Ethics Review

There are no changes being proposed related to the review of ethical considerations for cell and gene therapies; however, CADTH is providing additional details regarding this part of the process.

- At the process's initiation, CADTH develops a review plan to ensure that the review will capture pertinent ethical considerations. The plan specifies the following parameters of the review:
  - The technology and related technologies, populations, context, and types of publications that will be used to conduct a literature review.
  - The framework or guidance tool used to identify ethical considerations in the published literature.
- Where the scope of the ethics review includes broader technology or condition topics than the specific product and indication under assessment, CADTH ethics reviewers will work with the economic and clinical reviewers to scrutinize the proposed broader topics for their relevance. The rationale for expanding the scope to include related technologies and conditions with similar ethical considerations will be detailed in the final report.

- The ethics review will incorporate a description of the included publications, including a summary of the country in which the publication originated, the objective of the publication, its key ethical aspects, and its funding source.
- The reporting of ethical considerations will comprise a descriptive, narrative summary of ethical aspects derived from the considerations that are identified in the published literature.
- The ethics review report will be prepared in accordance with a template.

7.2.3 Implementation Plan Review

Sponsors will continue to be required to complete a template with key details about their plans to implement the drug in the Canadian system. The drug programs will be asked to review and comment on the sponsor's completed implementation plan. Their feedback on the implementation plan could help provide early identification of potential access issues within the different jurisdictions, potential issues with administration or distribution mechanisms (e.g., need for specialty clinics), and/or challenges with diagnostic testing requirements. This approach will allow CADTH and the participating jurisdictions to efficiently reflect on potential implementation issues and corresponding mitigation strategies. CADTH is not currently proposing any revisions to the implementation plan template or process, but welcomes any stakeholder comments to the implementation plan.

7.3 Tailored Reviews

CADTH is proposing that the existing tailored review process for select non-oncology drugs be expanded to oncology drugs as well. As with the existing processes for non-oncology drugs, tailored reviews will be conducted for a subset of new combination products and new formulations of existing drugs. There are no changes proposed to the existing *Tailored Review Application Form* or *Tailored Review Submission Template*. CADTH welcomes stakeholder commentary on the existing tailored review process.

8. RECOMMENDATION PROCEDURES

8.1 Expert Review Committees

CADTH will continue to use the same expert review committees for drug reimbursement reviews:

- the pan-Canadian Oncology Drug Review Expert Review Committee (pERC) will be used for drugs that are eligible for review through CADTH's pCODR program
- CDEC will be used for drugs that are reviewed through CADTH's CDR program
- the Canadian Plasma Protein Product Expert Committee (CPEC; a subcommittee of CDEC) will continue to be used for products that are reviewed through the PPP process.

CADTH is seeking to amend the structures of CDEC and pERC as follows:

- the size of the committee membership will be aligned
- an ethicist will be added to all committees
- the terms of reference for these committees are currently under development for alignment and will be posted at a later date.

8.2 Expert Committee Briefing Materials

CADTH will be aligning the structure and content of the briefing materials that are provided to the expert review committees. The committee briefing materials will be distributed to the expert review committee members at least 10 business days prior to the meeting date. This is consistent with process for non-oncology drug reviews and will be adopted for all drug reimbursement reviews (as this is currently five business for oncology drug reviews).

Table 9: Proposed Timelines for Issuing Committee Briefing Materials

Current processes		Proposed process
Oncology	Non-oncology	
Five business days prior to the expert review committee meeting	Ten business days prior to the expert review committee meeting	Ten business days prior to the expert review committee meeting

8.3 Deliberative Process and Framework

As communicated in November 2019 at the *CADTH Drug Portfolio Information Session*, CADTH is currently undertaking a review of the deliberative processes used by its expert review committees. The time frame for consulting on the proposed aligned deliberative process and framework for CADTH's drug reimbursement reviews has been adjusted due to the COVID-19 pandemic. Additional details will be announced at a later date.

8.4 Recommendation Framework

CADTH introduced an aligned recommendation framework for the CDR and pCODR processes in March 2016 (see *Common Drug Review Update — Issue 118* for the announcement). There are no changes being proposed to the recommendation framework at this time, so these recommendation options will remain that a drug be reimbursed; that a drug be reimbursed with conditions; or that a drug not be reimbursed. This framework is described in Table 10.

Table 10: Recommendations Framework

Category	Description
Reimburse	The drug under review demonstrates comparable or added clinical benefit and acceptable cost and cost-effectiveness relative to one or more appropriate comparators[a] to recommend reimbursement in accordance with the defined patient population under review, which is typically the patient population defined in the Health Canada–approved indication (as applicable).

Reimburse with conditions	Scenarios that could be considered under this category include: • The drug under review demonstrates comparable or added clinical benefit **and** acceptable cost and cost-effectiveness relative to one or more appropriate comparators in a subgroup of patients within the approved indication. In such cases, conditions are specified to identify the subgroup. • The drug under review demonstrates comparable clinical benefit **and** acceptable cost and cost-effectiveness relative to one or more appropriate comparators.[a] In such cases, a condition may include that the drug be listed in a similar manner to one or more appropriate comparators.[a] • The drug under review demonstrates comparable or added clinical benefit, **but** the cost and cost-effectiveness relative to one or more appropriate comparators[a] is unacceptable. In such cases, an included condition may be a reduced price. • The drug under review demonstrates clinical benefit, with a greater degree of uncertainty and an acceptable balance between benefits and harms, in a therapeutic area with significant unmet clinical need. In such cases, if the cost and cost-effectiveness relative to one or more appropriate comparators[a] is unacceptable, an included condition may be a reduced price.
Do not reimburse	There is insufficient evidence identified to recommend reimbursement. Scenarios that typically fit this recommendation category include: • The drug under review does not demonstrate comparable clinical benefit relative to one or more appropriate comparators.[a] • The drug under review demonstrates inferior clinical outcomes or significant clinical harm relative to one or more appropriate comparators.[a]

Note: Existing treatment options may include best supportive care and non-pharmaceutical health technologies or procedures.

[a] An appropriate comparator is typically a drug reimbursed by one or more drug programs for the indication under review. However, the choice of appropriate comparator(s) in the review is made on a case-by-case basis and considers input from both jurisdictions and clinical experts.

8.5 Draft Recommendations

A summary of CADTH's proposal for issuing and posting draft recommendations for drug reimbursement reviews is provided in Table 11. For comparison purposes, this table includes a summary of the existing oncology and non-oncology processes. Details regarding the proposed process steps and the rationale for any revisions are provided in the following sections.

Table 11: Proposed Timelines for Issuing and Posting Draft Recommendations

Key Milestones	Current processes		Proposed process
	Oncology	Non-oncology	
Issuance to sponsor and drug programs	Not applicable (non-redacted recommendation is not distributed to sponsor)	Eight to 10 business days after the expert review committee meeting	Eight to 10 business days after the expert review committee meeting
Identification of confidential information		One business day after issuance by CADTH	One business day after issuance by CADTH
Redaction by CADTH		One business day after receipt from sponsor	One business day after receipt from sponsor

Posting on CADTH's website	Ten business days after the expert review committee meeting	Not applicable (recommendations currently issued under embargo)	Next scheduled issuance of CADTH's program updates (13 to 14 business days after the expert review committee meeting)
Stakeholder feedback period	Ten business days after posting on CADTH's website		Ten business days after posting on CADTH's website

8.5.1 Issuing Draft Recommendations

To ensure that decision-makers have access to all relevant information regarding the drug under review, CADTH will continue to issue non-redacted recommendations to the sponsor and drug programs before public posting. As shown in Table 11, this is consistent with the existing process for non-oncology drugs and will be expanded to all drug reimbursement reviews, as under the existing oncology drug review process, the non-redacted recommendation is not currently distributed to the sponsor.

As described in Section 2.4.2, issuance of the draft recommendation to the sponsor and drug programs will represent the deadline for the 180-calendar day performance metric.

8.5.2 Redaction of Confidential Information in Draft Recommendations

Once the draft recommendation has been issued, the sponsor will have one business day to identify and request the redaction of any confidential information contained in the recommendation. CADTH will redact information in accordance with the confidentiality guidelines before posting for stakeholder feedback.

Stakeholders are reminded to please review the proposed revisions to the confidentiality guidelines when considering this consultation.

8.5.3 Posting Draft Recommendations

CADTH is proposing that all draft recommendations be posted for stakeholder feedback. This is part of the current review process for oncology drugs and will be expanded to all drug reimbursement reviews. CADTH believes this is an important revision to improve the transparency of its drug review processes. The posting of the draft recommendations will typically occur at the next scheduled issuance of CADTH's program updates (as described in Section 2.1.1, this will be consolidated and issued once per week). This will typically occur 13 to 14 days after the expert review committee meeting for non-oncology and oncology drug reviews, respectively.

8.5.4 Stakeholder Feedback on Draft Recommendations

a) Eligibility for Stakeholder Feedback

The following stakeholders will be eligible to provide feedback on the draft recommendations:

- the sponsor of the submission, resubmission, or reassessment
- the DIN holder of the drug under review (if the sponsor is a tumour group)
- patient groups that responded to the call for patient input
- clinician groups that responded to the call for clinician input
- the drug programs (including Canadian Blood Services, pCPA, and CAPCA).

b) Stakeholder Feedback Period

As with the existing oncology review process, CADTH is proposing that the stakeholder feedback period be 10 business days, with the feedback period beginning on the first day after the recommendation has been posted (i.e., the day the recommendation is posted will be day zero).

c) Format for Stakeholder Feedback

CADTH is proposing that stakeholder feedback on draft recommendations be obtained using a standardized template. This will be similar to the existing process for oncology drugs; however, the proposed form has been revised to accommodate the proposed changes to the reconsideration process described in Section 8.6. Interested stakeholders are asked to review and comment on the proposed form (see Table 12).

d) Filing Stakeholder Input

Similar to the process revisions described in sections 6.2.3 and 6.3.1, CADTH will no longer require patient groups or clinician groups to register and file their feedback using Collaborative Workspaces. This change offers efficiencies for CADTH as the agency will no longer be required to manage collaborative space accounts and provide technical support for patient and clinician groups.

Table 12: Proposed Stakeholder Feedback Form

Stakeholder agreement with the draft recommendation		
1. Please indicate if the stakeholder agrees with the expert review committee's recommendation.	Yes	☐
	No	☐
Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.		
Expert review committee consideration of the stakeholder input		
2. Does the draft recommendation demonstrate that the expert review committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐
If not, what aspects are missing from the draft recommendation?		
Accuracy of the summary of stakeholder input		
3. Does the draft recommendation accurately summarize the stakeholder's input for the drug under review?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification or has been omitted from the recommendation.		
Clarity of the draft recommendation		
4. Are the reasons for the draft recommendation clearly stated in the draft recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification.		
5. Have the implementation issues been clearly articulated and adequately addressed in the draft recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification.		
6. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the draft recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification.		

8.6 Reconsideration Process

8.6.1 New Reconsideration Options

CADTH is proposing that the existing reconsideration processes be aligned and updated to establish multiple options for reconsideration that allow greater flexibility for sponsors, drug programs, and CADTH. As shown in Table 13, reconsideration requests would be stratified depending on the focus, complexity, and effort required to address the request. Three categories are being proposed: major revisions, minor revisions, and editorial revisions. These categories have been developed by CADTH based on a retrospective review of the feedback received from sponsors over several years. CADTH has found that there are situations where sponsors are interested in discussing revisions to the recommendations, but are unwilling to participate in the complete reconsideration processes that are currently available (citing

concerns with overall timelines). The options proposed in Table 13 are primarily intended to provide additional flexibility before the recommendation is finalized.

Table 13: Proposed Reconsideration Options

	Major revisions	Minor revisions	Editorial revisions
Criteria	Reconsideration requests that are focused on the revised recommendation category (e.g., do not reimburse); or requests that would result in changes to the patient population that would be eligible for reimbursement with the drug under review (e.g., expansion of the patient population address in the initiation criteria).	Reconsideration requests that are focused on any of the following aspects of the recommendation: reimbursement conditions within the patient population for whom reimbursement of the drug under review has been recommended (e.g., renewal criteria, pricing conditions, or administration criteria); implementation guidance provided by the expert review committee; or reasons for recommendation.	Requests for CADTH to revise the text in the recommendation to provide additional clarity and details regarding the recommendation, evidence that was considered, the deliberative process, or reasons for recommendation.
Deliberation	All requests for major revisions to the recommendation would be addressed through discussion and deliberation with the full expert review committee.	CADTH proposes that the majority of requests for minor revisions would be addressed through discussion and deliberation with a subpanel of the expert review committee (e.g., chair, lead discussants, and patient and public members) with additional support from clinical experts, as required.	CADTH staff and the expert review committee chair will address the majority of requests for editorial revisions. Other committee members will be consulted, as required.
Outcomes	Should the recommendation be substantially revised following deliberation on the reconsideration request, CADTH would issue another draft recommendation for stakeholder feedback. A final recommendation would be issued if the committee upheld the existing recommendation or made only minor revisions to the recommendation.	To expedite the review timelines, CADTH would not issue another draft recommendation following deliberations on a request for minor revisions. A final recommendation would be issued whether or not the committee decided to uphold the existing recommendation or make minor revisions to the recommendation.	These will be limited to editorial revisions or corrections that do not impact the reimbursement recommendation.
Timelines	Requests for major revisions to a recommendation would typically require two to three months to address.	Requests for minor revisions to a recommendation would typically require one month to address.	A final recommendation would be issued in accordance with standard timelines (i.e., there would be no delay as a result of editorial revisions).

Eligibility	Due the resources required to address these requests and the implications for timelines, CADTH is proposing that only those stakeholders that will be directly involved in the negotiations for the drug under review be permitted to file these requests (i.e., the sponsor and the drug programs).		All stakeholders that are eligible to provide input on CADTH's recommendations may request editorial revisions.
Patient and clinician group feedback	Feedback from clinicians and patient groups on the recommendation would be considered by the committee in the deliberations for the reconsideration request.	Feedback from clinicians and patient groups on the recommendation would be considered by the committee in the deliberations for the reconsideration request.	Patient and clinician groups may request editorial revisions.
Fee schedule	Requests filed by sponsors would be subject to a schedule D application fee.		Not applicable.

8.6.2 Eligibility to Request Reconsideration

In the past, reconsideration procedures represented a major difference between the oncology and non-oncology drug review processes. In the non-oncology processes, a request for reconsideration could only be filed by the sponsor and was limited to a small minority of drug reviews (i.e., approximately 20% underwent reconsideration). In contrast, the decision to undertake a reconsideration in the oncology drug review process was determined by a panel of three members from pERC based on stakeholder feedback, and most drugs underwent reconsideration prior to finalization (approximately 70%). Reconsiderations result in a significant extension of the overall review timelines (typically two to three months) and have important resource implications for CADTH, as well as for the sponsors. As a result, CADTH is proposing that only those stakeholders that will be directly involved in the negotiations for the drug under review be permitted to file these requests (i.e., the sponsor and the drug programs). This will help provide greater predictability in the review timelines for sponsors, minimize the overall review timelines for decision-makers and patients, and help to avoid delays to accessing new medications. Feedback from clinicians and patient groups on the draft recommendation would be considered by the committee members in the deliberations for the reconsideration request.

8.6.3 Revised Recommendations Following a Reconsideration

In situations where the committee's recommendation has been substantially revised following a request for major revisions, CADTH would issue another draft recommendation for stakeholder feedback. This is similar to the current process used for non-oncology drugs to ensure that feedback is reflective of the most current recommendation. Specifically, this process would apply in following circumstances:

- a draft recommendation stating that a drug not be reimbursed was revised to state that the drug should be reimbursed with or without conditions
- a draft recommendation stating that a drug should be reimbursed with or without conditions was revised to state that the drug should not be reimbursed
- the patient population eligible for reimbursement has been expanded or narrowed following the reconsideration.

8.6.4 Reconsideration Meetings

CADTH currently offers sponsors the opportunity for a teleconference to elaborate on the issues that were raised in the request for reconsideration. As communicated at the *CADTH Drug Portfolio Information Session* in November 2019, CADTH is proposing that these reconsideration teleconferences be offered for all drug reimbursement reviews. Details of CADTH's proposed process are provided as follows.

a) Attendance

The sponsor would be free to select their attendees. Sponsors are welcome to invite clinical experts to participate in the teleconference, provided they have agreed to maintain the confidentiality of the proceedings, including any CADTH documents that have not been posted publicly. Key CADTH staff will attend the teleconference (e.g., program directors and review team members). With the exception of the review manager(s),the names of the review team members are not disclosed to the sponsor.

b) Meeting Logistics and Agenda

Reconsiderations meeting will only be offered via teleconference and will be a maximum of one hour. In-person meetings, video conferencing, or webinars will be not offered for reconsideration meetings. CADTH will provide the teleconference information prior to the meeting and may record the call for internal purposes. If providing a presentation, the sponsor must limit the number of slides to 30 or less.

c) Summary of the Discussion

The sponsor will be required to prepare a draft summary of the discussion using the template provided by CADTH. The summary must not exceed two pages and must be submitted to CADTH in accordance with the deadlines provided at the meeting. Delays in providing the summary could impact the target expert committee meeting. CADTH staff will review and finalize the summary (revising as required to ensure clarity). The final summary document will be provided to the sponsor and included in the committee briefing materials.

8.6.5 Application Fees for Reconsiderations

As described in Section 2.4.1, CADTH is proposing that requests for major or minor revisions to draft recommendations that are filed by sponsors be subject to a schedule D application fee. As part of CADTH's cost-recovery initiatives, a schedule D fee is currently applied only for reconsideration requests for non-oncology drugs. This would be expanded to all drug reimbursement reviews to help ensure the sustainability of CADTH's programs.

8.7 Final Recommendations

A summary of CADTH's proposal for issuing and posting final recommendations for drug reimbursement reviews is provided in Table 14. For comparison purposes, this table includes a

summary of the existing oncology and non-oncology processes. Details regarding the proposed process steps and the rationale for any revisions are provided in the following sections.

Table 14: Proposed Timelines for Issuing Final Recommendations

Milestones	Current processes		Proposed timing
	Oncology	Non-oncology	
Issuance to sponsor and drug programs where there is no reconsideration	Not applicable (non-redacted recommendation is not distributed to sponsor)	Five business days after the end of the embargo period	Five business days after the end of the stakeholder feedback period
Issuance to sponsor and drug programs following a reconsideration		Five business days after the expert review committee meeting	Eight to 10 business days after the expert review committee meeting
Sponsor identifies confidential information		Sponsor has one business day to identify confidential information	Sponsor has one business day to identify any confidential information
Redaction of confidential information by CADTH		CADTH redacts information one business day after receipt from sponsor	CADTH will redact information one business day after receipt from sponsor
Posting on CADTH's website when there has not been a reconsideration	Two business days after the end of the stakeholder feedback period	Two business days after the recommendation is issued to the sponsors and drug plans	Two business days after the recommendation is issued to the sponsors and drug plans
Posting on CADTH's website following a reconsideration	10 business days after the expert review committee meeting	Two business days after the recommendation is issued to the sponsors and drug plans	

8.7.1 Issuing Final Recommendations

To ensure that decision-makers have access to all relevant information regarding the drug under review, CADTH will continue to issue non-redacted recommendations to the sponsor and drug programs prior to public posting. Currently, there are differences in the timing for issuing final recommendations for oncology and non-oncology drugs; therefore, CADTH is proposing to align and streamline the processes for issuing final recommendations to sponsors and drug programs. As shown in Table 14, CADTH is proposing the following process:

- If there is no request for reconsideration, CADTH will issue final recommendations to the sponsor and drug programs five business days after the end of the stakeholder feedback period.
- If there is a request for reconsideration, CADTH will issue the final recommendation (provided the recommendation has not been substantially revised, as described in Section 8.6.3) eight to 10 business after the expert review committee meeting. This will introduce efficiencies for CADTH by streamlining the workflow for all recommendations being issued from each expert review committee meeting (i.e., both draft recommendations and final recommendations will be distributed according to the same schedule).

8.7.2 Redaction of Confidential Information in Final Recommendations

Once the final recommendation has been issued, the sponsor will have one business day to identify and request the redaction of any confidential information contained within it. CADTH will redact information in accordance with the confidentiality guidelines before posting for stakeholder feedback. Stakeholders are reminded to review the proposed revisions to the confidentiality guidelines when considering this consultation.

8.7.3 Posting Final Recommendations

As described in Section 8.7.2, sponsors may request the redaction of any confidential information in the final recommendation prior to its posting on the CADTH website. The posting of final recommendations will typically occur one to two business days following receipt of the sponsors completed *Identification of Confidential Information Form*. The recommendation will be available as soon as posted; however, posting will be communicated at the next scheduled issuance of CADTH's program updates (as described in Section 2.1.1, this will be consolidated and issued once per week).

9. TEMPORARY SUSPENSION PROCEDURES

CADTH's procedures for the temporary suspension of reviews is currently aligned across the oncology and non-oncology processes. No revisions are being proposed at this time; however, stakeholders are encouraged to consider the consultation regarding mandatory information sharing between Health Canada, CADTH, and INESSS for all submissions filed on a pre-NOC basis (as this proposal could provide additional opportunities for sponsors to have a file suspended rather than withdrawn in situations where a notice of deficiency or notice of non-compliance is issued by Health Canada).

10. WITHDRAWAL PROCEDURES

CADTH will be expanding the existing withdrawal procedures for non-oncology drugs to all drug reimbursement reviews. The following key changes will occur:

- The existing pCODR procedures state that a sponsor may voluntarily withdraw from CADTH's process at any time up until the final recommendation has been issued. Following stakeholder consultation in September 2015 (see *Common Drug Review Update – Issue 111* for details), CADTH revised this process for non-oncology submissions to set a clear deadline for voluntary withdrawal. This revision was made to ensure that CADTH's limited resources are used effectively. CADTH is proposing that sponsors may request voluntary withdrawal from CADTH's drug reimbursement review process at any time up until 4:00 p.m. EST three business days before the target expert committee meeting is scheduled.
- The existing pCODR procedures state that PAG may request that CADTH continue the review of a drug that has been voluntarily withdrawn by the sponsor. CADTH discontinued this process in 2014 for non-oncology submissions due to practical challenges with continuing a review process in the absence of participation or documentation from the

sponsor. CADTH is proposing that this be discontinued in the drug reimbursement review process, as well, and that voluntary withdraw result in cessation of work on the file by CADTH.

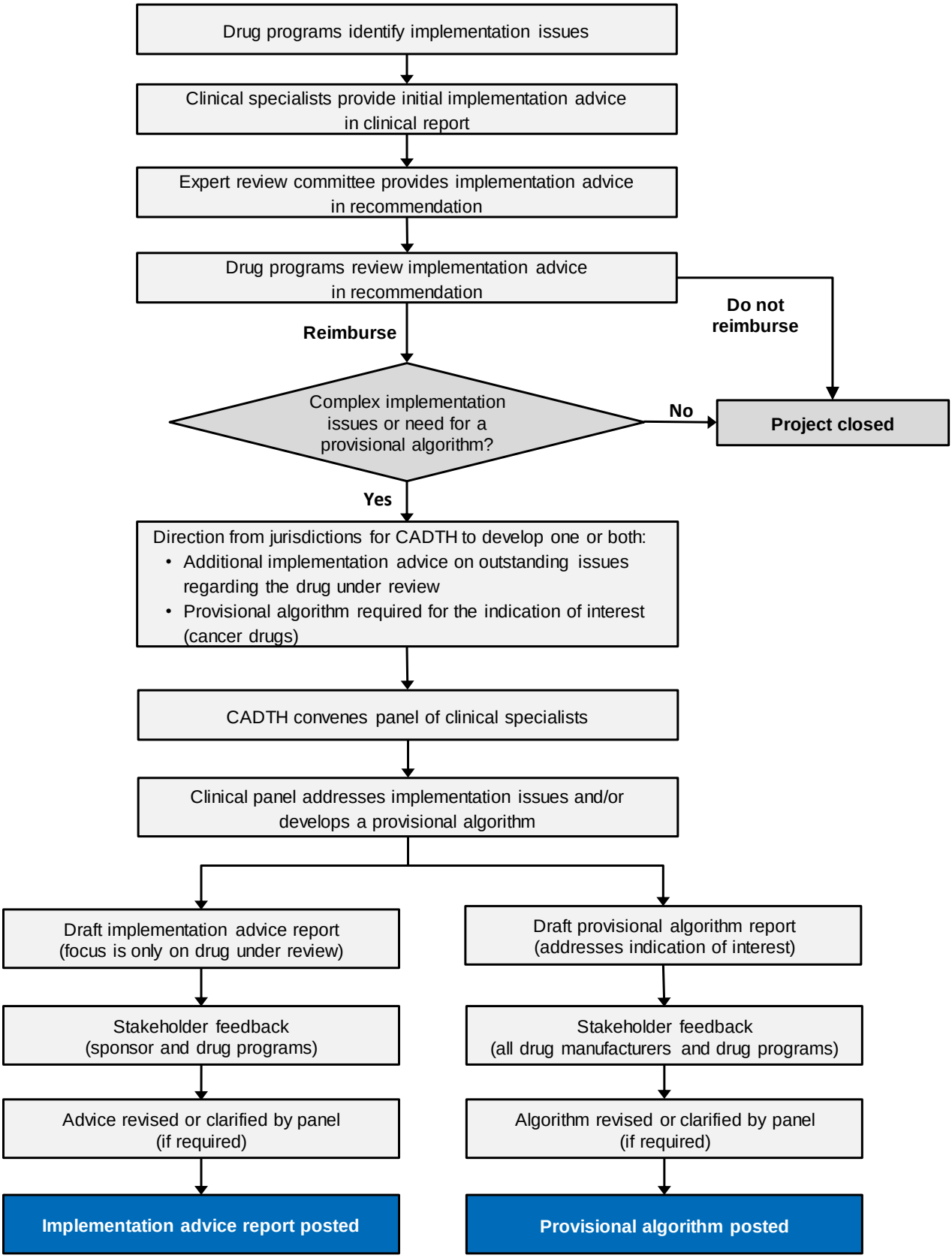
11. IMPLEMENTATION PROCEDURES

After a final recommendation has been issued, CADTH provides the drug programs with support in implementing the recommendation. This can include, but is not limited to, refining reimbursement conditions and developing advice on implementation issues for drugs that have been reviewed by CADTH. This support is distinct from the drug reimbursement review process and is offered for the purposes of assisting jurisdictions in addressing implementation issues that could not be addressed in the CADTH drug reimbursement recommendation due to a high degree of complexity, lack of clinical evidence, or other factors.

In the proposed aligned drug review processes, there will be two primary forms of implementation advice offered by CADTH:

- implementation advice regarding the drug under review (i.e., addressing any outstanding issues from the drug reimbursement review)
- development of provisional algorithms that address the sequencing of oncology treatments within a particular indication.

Figure 5: CADTH Implementation Advice and Provisional Algorithm Processes



11.1 Implementation Advice Regarding a Drug Reimbursement Recommendation

CADTH's goal is to ensure that all recommendations contain all of the information required for the drug programs to make a reimbursement decision regarding the drug under review; however, there may be instances where additional implementation advice is required due to limitations with the available evidence or the need for additional consultation with subject matter experts. In the existing non-oncology drug review processes, CADTH currently develops implementation advice reports at the request of the drug programs to advise on any outstanding issues. Following consultation with the drug programs, CADTH will be expanding this process to include oncology drugs as well.

Examples of when implementation advice is required may include, but are not limited to, the following:

- The expert review committee concludes that the comparative clinical benefit of the drug has been demonstrated, but that a panel of clinical specialists could be convened in order to specify the conditions that are essential to ensure that the treatment is reimbursed in the most appropriate manner (e.g., by taking into account issues such as budget constraints).
- The drug programs communicate that there is a need to investigate potential reimbursement criteria for patient populations that may not be addressed by the existing indications and/or recommendations (e.g., understudied populations where there may be an unmet therapeutic need).

Implementation advice reports will typically be prepared after CADTH has issued a recommendation that the drug under review be reimbursed by the drug programs (i.e., these reports will not typically be initiated in situations where the expert review committee has recommended that the drug under review not be reimbursed by the drug programs). The procedures for implementation advice reports will be the same as those currently described in Section 14.1 of the *Procedures for the CADTH Common Drug Review and Interim Plasma Protein Product Review*.

11.2 Development of Provisional Algorithms

As part of its ongoing initiative to align its drug reimbursement review process, CADTH has undertaken an internal review of the provisional algorithm process that was launched in July 2019. The objective of this review is to introduce efficiencies for CADTH, provide greater clarity to sponsors regarding the required documentation for the algorithm process, and further enhance the transparency of the process for pharmaceutical manufacturers. These revisions are summarized in Table 14 and described in detail in the following sections.

Table 15: Revisions to the Provisional Algorithm Process for Oncology Drugs

	Previous process	Revised process
Eligibility for provisional algorithm	Provisional algorithm work undertaken for all drugs filed for review through the pCODR process.	Provisional algorithm work will be undertaken for oncology drugs that receive a pERC recommendation in favour of reimbursement and CADTH receives direction from the drug programs that a provisional algorithm is required for implementation.
Required documentation	Filing a proposed algorithm is optional for the sponsor of the drug under review.	A new mandatory submission template for sponsors to clearly articulate their proposed place in therapy for the drug. This has detailed instructions for sponsors, will be screened by CADTH prior to acceptance for review, and will help inform the drug programs about the need for CADTH to develop a provisional algorithm.
Timing for initiation	Provisional algorithm work is initiated in the pre-submission phase (i.e., three to four months prior to an application being received by CADTH).	Provisional algorithm work will be initiated in the implementation phase (i.e., when a final recommendation has been issued in favour of reimbursement).
Timing for completion	Provisional algorithm work is completed at the time the pERC final recommendation has been issued.	Provisional algorithm work is completed two to three months after pERC final recommendation has been issued (depending on complexity, number of industry participants, and availability of clinical specialists).
Industry participants	Industry participation is limited to the sponsor of the drug under review through the pCODR process.	Industry participants will include the following: • sponsor of the drug under review through the pCODR process; and, • all other manufacturers whose products may be directly impacted by the algorithm established by CADTH.
Algorithm reporting	Provisional algorithms are to be reported in the pERC final recommendation (only if the recommendation is in favour of reimbursement).	Provisional algorithms will be reported in a distinct CADTH report that is separate from all documentation related to the oncology drug submission(s) that triggered the need for the development of the algorithm.

pCODR = pan-Canadian Oncology Drug Review; pERC = pCODR Expert Review Committee.

11.2.1 Eligibility and Initiation

CADTH has revised the provisional algorithm process and these projects will be initiated only in the following instances:

- following issuance of a recommendation in favour of reimbursement for a drug with the potential to impact the existing funding algorithm for the indication of interest; or
- identification of new evidence that may disrupt the sequencing of drugs; and
- the participating drug programs indicate that a provisional algorithm is required for implementation purposes.

These revisions will introduce important efficiencies for CADTH by ensuring that substantial effort is not invested in developing and refining provisional algorithms for drugs that are not recommended for reimbursement, which will allow CADTH to expand engagement with other drug manufacturers (as described in Section 11.2.2).

Since the initial launch of the provisional algorithm process, CADTH has encountered issues with the quality and quantity of information being filed by drug manufacturers. In addition, sponsors have expressed some uncertainty regarding their obligations when preparing the required documentation. As described in Section 4.2.2, CADTH has created a new mandatory submission template for sponsors to clearly articulate their proposed place in therapy for the drug. This template has detailed instructions for sponsors, will be screened by CADTH prior to acceptance for review, and will help inform the drug programs regarding the need for CADTH to develop a provisional algorithm if the drug under review is recommended for reimbursement.

11.2.2 Stakeholder Engagement

a) Industry Engagement

CADTH is revising the provisional algorithm process to align with its current therapeutic review processes with respect to engagement with drug manufacturers. As previously described, the revised process will now be undertaken after the completion of one or more drug reimbursement reviews. The revise process will be conducted in a manner that ensures that drug manufacturers whose products may be directly impacted by the provisional algorithm are aware of the review, and that one or more of their products may be impacted as a result; and that all drug manufacturers whose products may be directly impacted are given the opportunity to provide input into the process.

For drug manufacturers other than sponsor for the drug under review, the opportunity to participate in the implementation advice process will only apply in situations where CADTH has been asked to directly comment on one or more of that manufacturer's product(s). CADTH will notify all impacted manufacturers (i.e., DIN holders) with the following information:

- that CADTH will be developing a provisional algorithm for the indication of interest
- that one or more of their products may be impacted by CADTH's report.

Upon notification that the algorithm is being developed by CADTH, all manufacturers with products that fall with the scope of the provisional algorithm will have 10 business days to provide written input to CADTH regarding their perspective on the treatment algorithm and the

place in therapy for their product(s). This input must be provided using the template provided by CADTH and must not contain any confidential information (as all information included will be considered disclosable by CADTH).

Once CADTH has drafted the implementation advice report that includes the sequencing of treatments, the manufacturer(s) will be provided with an embargoed copy for review and comments. The feedback period will be five business days and all feedback must be provided using the standardized template provided by CADTH. CADTH will review and discuss the feedback from the manufacturer(s) with the implementation advice panel and the report will be revised as required.

b) Drug Program Engagement

The participating drug programs will be engaged throughout all phases of the provisional algorithm process. To help ensure that the issues are clearly addressed by the panel and to help expedite the overall process, representatives from CAPCA, pCPA, and/or the drug programs will have the opportunity to participate in panel meetings and comment on the draft report.

c) Patient and Clinician Group Engagement

The implementation panelists will be provided with a summary of the patient group and clinician group input submissions that were received as a result of the call for input and incorporated into the reimbursement review process for the drug(s) that triggered the need for the development of the provisional algorithm. This information will provide important context for the panel's deliberations. In order to expedite the algorithm development process, CADTH will not undertake additional calls for patient group input or clinician group input for these projects.

11.2.3 Implementation Panel and Deliberative Process

CADTH will convene clinical panels to advise on provisional algorithms. The panelists will be comprised of clinical specialists with expertise in the diagnosis and management of the condition for which the provisional algorithm is required. The clinicians will primarily be identified by CAPCA (e.g., clinical leads affiliated with provincial cancer agencies), and will join a panel chair that will be determined by CADTH. All panelists will be required to comply with CADTH's conflict of interest policies.

Panelists will be provided with details regarding the provisional algorithm process, including the deliberative framework, the existing provisional algorithm, the sponsor's proposed place in therapy for the drug(s) reviewed through pCODR that triggered the need for the algorithm review, and the input from other drug manufacturers.

The deliberations regarding the provisional algorithm will be focused on addressing a specific policy question raised by the jurisdictions. This will typically be related to understanding the implications of one or more new provisional therapies on the existing sequence of treatments that are funded by the jurisdictions. The following items will be considered by the expert panels when advising the jurisdictions on the provisional algorithm for the relevant indication:

- unmet therapeutic need for patients (particularly those in understudied populations)

- evidence supporting a particular sequence of therapies (if available)
- clinical experience and opinion that support a particular sequence of therapies
- clinical practice guidelines
- variability across jurisdictions regarding the reimbursement status of existing treatment options
- affordability and sustainability of the health care system
- implementation considerations at the jurisdictional level.

Clinical and economic evidence to inform the optimal treatment sequence is typically limited; therefore, the clinical experience and knowledge of Canadian specialists with expertise in the diagnosis and management of patients with the condition of interest will often form the basis of the advice offered by panel. The rationale for the panel's proposed provisional algorithm will be documented. Stakeholders will be consulted and provided with an opportunity to comment on the proposed provisional algorithm before it is finalized by CADTH.

11.2.4 Provisional Algorithm Reports

Under the process that was launched in July 2019, CADTH would include the provisional algorithm in the pERC final recommendation for the drug under review. The algorithm would only be included as part of the implementation considerations in the recommendation if pERC recommended to reimburse or reimburse with conditions. CADTH has revised this process and the provisional algorithms will be reported in a distinct CADTH report that is separate from all documentation related to the oncology drug submission(s) that triggered the need for the development of the algorithm. This change has been undertaken to accommodate the increased industry engagement described in Section 11.2.2 (i.e., involvement of all manufacturers whose products may be impacted by CADTH's provisional algorithm).

The final algorithm report from this process will be posted on the CADTH website. There will be no confidential information included in the implementation advice report. Manufacturers will not have the opportunity to request any redactions.

APPENDIX 1: PROPOSED CONFIDENTIALITY GUIDELINES

To further enhance and strengthen the transparency of CADTH's drug reimbursement review processes by minimizing the volume of redactions in CADTH's reports and recommendations, CADTH has developed the Confidentiality Guidelines. These guidelines will help ensure appropriate steps and procedures are in place so that the disclosure of information obtained through the drug reimbursement review processes is handled and managed in a consistent manner.

Together with the *Procedures for CADTH Drug Reimbursement Reviews*, the Confidentiality Guidelines provide clarity to CADTH and sponsors on how to appropriately protect and disclose information, allowing for a drug reimbursement review processes that is transparent and accountable. CADTH complies with these Confidentiality Guidelines when handling confidential information that are part of the drug reimbursement review processes. By filing a submission, resubmission, or reassessment, or by supplying other information to CADTH once a submission, resubmission, or reassessment has been filed, each sponsor hereby consents to comply with the requirements of these Confidentiality Guidelines and establishes an agreement between CADTH and the sponsor on its application.

A. Definition of Confidential Information

All sponsor-supplied information included in a submission, resubmission, reassessment, or anything received by CADTH related to the drug product after a submission, resubmission, or reassessment has been filed with CADTH will be deemed to be fully disclosable, unless such information has been clearly identified by a sponsor as confidential information. For greater clarity, confidential information does not include information that:

- is or becomes available to the public, other than as a result of a breach of the procedures contained herein (note that information available to the public includes but is not limited to published articles, presentations, drug prices, product monographs, clinical study information available from regulatory agency reports, other health technology assessment agency reports and recommendations, and www.clinicaltrials.gov)
- a third party (who is not under any obligation as to confidentiality or non-disclosure) rightfully discloses to CADTH
- is provided to an authorized recipient (as described in Section 3) without restriction as to its use, and the authorized recipient may disclose in accordance with its respective statutory requirements
- will address sequencing of therapies
- is derived from ad-hoc or post-hoc analyses or indirect treatment comparison conducted by the sponsor specifically for the purposes of informing the CADTH application
- is comprised of the disclosable price of the drug under review, its relevant comparators and companion diagnostics (if applicable)
- is comprised of a description of the design, methods, assumptions, limitations, and results of the economic model (e.g., incremental cost-effectiveness ratios)
- is comprised of a description of the design, methods, and summary statement about the budget impact analysis results

- is part of CADTH's own reanalyses.

The following types of information will be deemed by CADTH to be confidential information:

- sponsor's market research data, drug market share forecasts (from the sponsor's internal data), assumptions on competitor market share projections, and budget impact analysis numerical results
- information relating to the implementation plans provided by a sponsor on how the drug product may be delivered in the health care system (e.g., proposed launch date or facilities that may be built)
- information that meet with Health Canada's definition for confidential business information:
  - clinical information that was not used by the sponsor in the drug submission, supplement, or medical device application to support the proposed conditions of use or the purpose for which the drug or medical device is recommended
  - clinical information that describes the tests, methods, or assays used.

Sponsors must clearly identify any confidential information and provide the rationale for requesting the redaction of any of that information.

B. Handling Confidential Information

1. Responsibilities of CADTH

- CADTH will use reasonable care to prevent the unauthorized use, disclosure, publication, or dissemination of information received by CADTH as part of the drug reimbursement review processes that has been designated confidential.
- CADTH will not disclose confidential information in and related to a submission, resubmission, or reassessment to any third party except as permitted by the Confidentiality Guidelines, or as required by law or by order of a legally qualified court or tribunal.
- CADTH will use the confidential information solely for the purpose of carrying out its responsibilities with respect to the drug reimbursement review processes.

2. Responsibilities of Sponsors

- Information identified as confidential information within a submission, resubmission, or reassessment is expected to be kept to a minimum. It is not acceptable to mark an entire section as confidential. Sponsors should make sure that such information has not already been disclosed in documents posted by other health technology assessment agencies and/or regulatory authorities.
- It is the responsibility of the sponsor to clearly identify (using highlighting) any information that it considers to be confidential, and to list the confidential information and clearly state the reason(s) in a summary table provided by CADTH.
- Care should be taken when submitting information relating to individuals. Personal identifiers and sensitive information will be removed.

3. Release of Sponsor's Information

- CADTH may release any sponsor-supplied information received through the drug reimbursement review processes, including confidential information, to the following authorized recipients:

- CADTH staff and review team members (including contractors and clinical experts)
- CADTH expert committee members
- federal, provincial, and territorial government representatives (including their agencies and departments)
- pCPA office representative(s)
- CAPCA representative(s)
- Canadian Blood Services representative(s)
- members and observers of CADTH's advisory committees and their associated working groups.

- For drugs selected for joint engagement with clinical specialists by CADTH and INESSS, CADTH may release any sponsor-supplied information received through the drug reimbursement review processes, including confidential information, to INESSS expert committee members who are participating in meetings with the panel of clinical experts.
- While CADTH is an independent not-for-profit organization and is therefore not subject to access to information legislation, some of the authorized recipients listed previously have their own confidentiality procedures and are subject to freedom of information and access to information legislation over which CADTH has no control.
- CADTH staff members are required, as a condition of employment, to comply with CADTH's confidentiality requirements, Code of Conduct, and Conflict of Interest Guidelines. All of the previously described authorized recipients (with the exception of staff of federal, provincial, and territorial government representatives, including their agencies and departments; CAPCA; and pCPA) are required to sign a confidentiality agreement requiring them to comply with these Confidentiality Guidelines.

4. Documents Shared With Authorized Recipients

- The documents that CADTH may share with the authorized recipients include, but are not limited to:
  - pre-submission–related materials provided by the sponsor
  - the sponsor's submission, resubmission, or reassessment information
  - information provided by a sponsor for a drug-plan submission for a targeted reassessment
  - redacted and unredacted CADTH review report(s)
  - sponsor's comments about CADTH's review report(s)
  - CADTH's responses to the sponsor's comments about draft review report(s)
  - the draft recommendation
  - the redacted and unredacted final recommendation
  - the committee brief and reconsideration brief.

- CADTH provides the following documents to the sponsor (of which the sponsor must keep confidential until it is published on the CADTH website):
  - draft CADTH review report(s)
  - CADTH's responses to the sponsor's comments about draft review report(s)
  - an draft recommendation
  - the final recommendation (until posted on the CADTH website)
  - a response to request for clarification (if applicable).

- The documents that CADTH may post on its website include:
    - a tracking document indicating the status of the review, including a submission filed on a pre-NOC basis
    - CADTH review report(s) (with confidential information redacted, if specified)
    - a draft recommendation (with confidential information redacted, if specified)
    - a final recommendation (with confidential information redacted, if specified).

5. Making Reference to Confidential Information in Public CADTH Documents

CADTH may use confidential information supplied by the sponsor in the preparation of the review report(s) and recommendations. Before these documents are posted in the public domain, the sponsor will be asked to identify any confidential information for redaction in accordance with the Confidentiality Guidelines and the applicable sections of the *Procedures for CADTH Drug Reimbursement Reviews.*

The following principles and provisions will apply to any confidential information that the sponsor has identified and requests redacted from the review report(s), draft recommendation, or final recommendation:

- CADTH will redact the confidential information using redaction software and will indicate that the sponsor requested that the confidential information be redacted, pursuant to the Confidentiality Guidelines.
- CADTH may provide a general description of the type of information that was redacted and the reason(s), as provided by the sponsor.
- For greater clarity, information that does not meet the definition of confidential information as set out in section A of the Confidentiality Guidelines will not be redacted.
- In the case of a disagreement expressed by the sponsor regarding redactions made in the review report(s) and/or final recommendation, CADTH may require additional time to resolve the disagreement in consultation with the sponsor. This additional time could delay posting of these documents; however, any such delays will not affect the timelines for issuing the final recommendation to the authorized recipients.
- If the sponsor fails to respond to CADTH's request to identify confidential information for redaction within three business days, CADTH may proceed with posting the review report(s) and/or final recommendation in accordance with the *Procedures for CADTH Drug Reimbursement Reviews*.

C. Archiving of Documents Containing Confidential Information

- CADTH may retain copies of all documents associated with the review of a drug for as long as there may be a need to consult them.
- CADTH will determine at its sole discretion if there is a need to consult this information.
- CADTH staff undertakes regular reviews of archived material. Any material that CADTH determines to be no longer required will be disposed of. Any extra copies of documents at the completion of the review of the submission, resubmission, or reassessment will be destroyed.

APPENDIX 2: PROPOSED PROCEDURAL REVIEW PROCEDURE

A. Purpose

The purpose of this section is to define the steps CADTH will take to determine whether process was followed in the development of the final recommendation issued by a CADTH expert committee for a pharmaceutical review, and that the steps were consistent with the established process. It provides guidance for those who wish to make an application for a procedural review or who are considering doing so. A party that participated in the process relating to the final recommendation at issue may make an application for a procedural review; see Section 1.0 for further information on eligibility requirements.

CADTH will publish a notice on its website if a request for a procedural review is filed and accepted by CADTH. During this period, the drug programs and the pCPA will be advised by CADTH not to execute the final recommendation in question until a procedural review decision is concluded.

B. About Procedural Reviews

The ground for a procedural review relates only to whether the process was followed and not to the content or scientific issue that may or may not be included in the final recommendation (i.e., did CADTH fail to act in accordance with its procedures in conducting the review and issuing the final recommendation).

A procedural review is not an opportunity to reopen issues that CADTH's expert committee has decided on or to circumvent existing feedback mechanisms (e.g., request for reconsideration). A request for a procedural review will not be accepted because a requestor does not agree with a recommendation.

This procedure is not intended to address concerns related to the methodology used in the development of a CADTH process or in the interpretation and use of data during the review. This ground also does not cover fairness in the colloquial sense; for instance, that it is "unfair" that a recommendation is issued to not reimburse a treatment. For example, although it would be unfair to exclude a key step of the process (e.g., omitting an eligible stakeholder input), it would not be unfair if the expert committee considered the relevant data set and reached a view with which the applicant did not agree.

In addition, disagreement with CADTH's approach to managing confidential information that was provided in the submission, resubmission, therapeutic category or class review, or request for advice, including use or non-use in the review process, does not constitute grounds for a procedural review, provided processes were followed as outlined in the confidentiality guidelines (Appendix 1).

Requests for corrections of minor factual or typographical errors will not be grounds for a procedural review and will be addressed separately; CADTH may issue an erratum in these instances.

The review of a procedural review request will be conducted by a procedural review panel ("panel") that will be composed of individuals independent from the program directly responsible for the development of the final recommendation.

To promote transparency, processes for the development of the main types of CADTH recommendations issued by a CADTH expert committee are published on the CADTH website. Where there are concerns about perceived deviations from the procedure, parties are encouraged to contact and to resolve the matter with the CADTH Pharmaceutical Reviews Directorate as a first step.

C. Procedure

1. Requests for Formal Procedural Reviews

In cases where satisfactory resolution cannot be achieved through discussion with the CADTH Pharmaceutical Reviews Directorate, a formal request to CADTH may be made for a procedural review related to a final recommendation issued by a CADTH expert committee for a specific review. A procedural review cannot be lodged against other documents produced during the process (for example, the draft recommendation or draft report).

The following parties are eligible to submit a formal request to CADTH for a procedural review:

- a sponsor that filed the submission or resubmission for the review in question (applies to drug reimbursement reviews)
- a company whose review was assessed as part of a therapeutic category or a class review in question (applies to therapeutic reviews)
- a patient group that provided input in response to a call by CADTH for patient input for the review in question
- a clinician group that provided input in response to a call by CADTH for clinician input for the review in question.

Multiple parties, if eligible, may submit a request for a procedural review of a final recommendation issued by a CADTH expert committee for a specific review but each of these parties may submit only one request per final recommendation review at issue. In cases where a request may be made by more than one eligible party and is accepted for the same final recommendation review at issue, CADTH will conduct the requests jointly for the purpose of the procedural review proceeding.

Formal request for a procedural review must be made in writing using the designated CADTH Procedural Review Request Form (see section D) and must be received by CADTH within 20 business days of the final recommendation in question being posted on the CADTH website.

The completed CADTH Procedural Review Request Form must include the full name of the party making the request, the contact information of the party filing the prescribed request form, the name of the CADTH final recommendation in question, the involvement of the party with the final recommendation in question, and the details of the alleged deviation from procedure, including all supporting documents.

It is important that the prescribed request form is submitted correctly, is presented clearly, and contains the necessary information. If the request received is not appropriate (for example, the request does not have sufficient supporting information or the relevance of the issue is unclear), there is a possibility that the procedural review will be deemed "not valid" because it does not meet the ground for a procedural review. No extensions will be granted to the 20-business day period and all supporting documentation must be submitted within this period. Intent to submit supporting documentation after the 20-business day period will not be considered sufficient for initiation of the procedural review process.

Formal request using the designated CADTH Procedural Review Request Form may be submitted electronically to requests@cadth.ca.

2. Referring Requests for Procedural Reviews

Upon receipt by CADTH, formal requests for a procedural review will be forwarded to the CADTH official, or their delegate, who is responsible for leading the procedural review process and supporting the procedural review panel. CADTH will acknowledge receipt of the request.

3. Initiating a Procedural Review

Once the prescribed request form is received by CADTH, the CADTH official (or a delegate) will screen and assess the request for completeness and eligibility (i.e., that the request meets the requirements described in Section 1 and fits the definition of a procedural review). CADTH will notify the requestor in writing if the request has been accepted within 15 business days from the date of receipt of the prescribed request form by CADTH.

Where a request for a procedural review has been made by someone other than the company that made the original submission or resubmission for the review in question (if applicable), CADTH will notify the company and the drug programs that a procedural review has been initiated.

If a request is accepted, a notice indicating that a procedural review is in progress will be co-located with the file in question on the CADTH website. Efforts will be made to complete this step within five business days from the date that the request is granted for a procedural review. CADTH will convene a panel to conduct the review.

4. Procedural Review Panel

The mandate and responsibilities of the panel are set out in a CADTH Charter. The panel will have responsibility for adjudicating all procedural reviews.

The panel will aim to invite the applicant(s) to make a brief presentation within 20 business days of the published notice indicating that a procedural review is underway in order to uncover as much information as possible about the alleged breach of process. A maximum of 90 minutes will be allocated to present the issues that were submitted and to respond to questions from the panel. The maximum allowable time applies equally to joint requests. Each requesting organization may bring two representatives knowledgeable about the issue at hand to the meeting. No legal representation is permitted at the meeting. The meeting may be conducted in person or via teleconference at the sole discretion of the panel and will not be open to the public. The meeting may be recorded for internal use purposes. The panel may request additional information from the

applicant and may also engage in additional internal fact-finding activities (e.g., interviews with the relevant director, other staff members, or other parties), as needed.

5. Making Decisions on Procedural Reviews

The panel has sole and absolute discretion for determining whether the established process was properly followed. Findings will be made based on the consensus of the panel members. Should a consensus not be reached, a decision will be made by a majority vote of the panel members. Decisions of the panel are final, and there is no possibility of making further procedural review requests against the decision of the panel.

The duration of the procedural review may vary, depending on the complexity and nature of the request. While efforts will be made to issue a decision in the shortest possible time period, it may take up to a maximum of 60 business days to issue a decision from the date of receipt of the request for a formal procedural review by CADTH.

A maximum of one procedural review per final recommendation will be undertaken (i.e., no additional procedural review requests may be filed against the same recommendation at issue).

6. Outcomes of Decision on Procedural Reviews

The panel may issue the following decision:

- No change to the existing CADTH final recommendation for the specific review; or
- Steps in the review process for the specific review at issue must be revisited and/or the submission, resubmission, therapeutic review, or reassessment must be redeliberated by the expert committee at the next available meeting. A re-deliberation may result in the expert committee final recommendation being upheld or being revised.
    - If the original final recommendation is upheld following the re-deliberation, the original final recommendation will remain posted unchanged on the CADTH website and a note will be added to indicate that the procedural review was completed and that no changes were made to the original recommendation.
    - If the final recommendation is changed following the re-deliberation, the revised final recommendation will supersede the previous recommendation and will be publicly posted.

7. Communicating Decisions on Procedural Reviews

The applicant(s) will be informed of the decision of the panel. In cases where the panel finds that a deviation from process has occurred, CADTH will identify the steps required to rectify the situation and will inform the applicant(s) of the decision and next steps, if applicable.

In cases where the panel finds that a deviation from process has occurred, the final recommendation at issue will be removed from the website and replaced with a notice indicating that additional work is underway and new targeted timelines due to the findings of the procedural review, until the matter can be appropriately remedied. High-level details about the submitted procedural review request, including the name of the applicant(s), and the decision and reason for

the decision, will be publicly posted on the CADTH website. No further procedural review request will be permitted against the final recommendation at issue.

D. Proposed Procedural Review Request Form

The following form must be submitted, along with supporting documentation, to CADTH via email at requests@cadth.ca within 20 business days of a final recommendation being issued. No extensions will be granted to the 20-business day period and all supporting documentation must be submitted within this period.

Section 1: About the Applicant	
Organization	
Role in the review process	☐ A sponsor that filed the submission, resubmission, or reassessment for the review in question (applies to drug reimbursement review products) ☐ A company whose product was assessed as part of a therapeutic category or a class review in question (applies to optimal use drug reviews) ☐ A patient group that provided input in response to a call by CADTH for the review in question ☐ A clinician group that provided input in response to a call by CADTH for the review in question
Contact information	Name: Email: Phone:
Date of procedural review request:	
Section 2: Final recommendation for which procedural review is being requested	
CADTH project number	
Therapeutic class or drug name(s) (as applicable)	
Indication(s)	
Date final recommendation issued	
Section 3: Ground for the procedural review request	
Important note*: Provide a detailed description, along with any relevant documentation, related to how you perceive that CADTH failed to act in accordance with its procedures. Relevant CADTH process steps should be clearly identified. Please provide a list of all supporting documentation. This section should be written clearly and succinctly and should not exceed 10 pages.*	

☐ By submitting this application, I hereby confirm that the information provided herein is accurate, correct, and complete, and that the documents submitted along with this form are relevant and complete.

APPENDIX 3: PROPOSED PRE-SUBMISSION PHASE TEMPLATES

Submission Eligibility and Complexity Assessment Form

Purpose

This form is used by CADTH to determine if a product is eligible for review through one of the single drug review pathways and to assess the complexity of the pending submission. This form must be completed by sponsors before filing a submission in the following situations:

- the sponsor is seeking direction regarding whether or not a product is eligible for review through CADTH's drug reimbursement review processes
- the sponsor is planning to file a submission for a cell or gene therapy.

SECTION 1: BACKGROUND INFORMATION

Details	Sponsor's responses
Sponsor name	*Please provide the complete company name of the submission sponsor.*
Product name	*Please state the brand name (if known).*
Generic name	*Please list the non-proprietary names of the active substance(s) included in the drug of interest.*
Dosage forms and strengths	*Please identify the dosage forms and strengths (if applicable).*
Indication(s) for consideration by CADTH	*Please list the indications that are approved or undergoing review by Health Canada for the drug of interest.*
Health Canada approval status	☐ Pre-NOC ☐ Post-NOC Date of approval: *Date or anticipated date of Health Canada approval.*
Contact information	
Questions for CADTH	*Please list the specific questions you have regarding CADTH's processes:*

NOC = Notice of Compliance

SECTION 2: ELIGIBILITY FOR CADTH DRUG REIMBURSEMENT REVIEW PROCESS

Product characteristics	Sponsor's responses
Please complete this section for all products that are regulated as drugs	
What is the prescription status of the drug in question?	☐ Prescription drug ☐ Over the counter ☐ Ethical ☐ Other, please specify:
Which of the following best describes the product and indication(s) in question?	☐ New active substance ☐ New indication for existing drug ☐ New combination product ☐ New dosage form or strength of an existing drug ☐ Subsequent entry non-biologic complex drug ☐ Other, please specify:
Which of the following best describes the drug in question?	☐ Chemically synthesized drug ☐ Biologic ☐ Radiopharmaceutical ☐ Gene therapy ☐ Cell therapy (e.g., chimeric antigen receptor T cells) ☐ Preventive vaccine ☐ Therapeutic vaccine ☐ Other, please specify:
Please state the route of administration for the drug	☐ Oral ☐ Intravenous ☐ Intramuscular ☐ Inhalation ☐ Subcutaneous ☐ Sublingual ☐ Other, please specify:
What type of submission has been or will be filed with Health Canada?	☐ New drug submission (NDS) ☐ Supplemental new drug submission (S/NDS) ☐ Abbreviated new drug submission (A/NDS or S/ANDS) ☐ Other, please specify:
Is the drug in question used in the treatment of cancer?	☐ No ☐ Drug is used in the active treatment of cancer ☐ Drug is used as a supportive therapy for cancer patients
Is the drug in question a blood or a plasma-related product?	☐ No ☐ Drug is derived from human blood or plasma ☐ Drug is not derived from human blood or plasma, but has the potential to displace existing drugs that are derived from human blood or plasma ☐ Drug is not derived from human blood or plasma, but has the potential to impact the need for the transfusion of blood in Canada

Does the product in question fit within the reimbursement mandate of one or more the following? (Check all that apply)	☐ Public drug plans and/or cancer agencies ☐ Canadian Blood Services ☐ Hospital formularies ☐ Public health agencies ☐ Uncertain ☐ Other, please specify:

SECTION 3: COMPLEXITY OF THE DRUG SUBMISSION

Product characteristics	Sponsor's responses
Regulatory review	
Please indicate if the drug is undergoing or underwent review by Health Canada through an expedited pathway	☐ No (standard review pathway) ☐ Yes (priority review) ☐ Yes (Notice of Compliance with Conditions [NOC/c] filed at the outset) ☐ To be confirmed (requested or will be requested) ☐ Other expedited pathway, please specify:
Information about how the drug is administered to patients	
Please identify the location of administration	☐ Home administration ☐ Outpatient clinic or infusion centre ☐ Hospital setting ☐ Physician's office ☐ Other setting, please specify:
Please provide details regarding the peri-treatment period for the drug	**Pre-treatment period** *Please provide details regarding the pre-treatment regimen for the drug under review (if applicable). For example, details about the setting and specific therapeutic regimen that patients would need to undergo in order to prepare to receive the drug of interest.* **Treatment period** *Please provide details regarding the administration of the drug of interest, including the treatment setting.* **Post-treatment period** *Please provide details regarding the post-treatment follow-up period, including the setting (e.g., need for hospitalization) and all details regarding monitoring for adverse events.*
Is administration limited to specialized centres in Canada?	☐ No ☐ Yes Please explain your answer:
Are prescribing physicians required to undergo training specific to the drug treatment?	☐ No ☐ Yes Please explain your answer:

Information about the indication for drug of interest	
Does the drug have a companion diagnostic test?	☐ No ☐ Yes If yes, please provide a brief description of the following: • Do all patients require testing to be eligible for the drug? • Is the test currently available in all or some Canadian provinces and territories?
Has the drug been given orphan drug designation?	*Please check all that apply* ☐ No ☐ Yes (United States Food and Drug Administration) ☐ Yes (European Medicines Agency) ☐ To be confirmed (requested or will be requested)
Epidemiological information	Estimated prevalence in Canada: Estimated incidence in Canada:
Information about the comparators	
Comparator(s)	*Please provide a brief list of the comparators for the drug of interest and provide a description of how they are currently reimbursed (if applicable)*.
Does the drug in question have a novel mechanism of action relative to comparators?	☐ No ☐ Yes Please explain your answer:
Clinical development program and comparative efficacy	
Overview	*Please provide a brief description of the clinical development program for the drug and indication.*
Are comparative efficacy data available for the drug versus appropriate comparators?	☐ No ☐ Yes (direct comparison) ☐ Yes (indirect comparison)

Resubmission Eligibility Form

Purpose

Prior to filing a resubmission, sponsors are required to have its eligibility assessed by CADTH. To do so, sponsors must complete this form and submit it to requests@cadth.ca for evaluation. CADTH will assess the information in consultation with its advisory committees and working groups, as required, and notify the sponsor of its eligibility.

Template

1. SPONSOR INFORMATION
Name of sponsor: **Primary contact for resubmission:** *Provide name, title, email, phone number* **Back-up or secondary contact for resubmission:** *Provide name, title, email, phone number*
2. DRUG INFORMATION
Name of drug (non-proprietary and brand): **Indication:** **Requested reimbursement criteria**: **Anticipated resubmission filing date**:
3. RATIONALE FOR THE RESUBMISSION INFORMATION
Indicate if the reason for the resubmission is due to new clinical and/or new economic evidence. Check all that apply for the pending resubmission: **New clinical information** ☐ **Improved efficacy** ☐ **Improved safety** ☐ **New economic information** ☐
4. ISSUES ADDRESSED BY THE NEW INFORMATION
Using the following table, identify the issues raised in the CADTH recommendation that the new information addresses. Add or remove rows as required.

Issue in recommendation	New evidence that addresses the issue
Clearly state the issue raised in the recommendation	*Add brief summary of new evidence*
Clearly state the issue raised in the recommendation	*Add brief summary of new evidence*

Clearly state the issue raised in the recommendation	*Add brief summary of new evidence*

5. SUMMARY OF NEW CLINICAL INFORMATION

This section should not exceed THREE pages and should include:

- *a description of any new clinical information that was not available at the time of the last review*
- *a brief overview of new clinical studies, including a description of the study design, population, intervention, comparators, and outcomes*
- *a brief summary of the key results from the new studies*
- *citations to main articles if clinical data are published.*

6. SUMMARY OF NEW ECONOMIC INFORMATION

This section should not exceed THREE pages and should include a description of any new economic information that was not available at the time of the last review.

7. ELIGIBILITY ASSESSMENT (FOR CADTH USE ONLY)

Issue in recommendation	**CADTH assessment**
Issue raised in the recommendation	*To be completed by CADTH*
Issue raised in the recommendation	*To be completed by CADTH*
Issue raised in the recommendation	*To be completed by CADTH*

8. CONCLUSION (FOR CADTH USE ONLY)

Based on the information provided by the sponsor, CADTH has concluded that the resubmission:

- **meets the eligibility criteria for a resubmission** ☐
- **does not meet the eligibility criteria for a resubmission** ☐

Date:

Tailored Review Application Form

Purpose

Sponsors must complete this form and submit it to CADTH at requests@cadth.ca before filing a submission for new combination products (complete sections 1 and 2) and new formulations of existing drugs that are eligible for review (complete sections 1 and 3). CADTH will review the information and, with input from the drug plans (as needed), confirm whether a standard or tailored review should be filed.

Template

SECTION 1: BACKGROUND INFORMATION

Drug characteristics	Sponsor's responses
Sponsor name	*Please provide the complete company name of the submission sponsor.*
Brand name	*Please state the brand name (if known).*
Generic name	*Please list the non-proprietary name(s) of the active substance(s) included in the drug of interest.*
Route of administration	*Please state the route of administration for the drug of interest.*
Dosage form and strengths	*Please identify the dosage forms and strengths for the drug of interest.*
Indication(s)	*Please list the indications that are approved or undergoing review by Health Canada for the drug of interest.*
Location of administration	*Please identify the location of administration (e.g., community and/or hospital).*
Date of Health Canada approval	*Please provide the date or anticipated date of Health Canada approval for the drug of interest.*
Clinical development program	*Please provide a brief description of the clinical development program for the drug and indication.*
Comparator(s)	*Please provide a brief list of the comparators for the drug of interest.*
Contact information	Name: Title: Email: Phone:

SECTION 2: NEW COMBINATION PRODUCTS

Questions	Sponsor's responses
1. Have the individual components been reviewed by CADTH for the same indication?	**☐ Yes ☐ No** **If yes, please state which components have been reviewed:**
2. Does the combination product contain at least one new active substance?	**☐ Yes ☐ No** **If yes, please state which components are new active substances:**
3. Are all of the individual components reimbursed by the drug plans?	**☐ Yes ☐ No** **Please provide a brief summary of the reimbursement status of the individual components, indicating any differences between the drug plans:**
4. Are the individual components currently indicated for use in combination therapy with one another?	**☐ Yes ☐ No** **Please provide details regarding the approved indications for combination usage of the individual components:**
5. Are the components marketed in Canada in the same dosage strength?	**☐ Yes ☐ No** **Please provide details regarding the dosage strengths for the combination product and the individual components:**
6. Based on publicly available prices, is the price of the combination product the same or less than the sum of the individual components?	**☐ Yes ☐ No**

SECTION 3: NEW FORMULATIONS OF EXISTING DRUGS THAT ARE ELIGIBLE FOR REVIEW

Questions	Sponsor's responses
1. Does the new formulation have the same indication as other existing formulation(s) of the drug?	**☐ Yes ☐ No** **If no, please state the indications and comment on the rationale for the differences in the indications:**
2. Has the active substance been reviewed by CADTH for the indication of interest?	**☐ Yes ☐ No** **If yes, please state which formulations have been reviewed and for what indications:**
3. Is the active substance currently reimbursed by the participating drug plans for the indication of interest?	**☐ Yes ☐ No** **Please provide details regarding the reimbursement status of the active substance, indicating any differences between the drug plans:**
4. Please describe the comparative clinical evidence available for the new formulation.	**Direct evidence versus other formulation(s): ☐ Yes ☐ No** **Indirect evidence versus other formulation(s): ☐ Yes ☐ No** **Please provide details regarding the comparative evidence:**
5. Are there specific challenges with meeting the requirements for a standard review as described in CADTH's procedures?	**☐ Yes ☐ No** **Please describe the specific requirements with which there are challenges and provide an explanation for each:**

Proposed Place in Therapy for Drug Under Review

Purpose

The purpose of this template is for the sponsor to clearly indicate where it believes the drug under review should be used compared to existing treatments that are currently reimbursed, as well as the impact of reimbursing the drug under review on the sequence of use for other available therapies used before, after, or as alternatives to the submitted therapy. Sponsors planning to file a submission or resubmission must complete this template and submit it to CADTH at the same time they are providing advance notification (i.e., at least 30 business days prior to the anticipated date of filing).

Template

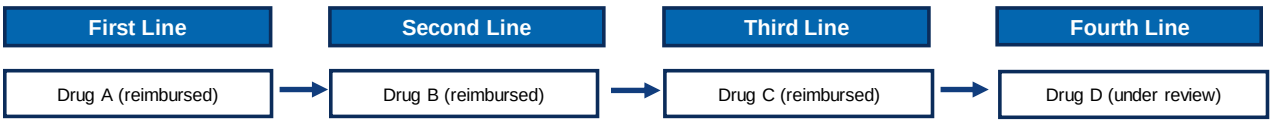
SECTION 1: BACKGROUND INFORMATION

Background	Information
Sponsor	*Please provide the complete company name of the submission sponsor.*
Drug under review	Brand name: *Please state the brand name (if known)* Generic name: *Please state the generic name*
Approved or anticipated indication to be reviewed by CADTH	*Please list the indications that are approved or undergoing review by Health Canada for the drug of interest.*
Sponsor's requested reimbursement criteria	☐ As per indication(s) to be reviewed by CADTH ☐ Other, please specify:
Anticipated date of filing with CADTH	DD-MM-YYYY
Contact information	Name: Title: Email: Phone:

SECTION 2: CURRENT TREATMENT ALGORITHM

2.1 Current Treatment Algorithm Diagram

In this section, the sponsor must provide complete details regarding the current treatment algorithm for the indication of interest. A sample table for reporting current treatment algorithm is provided as follows.



2.2 Current Treatment Algorithm Details

In this section, the sponsor must provide complete details regarding the current treatment algorithm for the indication of interest. Please clearly state the drugs and/or treatment regimens that are used, or likely to be used, for the indication of interest. The sponsor can clarify whether some options are only available for a subset of patients. Alternatively, multiple tables can be created to expand on the different subsets. Clearly identify all current treatment options as being reimbursed or undergoing review by CADTH, under negotiation by the pan-Canadian Pharmaceutical Alliance (pCPA), or under consideration by the drug programs. In the reimbursement status column, please identify the status as follows: reimbursed by a majority of drug programs; reimbursed by a minority of drug programs; under review for reimbursement.

Sample table for reporting current treatment algorithm

Drugs	Reimbursement status
First-line treatment options	
List drug or regimen	
Add rows as required	
Second-line treatment options	
List drug or regimen	
Add rows as required	
Third-line treatment options	
List drug or regimen	
Add rows as required	
Fourth-line treatment options	
List drug or regimen	
Add rows as required	

Please use this space to define any abbreviations used within the table.

SECTION 3: SPONSOR'S PROPOSED PLACE IN THERAPY ALGORITHM

3.1 Proposed Place in Therapy

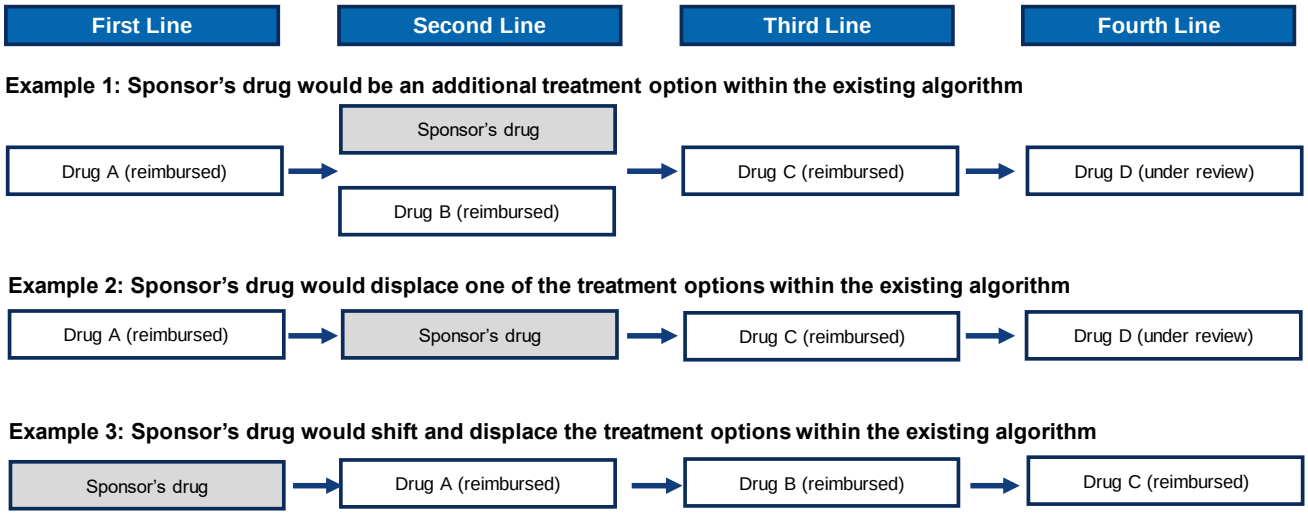
In this section, the sponsor is required to provide its proposed place in therapy for the drug under review. Please provide a clearly stated rationale for the proposed place in therapy, noting if the rationale is based on evidence from clinical studies, clinical expert opinion, cost-effectiveness relative to alternative treatments, and so forth.

3.2 Potential Impact on Currently Reimbursed Treatments

Please briefly describe the potential impact (if any) of the indication of interest on currently reimbursed treatments. Examples of impact include different position in sequence, replacement or elimination of treatment, change in reimbursement criteria, and so forth. Please ensure that this section of the document contains references to all relevant documentation supporting the sponsor's rationale for the place in therapy.

3.3 Provisional Algorithm Diagram

In this section, the sponsor is required to provide one or more figures illustrating the proposed place in therapy of the drug or regimen under review and to demonstrate the potential impact (if any) on currently reimbursed treatments for the indication.



References

APPENDIX 4: PROPOSED APPLICATION PHASE TEMPLATES

Application Overview Template

Purpose

This form provides CADTH with a simple reference document to improve the efficiency of the application intake process.

Template

Name of product	Non-proprietary name: Brand name: Is the brand name confidential until a NOC is issued? Yes ☐ No ☐ NA ☐
Sponsor(s)	Sponsor name(s): Submitting consultant (if applicable):
Indication(s) to be reviewed by CADTH	1. 2.
Sponsor requested reimbursement criteria	☐ As per indication(s) to be reviewed by CADTH ☐ Other, please specify:
Type of submission	☐ New drug ☐ New indication ☐ New combination product ☐ New formulation that is eligible for review by CADTH ☐ Subsequent entry non-biologic complex drug
Cell or gene therapy	☐ No ☐ Cell therapy ☐ Gene therapy
Review program	☐ CADTH Common Drug Review ☐ CADTH pan-Canadian Oncology Drug Review ☐ CADTH Interim Plasma Protein Product Review
Resubmission	☐ Yes ☐ No If yes, please indicate: ☐ Resubmission based on new cost information ☐ Resubmission based on new clinical information ☐ Resubmission based on new cost and clinical information
Health Canada review type	The drug is undergoing or underwent review by Health Canada through an expedited pathway: ☐ No (standard review pathway) ☐ Priority review ☐ Advance consideration under NOC/c ☐ To be confirmed (requested, Health Canada decision pending) ☐ Other expedited pathway (please specify)

NOC status	☐ Pre-NOC ☐ Post-NOC ☐ Unlabeled indication
Date of NOC (issued or anticipated)	DD-MM-YYYY
Health Canada information sharing	☐ Yes, Health Canada will be or has been provided with a completed consent form ☐ No, Health Canada will not be provided with a completed consent form ☐ Not applicable (post-NOC submission or a resubmission)
Has this drug previously received an NOD or NON?	☐ Yes ☐ No
Has this drug previously been filed with CADTH and withdrawn?	☐ Yes ☐ No
Primary contact	Name: Title: Email: Phone:
Secondary contact	Name: Title: Email: Phone
Application fee contact (if not primary contact)	Name: Title: Email: Phone:

NA = not applicable; NOC = Notice of Compliance; NOD = Notice of Deficiency; NON = Notice of Non-Compliance.

Declaration Letter Template

Purpose

This form ensures that the sponsor acknowledges the terms and conditions of CADTH's procedures, as well as the procedures related to submitted prices, disclosure of known clinical studies, and communications.

Template

Reference: [Brand name/generic name]

Agreement to supply at the submitted price

This letter confirms that [name of sponsor] will supply the above-named drug at a price no greater than the submitted price, as provided in the [submission; resubmission – select appropriate], to all of the drug programs that participate in CADTH's drug reimbursement review processes (i.e., CADTH Common Drug Review, CADTH pan-Canadian Oncology Drug Review, or CADTH Interim Plasma Protein Product Review process).

We understand that the submitted price is the price per smallest dispensable unit that is submitted to CADTH and that must not be exceeded for any of the drug programs or cancer agencies following completion of the review processes. The submitted price will be disclosed in all applicable CADTH reports.

Disclosure of all studies

This letter confirms that [name of sponsor] has disclosed all unpublished studies known to [name of sponsor], including those undertaken by other companies that distribute, market, and license this drug in Canada or in other countries and those undertaken by other groups or individuals as of [insert date].

Authorizing unrestricted sharing of information

This letter acknowledges that CADTH may communicate, without restriction with respect to the product under review, with the authorized recipients in accordance with the *CADTH Drug Reimbursement Reviews Confidentiality Guidelines*. This includes, but is not limited to:

- federal, provincial, and territorial government representatives (including their agencies and departments)
- the pan-Canadian Pharmaceutical Alliance office (pCPA)
- the Canadian Association of Provincial Cancer Agencies (CAPCA)
- Canadian Blood Services.

Consenting to terms and conditions

This letter acknowledges that by filing a submission or resubmission with CADTH, the sponsor consents to be bound by the terms and conditions specified in the *Procedures for CADTH Drug Reimbursement Reviews* and all provisions regarding withdrawal from the CADTH review process. Consent to the terms and conditions cannot be revoked by the sponsor at any time during or after the CADTH's review.

[Signature]
[Name and Title of Senior Company Official of Sponsor]

Sponsor's Executive Summary Template

Purpose

The executive summary should provide a high-level synopsis of the resubmission or resubmission. While all required headings and subheadings have been provided in the template, additional sections may be added, as needed. The amount of space used for each section is at the discretion of the applicant.

Section 1: Executive Summary for Submission

1. Brief Description of the Drug

2. Place in Therapy

3. Summary of Clinical Evidence

3.1 Overview of Studies

3.2 Efficacy Results

3.3 Safety Results

4. Summary of Pharmacoeconomic Evidence

5. Requested Reimbursement Criteria *(include this section if applicable)*

5.1 Requested Reimbursement Criteria

5.2 Rationale for Requested Reimbursement Criteria

6. Conclusions

References

Section 2: Executive Summary for a Resubmission

1. Brief Description of the Drug

2. Place in Therapy

3. Rationale for Filing the Resubmission or Reassessment

4. Summary of New Clinical Evidence

4.1 Overview of New Studies

4.2 New Efficacy Results

4.3 New Safety Results

5. Summary of New Pharmacoeconomic Evidence

6. Requested Reimbursement Criteria *(include this section if applicable)*

6.1 Requested Reimbursement Criteria

6.2 Rationale for Reimbursement Criteria

7. Conclusions

References

Table of Studies Template

Purpose

The purpose of this table is to provide CADTH with an overview of all published and unpublished studies for the drug and indication under review.

Template

Study ID(s)	Sponsor	Description	Phase	Start and end date	Abstracts, publications, and errata
1. List of all pivotal for the indication(s) to be reviewed by CADTH					
		Title: **Study design:** *Brief description* **Randomized N:** *Total sample size* **Population:** *Brief description* **Intervention(s):** *Drug, dosage, administration frequency* **Comparator(s):** *Comparator(s) dosage, administration frequency* **Outcomes:** *Primary and key secondary end points*		**Start:** MM/YYYY **End:** MM/YYYY	1. Citation #1 2. Citation #2 Note: All citations must use the JAMA oncology format
2. List of all additional completed RCTs for the indication(s) to be reviewed by CADTH					
		Title: **Study design:** *Brief description* **Randomized N:** *Total sample size* **Population:** *Brief description* **Intervention(s):** *Drug, dosage, administration frequency* **Comparator(s):** *Comparator(s) dosage, administration frequency* **Outcomes:** *Primary and key secondary end points*		**Start:** MM/YYYY **End:** MM/YYYY	1. Citation #1 2. Citation #2 Note: All citations must use the JAMA oncology format
3. List of completed non-randomized studies for the indication(s) to be reviewed by CADTH					
		Title: **Study design:** *Brief description* **Total sample size:** **Population:** *Brief description* **Intervention(s):** *Drug, dosage, administration frequency* **Comparator(s):** *Comparator(s) dosage, administration frequency* **Outcomes:** *Primary and key secondary end points*		**Start:** MM/YYYY **End:** MM/YYYY	1. Citation #1 2. Citation #2 Note: All citations must use the JAMA oncology format
4. List of all ongoing studies for the indication(s) to be reviewed by CADTH					
		Provide a brief description	II, III, or IV	**Start:** MM/YYYY **End:** MM/YYYY	1. Citation #1 Note: All citations must use the JAMA oncology format

(Add to the following alphabetical list any abbreviations added to the table): N = total number of patients; RCT = randomized controlled trial.

Number of Patients Accessing a New Drug Template

Purpose

The purpose of this table is to provide CADTH and participating drug plans with information regarding the number of patients in Canada currently accessing the drug under review.

Template

The following table summarizes information regarding the number of patients in Canada currently accessing [insert drug brand name], [a new drug/a new combination product containing a new drug; select appropriate], to within 20 business days of the filing date of this submission with CADTH.

Mechanism for patient access	Number of patients
Compassionate supply from the sponsor[a]	
Health Canada's Special Access Programme	
Clinical trial(s)	
Add lines as needed to identify any other applicable means by which patients are currently accessing the drug.	

[a] Include a brief description of the compassionate supply program(s) and whether or not the drug is provided to patients free of charge.

Reimbursement Status for Comparators

Purpose

The purpose of this table is to provide CADTH and participating drug plans with information regarding the number of patients in Canada currently accessing the drug under review. The template is to be completed based only on publicly available information; the individual drug programs or CADTH are not to be contacted for information on the reimbursement status of comparators.

Template

Complete the reimbursement status for comparators tables as follows:

Abbreviation	Description
–	Information not available
CADTH	Under review by CADTH
EX	Exception item for which coverage is determined on a case-by-case basis
FB	Full benefit
FPT	Under consideration by the federal, provincial, and territorial drug plans
NB	Not a benefit
RES	Restricted benefit with specified criteria (e.g., special authorization, exception drug status, limited use benefit)
pCPA	Under negotiation by the pan-Canadian Pharmaceutical Alliance

1. CADTH Common Drug Review Submissions

Reimbursement Status for Comparators for the Treatment of [State the Indication]

Comparators	Public drug programs														
	BC	AB	SK	MB	ON	NB	NS	PE	NL	YT	NT	NIHB	CAF	VAC	CSC
Brand (generic)															
Brand (generic)															

AB = Alberta; BC = British Columbia; CSC = Correctional Services Canada; DND = Canadian Armed Forces; MN = Manitoba; NIHB = Non-Insured Health Benefits Program; NL = Newfoundland and Labrador; NS = Nova Scotia; NT = Northwest Territories; ON = Ontario; PE = Prince Edward Island; SK = Saskatchewan; VAC = Veterans Affairs Canada; YT = Yukon.

2. CADTH pan-Canadian Oncology Drug Review Submissions

Reimbursement Status for Comparators for the Treatment of [State the Indication]

Comparators	Public drug programs								
	BC	AB	SK	ON	NB	NS	PE	NL	NIHB
Brand (generic)									
Brand (generic)									

AB = Alberta; BC = British Columbia; MN = Manitoba; NIHB = Non-Insured Health Benefits Program; NL = Newfoundland and Labrador; NS = Nova Scotia; NT = Northwest Territories; ON = Ontario; PE = Prince Edward Island; SK = Saskatchewan.

Reimbursement Criteria for (Comparator) for (State the Indication)

Drug plan	Criteria for restricted benefit
Add name	State the exact criteria (if publicly available)
Add name	State the exact criteria (if publicly available)

Implementation Planning for a Cell or Gene Therapy Template

Purpose

This form must be completed by sponsors for all submissions for cell or gene therapies. The drug programs will be asked to review and comment on the completed implementation plan template. Their feedback on the implementation plan could help provide early identification of potential access issues within the different jurisdictions, potential issues with administration or distribution mechanisms (e.g., need for specialty clinics), and/or challenges with diagnostic testing requirements. This will approach will allow CADTH and the drug programs to efficiently reflect on potential implementation issues and corresponding mitigation strategies.

Template

1. BACKGROUND INFORMATION

1.1. Product Information

Non-proprietary name	*Please state the non-proprietary name of the drug under review*
Brand name	*Please state the confirmed or anticipated brand name of the drug under review*
Dosage form and strengths	*Please provide all formats and strengths included in the submission to CADTH*
Sponsor(s)	*Please state the name of the submission sponsor*
Indication(s)	*Please list all indications to be reviewed by CADTH*
Sponsor requested reimbursement criteria	☐ As per indication(s) to be reviewed by CADTH ☐ Other, please specify:
Drug is undergoing or underwent review by Health Canada through an expedited pathway	☐ No (standard review pathway) ☐ Priority review ☐ Notice of Compliance with Conditions (NOC/c) filed at the outset ☐ Another expedited pathway (please specify) ☐ To be confirmed (requested, Health Canada decision pending)
Date of Notice of Compliance (issued or anticipated)	DD-MM-YYYY

1.2. Disease Information

1.2.1. Overview of the Condition

In this section, the sponsor is asked to provide a brief description of the disease condition.

1.2.2. Estimated Disease Prevalence

In this section, provide a breakdown of prevalence by participating province and territory. If the drug under review is expected to fall within the coverage mandate of the Non-Insured Health Benefits program of the First Nations and Inuit Health Branch, please provide a separate estimate for the estimated prevalence in the First Nations and Inuit populations (if available).

Sample Table for Presenting the Estimated Prevalence in Each Region

Region	Estimated prevalence		
	Lower estimate	Best estimate	Upper estimate
Canada			
Alberta			
British Columbia			
Manitoba			
New Brunswick			
Newfoundland and Labrador			
Northwest Territories			
Nova Scotia			
Nunavut			
Ontario			
Prince Edward Island			
Quebec			
Saskatchewan			
Yukon			
First Nations			

1.3. Diagnosis of the Condition

1.3.1. Diagnostic Testing Requirements

In this section, the sponsor is asked to provide a description of the diagnostic testing requirements for the indication(s) under review by CADTH. Please clearly describe the diagnostic tests that would be required or recommended to identify the patient population that could be eligible for treatment with the drug under review. This should include:

- name and rationale for each diagnostic test
- timing of the testing procedures relative to receiving the drug under review (e.g., would the test results only be valid for a finite period of time due to anticipated progression of the disease?)
- setting for the diagnostic testing (e.g., hospitals or outpatient clinics)
- for any invasive testing procedures, the anticipated time and setting for recovery from the procedures and any factors that could influence recovery time
- the sponsor's perspective on the appropriate health care professionals in Canada to confirm the diagnosis.

Please note if there are any confirmed or anticipated statements in the Canadian product monograph regarding specific diagnostic testing that is recommended for the drug under review.

1.3.2. Availability of Diagnostic Testing

In this section, the sponsor is asked to provide a description of the availability of the diagnostic testing requirements for the indication(s) under review by CADTH. Please provide a brief overview of the following:

- availability of the diagnostic testing requirements at the time the submission is filed with CADTH and by the time the review of the submission has been completed (i.e., when a final recommendation has been issued)
- any provinces or territories where there is likely to be limited access to the diagnostic testing requirements for the indication(s) of interest at the time CADTH's review is targeted to be completed
- any initiatives being undertaken by the sponsor to increase the availability of the diagnostic test in Canada
- any known initiatives being undertaken by others to increase the availability of the diagnostic test in Canada.

2. ACCESSIBILITY CONSIDERATIONS

2.1. Ability to Supply

Irrespective of CADTH's reimbursement recommendation, please briefly comment on the ability to supply the drug to all eligible patients across Canada at the time CADTH's review is targeted for completion (e.g., within six months of the filing date).

2.2. Canadian Treatment Centres

In this section, the sponsor is asked to provide a description of where the treatment will be available in Canada. If relevant, please provide details regarding any certification or qualification activities that are required for the drug to be administered at a particular treatment centre. If the treatment will be limited to selected treatment centres (e.g., specialty clinics or tertiary hospitals), please provide a summary table that shows the number of centres in each of the provinces and territories.

Sample Table for Presenting the Number of Treatment Centres

Province or territory	Treatment centres		
	Year 1	Year 2	Year 3
Alberta			
British Columbia			
Manitoba			
New Brunswick			
Newfoundland and Labrador			
Northwest Territories			
Nova Scotia			
Nunavut			
Ontario			
Prince Edward Island			
Quebec			
Saskatchewan			
Yukon			

2.3. Patient Support Programs

In this section, the sponsor is asked to briefly describe any patient support programs that are planned for the drug under review.

3. HEALTH SYSTEM CONSIDERATIONS

3.1. Health Care Professionals

3.1.1. Prescribing Limitations

Please identify any confirmed or anticipated statements in the Canadian product monograph regarding restricting the prescribing and/or administration of the drug to certain health care professionals. If applicable, outline any prescribing conditions proposed by the sponsor that are related to limiting the prescribing and/or administration of the drug to certain health care professionals.

3.1.2. Specialized Training for Health Care Professionals

In this section, the sponsor is asked to provide a description of any specialized training programs or certification requirements for health care professionals who would prescribe and/or administer the drug under review. Please focus on training that is specific to the drug under review. If applicable, provide a brief overview of the accessibility of any specialized training programs, certification, or qualification requirements across Canada.

3.2. Health Care Resources

3.2.1. Pre-Treatment Phase

Please describe the health care resources required in the pre-treatment phase for patients preparing to undergo treatment with the drug under review.

- Provide the following information for any drugs that are required in order to prepare the patient to receive the drug under review:
  - non-proprietary name, dosage, route of administration
  - timing relative to the receiving the drug under review
  - setting to administer the pre-treatment drugs (e.g., home, physician's office, outpatient clinic, inpatient hospital setting).
- Provide the following information for any medical procedures that are required to prepare the patient to receive the drug under review:
  - name and rationale of the procedure
  - timing of the procedure relative to receiving the drug under review
  - setting for the procedure (e.g., physician's office, outpatient clinic, inpatient hospital setting)
  - anticipated duration and setting expected for recovery from the procedures (e.g., hospitalization for a particular period of time) and factors that could influence recovery time.
- Provide the details of any additional diagnostic and clinical testing required to ensure the patient is a candidate for the treatment.
  - Please focus on any testing that is additional to the initial diagnostic criteria that were used to identify the patient as a candidate for treatment (e.g., physical examinations, laboratory testing, diagnostic imaging).

3.2.2. Treatment Phase

Please describe the health care resources, including medications and hospitalization, required for patients to receive the drug under review.

- Include the following information for any concomitant drugs required or recommended for patients receiving the drug under review:
  - non-proprietary name, dosage, route of administration, timing relative to the receiving the drug under review
  - rationale for the concomitant medications
  - Health Canada approval status for the concomitant drugs (i.e., approved or off-label usage for the indication of interest).
- Describe the need for the drug to be administered by a physician or a clinical team and the setting of the treatment (e.g., physician office, outpatient clinic, inpatient hospital setting).

3.2.3. Post-Treatment Phase

Please describe the health care resources required for patients in the post-treatment phase, including (but not limited to):

- any drugs required to prevent or reduce the risk of adverse events associated with the drug under review and/or the administration procedure(s)
  - non-proprietary name, dosage, route of administration
  - timing relative to the receiving the drug under review and duration of treatment
  - setting for the post-treatment drugs (e.g., home administration, physician's office, outpatient clinic, inpatient hospital setting)
- any additional monitoring requirements to ensure the safety and well-being of the patient after receiving the drug
- anticipated duration and setting for recovery from the procedures (e.g., hospitalization or need to be near a specialized treatment centre for a particular period of time) and factors that could influence recovery time.

3.3. Ancillary Requirements

In this section, the sponsor is asked to briefly describe any ancillary resources that may be required for patients who will receive the treatment and their caregivers (e.g., travel and lodging requirements). If applicable, please note the following:

- support for ancillary resources expect to be offered by the sponsor
- support for ancillary resources expect to be offered through other third-party organizations.

4. AFFORDABILITY CONSIDERATIONS

4.1. Budget Impact Analysis

In this section, the sponsor is asked to briefly summarize the reference-case results for its budget impact analysis. Please note that jurisdictions will be provided with the complete reports and models for the budget impact analyses; therefore, please provide a clear and concise summary that focuses on the key results.

Sample Table for Summarizing the Reference Case of the Budget Impact Analysis

Province or territory	Estimated budget impact		
	Year 1	Year 2	Year 3
Pan-Canadian[a]			
Alberta			
British Columbia			
Manitoba			
New Brunswick			
Newfoundland and Labrador			
Northwest Territories			
Nova Scotia			
Nunavut			
Ontario			
Prince Edward Island			
Saskatchewan			
Yukon			
First Nations and Inuit			

[a] Estimated aggregate budget impact for all of the provinces and territories with the exception of Quebec.

4.2. Other Considerations

In this section the sponsor may include any additional information it feels could be informative for the participating jurisdictions and pan-Canadian Pharmaceutical Alliance (pCPA). **This section of the document is optional for sponsors.**

Status in Other Countries

Examples of information that could be included:

- pricing information from other countries
- reimbursement conditions in other countries
- uptake of the drug being reviewed in other countries.

Confidential Pricing Elements

Examples of information that could be included:

- information in the economic model submitted to CADTH (e.g., cap per patient year)
- caps used in the other countries.

REFERENCES

Please provide a numbered list of references using the JAMA Oncology citation format.

Letter for Sending NOC or NOC/c Template

Purpose

The purpose of this letter is to indicate that the NOC or NOC/c is being provided, and to confirm whether or not there are any changes to the final product monograph wording that may necessitate revisions to the clinical and/or pharmacoeconomic information filed with CADTH.

Letter Template

Reference: Brand Name (Non-Proprietary Name)

1. Confirmation That NOC or NOC/c Has Been Received

This letter confirms that the [Health Canada NOC/NOC/c; select appropriate] for the previously noted CADTH submission filed on a pre-NOC basis is being provided to CADTH along with this letter.

2. Summary of Product Monograph Revisions

The following table summarizes product monograph wording changes that may impact the clinical and/or pharmacoeconomic information that was filed with CADTH.

Summary of Product Monograph Changes That May Impact Clinical and/or Pharmacoeconomic Information		
Section	**Draft product monograph[a]**	**Final product monograph[b]**
Indication		
Dosage and administration		
Other[c]		

[a] Provide the exact wording used in the draft product monograph at the time of acceptance for review by CADTH.
[b] Provide the exact wording from the Health Canada–approved final product monograph.
[c] Specify all other changes that may impact the clinical and/or pharmacoeconomic information. Add additional rows as necessary.

3. Impact of Product Monograph Revisions

Option 1

[Insert sponsor's name] confirms that there are no wording changes to the final Health Canada–approved indication or any other pertinent sections of the product monograph information, as compared to the draft product monograph provided at the time the file was accepted for review by CADTH.

Option 2

There are wording changes to the final Health Canada–approved product monograph. In [insert sponsor's name]'s opinion, the wording changes to the final Health Canada–approved indication [and/or; specify any other or additional pertinent sections of the product monograph with changes], as compared to the draft product monograph provided at the time the file was accepted for review by CADTH (and summarized in the previously included table), [has/have] no impact on the clinical and/or pharmacoeconomic information that was filed with CADTH. The rationale is as follows: [please provide a clear rationale].

Option 3

There are wording changes to the final Health Canada–approved product monograph. In [insert sponsor's name]'s opinion, the wording changes to the final Health Canada–approved indication [and/or; specify any other or additional pertinent sections of the product monograph with changes], as compared to the draft product monograph provided at the time the file was accepted for review by CADTH (and summarized in the previously included table), have an impact on the [clinical and/or pharmacoeconomic; indicate as appropriate] information that was filed with CADTH. [Insert sponsor's name]'s therefore confirms that additional documentation to address the impact will be provided to CADTH by [insert date].

[Signature]
[Name, and title of senior company official for the sponsor]

Tailored Review Submission Template

Purpose

A tailored review consists of CADTH conducting an appraisal of the clinical evidence and pharmacoeconomic evaluation filed by the sponsor using this template, which will be validated and critically appraises by CADTH.

Template

SPONSOR'S SUMMARY OF THE CLINICAL EVIDENCE

Pivotal Studies

Table 1: Details of Included Studies

		Study name	Study name
DESIGNS AND POPULATIONS	**Study design**		
	Locations	*List the number of centres and the countries involved*	
	Randomized (N)	*Provide total randomized patients*	
	Inclusion criteria	*Provide a bulleted list of the key inclusion criteria*	
	Exclusion criteria	*Provide a bulleted list of the key exclusion criteria*	
DRUGS	**Intervention**	*Specify the drug, dose, route and frequency of administration*	
	Comparator(s)	*Specify the drug, dose, route and frequency of administration for each comparator*	
DURATION	**Phase**		
	Run-in	*Specify the duration*	
	Double-blind	*Specify the duration*	
	Follow-up	*Specify the duration*	
OUTCOMES	**Primary end point**	*Define the end point*	
	Secondary and exploratory end points	*Secondary end points:* • *Provide a bulleted list* *Exploratory end points:* • *Provide a bulleted list*	
NOTES	**Publications**	• *Provide references for all publications related to this study* • *Provide the clinicaltrials.gov identification code*	

Please add here any abbreviations used in the table and their definitions (e.g., AE = adverse event; RCT = randomized controlled trial).
Source: For all tables reporting information from included studies, include the data source with citation.

Description of Studies

Please provide a brief summary of the following key trial information: the study objective(s), a description of the study design, eligible patients, sample size, locations including number of sites in Canada, study treatments, and randomization methodology (if applicable). If available, please include a figure showing the duration and characteristics of the different phases of the study (e.g.,

run-in period, treatment period, follow-up). CADTH does not typically report data for treatment groups that evaluated dosages that are not aligned with the recommendations in the product monograph. Where relevant, please include a statement that data will not be presented for treatment groups that are not aligned with the Health Canada–approved dose.

Populations

Inclusion and Exclusion criteria

Please describe the key inclusion and exclusion criteria of the study. Clearly state if there any differences in the inclusion and exclusion criteria between the studies.

Baseline Characteristics

Please summarize major and relevant baseline demographic and clinical characteristics using a table (please keep this to a maximum of one page). Comment on the similarity and differences between treatment groups within each study, and note any key differences in the demographic and clinical characteristics of the included populations across studies. CADTH typically only presents baseline characteristics for treatment groups that reflect the dosage(s) that will be recommended in the product monograph for the drug under review. Indicate in the table which analysis set the baseline characteristics have been summarized for (e.g., intention-to-treat set).

Table 2: Summary of Baseline Characteristics

Characteristics	Treatment 1	Treatment 2

Please add here any abbreviations used in the table and their definitions (e.g., RCT = randomized controlled trial; SD = standard deviation).
Source: Please report the source of the data here.

Interventions

Briefly describe the interventions employed in the included trials, including dose, frequency, duration, and so forth. If the trial is blinded, indicate the use of matched placebos and/or double-dummy controls, and provide a description of the placebo. Describe any concomitant medications or co-interventions required or permitted during the study.

Include any criteria for rescue medication use, where applicable, along with dosing schedules and maximum dosages permitted. Describe any stopping criteria for the intervention, if relevant. For non-oral medications or medications requiring a device for administration (e.g., insulin pen, auto-injector, inhalation device), include details related to the device, training, and administration. For drugs that require titration, please include a description of the titration schedule and the criteria used for determining the titration schedule (e.g., at the investigators discretion, a fixed schedule, or titration to target).

Outcomes

Briefly describe the efficacy outcomes for the included studies in sufficient detail for the reader to be able to understand and interpret the outcome data (definitions and measurement). Please do not include aspects of the statistical analysis or results in this section. Descriptions of scale measures should include a brief overview of the scale, including:

- construct(s) or domain(s) measured
- structure of the scale (i.e., is there one single overall score or individual domain scores or both)
- range of scores
- direction of the scale (e.g., do higher scores indicate greater or lesser impairment)
- the range of estimated minimal clinically important differences for the end point (if known) for the overall and individual domain scores.

Statistical analysis

Please provide a brief description of the statistical analysis for each study that includes the subsequently outlined items. Repetition should be avoided where possible. If methods for the secondary outcomes are similar to those for the primary outcome, simply state this and highlight any differences. The same applies if more than one secondary outcome is analyzed using similar methodology. Where appropriate, items may be summarized in a table where appropriate.

Primary Outcome(s) of the Studies

Power Calculation

Assumptions regarding expected differences in treatment effect and variation (e.g., standard deviation), as well as the rationale for selecting the parameters used in the calculation, should be reported.

Statistical Test or Model

The rationale for selection of the statistical test or model should be reported. The covariates and/or baseline values that were included in the statistical models should be specified. For co-primary end points or composite end points, it should be specified if the analysis approach accounted for multiple testing with an appropriate control of the type I error rate. It should be stated if the analysis was based upon the intention-to-treat or per-protocol population.

Data Imputation Methods

Please report the methods used for handling missing data (e.g., last observation carried forward, mixed-effect model with repeated measures, non-responder imputation).

Subgroup Analyses

Key details of subgroup analyses should be reported, including whether they are pre-specified, whether the comparability of the treatment groups was checked, and whether the type I error rate was controlled for multiple testing.

Sensitivity Analyses

The main sensitivity analyses, if any, and the rationale for the analyses should be described.

Secondary Outcomes of the Studies

The description of the statistical analysis for secondary outcomes should generally cover the same points described in the statistical test or model section, particularly when the main outcomes of

interest for the CADTH review are secondary outcomes in the clinical trial. Details of the method of adjustment for multiple testing or control of type I error rate must be provided. The description must identify which tests or outcomes were included in the testing strategy and identify those outcomes that were not included.

Analysis Populations

Define analysis sets (e.g., intention-to-treat, per-protocol, safety set) for each study. Actual numbers in each analysis population should be presented under Patient Disposition.

SPONSOR'S SUMMARY OF THE RESULTS

Patient Disposition

Please summarize the disposition for each included study in this section of the template. Please comment on the common reasons for screening failures as well as reasons for study discontinuation and note any differential dropout rates or large percentage of screening failures.

Table 3: Sample Table for Patient Disposition

	Study A		Study B	
	Treatment 1	**Treatment 2**	**Treatment 1**	**Treatment 2**
Screened, N				
Randomized, N				
Discontinued, N (%)				
Reason for discontinuation, N (%)				
Adverse events				
Lost to follow-up				
ITT, N				
PP, N				
Safety, N				

Please add here any abbreviations used in the table and their definitions (e.g., ITT = intention to treat)
Source: Please report the source of the data here.

Exposure to study treatments

Study Treatments

Summarize exposure, focusing on any discrepancies among treatment group or across trials. Include information on adherence to the study treatments.

Concomitant Medications

Please summarize exposure to concomitant interventions (e.g., rescue therapy, if relevant). Please note any imbalances between the treatment groups.

Efficacy

Please include a separate subsection for each of the key outcomes that were included in the study.

Efficacy Outcome One

The text of the efficacy section should clearly and concisely convey the main messages of the data that are presented in tables or graphs. Present the results in a manner that emphasizes the magnitude of the treatment effect and precision of the estimate (i.e., confidence interval), rather than only focusing only on statistical significance. Please focus on key results within the text; it is not necessary to repeat all of the data that are reported within tables.

Table 4: Sample Table for a Continuous Outcome

	Total N	Baseline	End of treatment time point (specify)		Treatment group difference versus control		
		Mean (SD)	Mean (SD)	Mean change from baseline (SE)	N	Mean difference (95% CI)[b]	*P* value
Outcome 1 (units) [a]							
Study 1							
Treatment 1							[c]
Treatment 2							
Study 2							
Treatment 1							[c]
Treatment 2							

Add here any abbreviations used in the table and their definitions (e.g., CI = confidence interval).
[a] Specify model, covariates, analysis population, and time point for each outcome.
[b] Indicate which group is the reference treatment.
[c] Specify if the outcome was within or outside of the statistical testing hierarchy.
Source: report the source of the data here.

Table 5: Sample Table for a Dichotomous Outcome

	Total N	Outcome 1[a]		
		n (%)	RR or OR (95% CI)[b]	*P* value
Study 1				
Treatment 1				[c]
Treatment 2				
Study 2				
Treatment 1				[c]
Treatment 2				

Add any abbreviations used in the table and their definitions (e.g., CI = confidence interval; RR = risk ratio).
[a] Specify model, covariates, analysis population, and time point for each outcome.
[b] Indicate which group is the reference treatment.
[c] Specify if the outcome was within or outside of the statistical testing hierarchy.
Source: Please report the source of the data here.

Harms

This section must not exceed five pages of 9-point Arial font. The required information or evidence must be succinct and entered directly into the template. In this section, whenever possible, please focus on integrated safety data.

Safety Evaluation Plan

Provide a brief overview of the overall safety evaluation plan for the drug under review. Please keep this description to a maximum of a half page.

Overview of Safety

Summarize the key findings of the safety evaluation for the drug under review. Please provide an overall summary table of key harms data (per the following example).

Table 6: Sample Table for Summarizing Harms Data

Adverse events	Study 1		Study 2	
	Treatment 1	Treatment 2	Treatment 1	Treatment 2
Patients with at least one adverse event				
n (%)				
Most common events				
Patients with at least one serious adverse event				
n (%)				
Most common events				
Withdrawals due to adverse events				
n (%)				
Most common events				
Adverse events of special interest				
[specify event], n (%)				

Add any abbreviations used in the table and their definitions (e.g., n = number of patients with event).
Source: report the source of the data here.

Adverse Events

Please focus on treatment-emergent adverse events. State findings overall (across studies).

Serious Adverse Events

Please summarize treatment-emergent serious adverse events in this section. Do not limit this section to treatment-related adverse events.

Withdrawals Due to Adverse Events

Please summarize withdrawals due to adverse events as well as adverse events that resulted in an interruption of the study treatment(s). Please clearly identify if the adverse events resulted in discontinuation of the study treatment and/or complete discontinuation from the study.

Adverse Events of Special Interest

Please provide a brief summary of any adverse events of special interest.

Bioequivalence (If Applicable)

This section can be used to summarize relevant bioequivalence trials that are considered to be pivotal or supportive for the regulatory submission for the drug under review. Information provided must be succinct and not exceed three pages. References must be provided and are to be included in a list of references at the end of the template.

Table 7: Sample Table for Bioequivalence Data

Pharmacokinetics	Drug Under Review	Comparator	Comparison
AUC			Difference (CI); *P* value

Cmax			
Tmax (h)			
T1/2 (h)			
Bioavailability			
Degradation			

Add any abbreviations used in the table and their definitions (e.g., AUC = area under the curve; CI = confidence interval).
Source: report the source of the data here.

PHARMACOECONOMIC EVALUATION

Sponsor-Submitted Cost Information

New Combination Products

- The required information must be succinct and entered directly into the template.
- The cost comparison should include all relevant comparators. For new combination products, this includes the individual components of the new combination product.
- The sources of price information and recommended dosage regimen must be provided and included as footnotes below the tables.
- Provide the price of the drug under review (price for all strengths per smallest unit to four decimal places) and its daily (or weekly or monthly) cost compared with the price of all relevant comparators (see Table 8).
- For new combination products, please ensure that the prices of the individual components are reported in the summary table. Include the cost differences and potential cost savings of the drug under review compared with the individual components.
- Quantify the price difference of the drug under review compared with each of the comparators listed in the table.

New Formulations of Existing Drugs

- The required information must be succinct and entered directly into the template.
- The cost comparison should include all relevant comparators. For new formulations of existing drugs, this includes the originator product(s) in addition to all relevant comparator treatments.
- The sources of price information and recommended dosage regimen must be provided and included as footnotes below the tables.
- Provide price of the drug under review (price for all strengths per smallest unit to four decimal places) and its daily (or weekly or monthly) cost compared with the price of all relevant comparators (see Table 8).
- Provide details if the drug under review is expected to result in any differences in health care resource use within the public payer perspective.
- State the assumptions for any differences in health care resource use and the justification for these assumptions (see Table 9).
- State the health care resources that will be used and which treatments these apply to (see Table 10).
- Quantify the difference in health care costs for the drug under review compared with each comparator (see Table 11)

- Present the aggregated differences in drug acquisition and health care costs in a summary table (see Table 12).

Table 8: Sample Table for Drug Acquisition Cost Comparison

Generic name (brand name)	Strength	Dosage form	Price ($)	Recommended dosage regimen	Annual[a] drug cost ($)	Difference in annual[a] cost
Drug under review						
Comparators						
Comparator 1						
Comparator 2						

Note: The drug under review should be the reference cost for the incremental comparison.
[a] Annual cost should be reported unless the drug is used for a specified period, then a cost per course can be stated (revise the terminology in the table and provide clarity on the course duration in a footnote[s]).

Table 9: Sample Table for Assumptions

Assumption	Justification
Assumption 1	*Provide references to support the justification where possible*
Assumption 2 *(add or remove as required)*	

Table 10: Sample Table for Health Resource Use

Health care resource	Frequency (and duration, if required) per year[a]	Unit cost	Treatment(s)
State health care resource			*State which treatments the resource is applicable to*
If more than one, state additional resources on each new row			
Add or remove rows as required			

Note: Reference sources for frequency/duration and unit cost clearly within the table and/or via footnote(s).
[a] Information should be reported on an annual basis, unless the drug is used for a specified period, then information based on the course duration can be stated (revise the terminology in the table and provide clarity on the course duration in a footnote[s]).

Table 11: Sample Table for Associated Health Care Costs

Generic name (brand name)	[State health care cost and resource]	[State health care cost and resource] *(add/remove columns as required)*	Aggregated health care cost[a] per year[b]	Difference in health care costs per year[b]
Drug under review				
Comparators				
Comparator 1				
Comparator 2				

Note: The drug under review should be the reference cost for the incremental comparison.
[a] Based on health care components included in the table.
[b] Annual cost should be reported unless the drug is used for a specified period, then a cost per course can be stated (revise the terminology in the table and provide clarity on the course duration in a footnote[s]).

Table 12: Sample Table for Summary of Comparative Treatment Costs

Generic name (brand name)	Difference in drug acquisition costs per year[a]	Difference in total health care costs per year[a]	Difference in total costs per year[a]
Drug under review			
Comparators			
Comparator 1			
Comparator 2			

Note: The drug under review should be the reference cost for the incremental comparison.
[a] Annual cost should be reported unless the drug is used for a specified period, then a cost per course can be stated (revise the terminology in the table and provide clarity on the course duration in a footnote[s]).

APPENDIX 5: PROPOSED TEMPLATES FOR STAKEHOLDER INPUT

Patient Input Template

Name of the drug and indication	
Name of the patient group	
Author of the submission	
Name of the primary contact for this submission	
Email	
Telephone number	

1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives (for example, by interviews, focus groups, or survey; personal experience; or a combination of these). Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug under review contributed insights. We will use this background to better understand the context of the perspectives shared.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, through clinical trials or private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways? If applicable, please provide the sequencing of therapies that patients would have used prior to and after the new drug under review. Please also include a summary statement of the key values that are important to patients and caregivers with respect to the drug under review.

7. Companion Diagnostic Test

Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments. **If** the drug under review has a companion diagnostic, please comment.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with the drug under review?

Consider:

- Access to testing: For example, proximity to testing facility, availability of appointment.
- Testing: For example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?

- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: For example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

8. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH Common Drug Review (CDR) and pan-Canadian Oncology Drug Review (pCODR) programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check appropriate dollar range			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name:
Position:
Date:

Clinician Group Input Template

CADTH project number	
Generic drug name (brand name)	
Indication	
Name of the clinician group	
Author of the submission	
Contact information	Name: Title: Email: Phone:

1. About Your Clinician Group

Please describe the purpose of your organization. Include a link to your website (if applicable).

2. Information Gathering

Please describe how you gathered the information included in the submission.

3. Current treatments
3.1. Describe the current treatment paradigm for the disease
Focus on the Canadian context. *Please include drug and non-drug treatments.* *Drugs without Health Canada approval for use in the management of the indication of interest may be relevant if they are routinely used in Canadian clinical practice. Are such treatments supported by clinical practice guidelines?* *Treatments available through special access programs are relevant.* *Do current treatments modify the underlying disease mechanism? Target symptoms?* ***Response:*** Click here to enter response.

4. Treatment goals

4.1. What are the most important goals that an ideal treatment would address?

Examples: Prolong life, delay disease progression, improve lung function, prevent the need for organ transplant, prevent infection or transmission of disease, reduce loss of cognition, reduce the severity of symptoms, minimize adverse effects, improve health-related quality of life, increase the ability to maintain employment, maintain independence, reduce burden on caregivers.

Response:

Click here to enter response.

5. Treatment gaps (unmet needs)

5.1. Considering the treatment goals in Section 4, please describe goals (needs) that are not being met by currently available treatments.

Examples:

- *Not all patients respond to available treatments*
- *Patients become refractory to current treatment options*
- *No treatments are available to reverse the course of disease*
- *No treatments are available to address key outcomes*
- *Treatments are needed that are better tolerated*
- *Treatment are needed to improve compliance*
- *Formulations are needed to improve convenience*

Response:

Click here to enter response.

5.2. Which patients have the greatest unmet need for an intervention such as the drug under review?

Would these patients be considered a subpopulation or niche population?

Describe characteristics of this patient population.

Would the drug under review address the unmet need in this patient population?

Response:

Click here to enter response.

6. Place in therapy

6.1. How would the drug under review fit into the current treatment paradigm?

Is there a mechanism of action that would complement other available treatments, and would it be added to other treatments?

Is the drug under review the first treatment approved that will address the underlying disease process rather than being a symptomatic management therapy?

Would the drug under review be used as a first-line treatment, in combination with other treatments, or as a later (or last) line of treatment?

Is the drug under review expected to cause a shift in the current treatment paradigm?

Response:

Click here to enter response.

6.2. Please indicate whether or not it would be appropriate to recommend that patients try other treatments before initiating treatment with the drug under review? Please provide a rationale for your perspective.

If so, please describe which treatments should be tried and include a brief rationale.

Response:

Click here to enter response.

6.3. Which patients would be best suited for treatment with the drug under review?

Which patients are most likely to respond to treatment with the drug under review?

Which patients are most in need of an intervention?

Would this differ based on any disease characteristics (e.g., presence or absence of certain symptoms, stage of disease)?

Response:

Click here to enter response.

6.4. How would patients best suited for treatment with the drug under review be identified?

Examples: *Clinician examination or judgement, laboratory tests (specify), diagnostic tools (specify)*

Is the condition challenging to diagnose in routine clinical practice?

Are there any issues related to diagnosis? (e.g., tests may not be widely available, tests may be available at a cost, uncertainty in testing, unclear whether a scale is accurate or the scale may be subjective, variability in expert opinion.)

Is it likely that misdiagnosis occurs in clinical practice (e.g., underdiagnosis)?

Should patients who are pre-symptomatic be treated considering the mechanism of action of the drug under review?

Response:

Click here to enter response.

6.5. Which patients would be least suitable for treatment with the drug under review?

Response:

Click here to enter response.

6.6. Is it possible to identify those patients who are most likely to exhibit a response to treatment with the drug under review?

If so, how would these patients be identified?

Response:

Click here to enter response.

6.7. What outcomes are used to determine whether a patient is responding to treatment in clinical practice?

Are the outcomes used in clinical practice aligned with the outcomes typically used in clinical trials?

Response:

Click here to enter response.

6.8. What would be considered a clinically meaningful response to treatment?

Examples:

- *Reduction in the frequency or severity of symptoms (provide specifics regarding changes in frequency, severity, and so forth)*
- *Attainment of major motor milestones*
- *Ability to perform activities of daily living*
- *Improvement in symptoms*
- *Stabilization (no deterioration) of symptoms*

Consider the magnitude of the response to treatment. Is this likely to vary across physicians?

Response:

Click here to enter response.

6.9. How often should treatment response be assessed?

Response:

Click here to enter response.

6.10. What factors should be considered when deciding to discontinue treatment?

Examples:

- *Disease progression (specify; e.g., loss of lower limb mobility)*
- *Certain adverse events occur (specify type, frequency, and severity)*
- *Additional treatment becomes necessary (specify)*

Response:

Click here to enter response.

6.11. What settings are appropriate for treatment with the drug under review?

Examples: Community setting, hospital (outpatient clinic), specialty clinic

Response:

Click here to enter response.

6.12. For non-oncology drugs, is a specialist required to diagnose, treat, and monitor patients who might receive the drug under review?

If so, which specialties would be relevant?

Response:

Click here to enter response.

7. Additional information

7.1. Is there any additional information you feel is pertinent to this review?

Response:

Click here to enter response.

Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check appropriate dollar range			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician group with a company, organization, or entity that may place this clinician group in a real, potential, or perceived conflict of interest situation.

Name:
Position:
Date:

Sponsor Comments Template

Purpose

This template is to be used by sponsors when providing their comments on the draft CADTH reports and by CADTH when providing responses to the commentary. The maximum table length is 10 pages (the reference list is not included in this total).

Template

SECTION 1: STANDARD REVIEWS

Sponsor's comments		CADTH response
CADTH clinical report		
1	*Your text here*	*Leave blank – for CADTH use*
2	*Your text here*	*Leave blank – for CADTH use*
CADTH pharmacoeconomic report		
3	*Your text here*	*Leave blank – for CADTH use*
4	*Your text here*	*Leave blank – for CADTH use*

SECTION 2: CELL AND GENE THERAPY REVIEWS

Sponsor's comments		CADTH response
CADTH clinical report		
1	*Your text here*	*Leave blank – for CADTH use*
2	*Your text here*	*Leave blank – for CADTH use*
CADTH pharmacoeconomic report		
3	*Your text here*	*Leave blank – for CADTH use*
4	*Your text here*	*Leave blank – for CADTH use*
CADTH ethics report		
5	*Your text here*	*Leave blank – for CADTH use*
6	*Your text here*	*Leave blank – for CADTH use*

SECTION 3: TAILORED REVIEWS AND TARGETED REASSESSMENT

Sponsor's comments		CADTH response
CADTH review report		
1	*Your text here*	*Leave blank – for CADTH use*
2	*Your text here*	*Leave blank – for CADTH use*

Sponsor's References

a. First citation here
b. Second citation here

CADTH References

1. For CADTH use

Identification of Confidential Information Form

Purpose

This template is used by sponsors when formally identifying confidential information contained within CADTH reports and recommendations.

Template

SECTION 1: STANDARD REVIEWS

CONFIDENTIAL INFORMATION TO BE REDACTED FROM CADTH CLINICAL REPORT		
Specify exact wording and page number	**Sponsor's rationale for removing information**	**CADTH response**
CONFIDENTIAL INFORMATION TO BE REDACTED FROM CADTH PHARMACOECONOMIC REPORT		
Specify exact wording and page number	**Sponsor's rationale for removing information**	**CADTH response**

SECTION 2: CELL AND GENE THERAPY REVIEWS

CONFIDENTIAL INFORMATION TO BE REDACTED FROM CADTH CLINICAL REPORT		
Specify exact wording and page number	**Sponsor's rationale for removing information**	**CADTH response**
CONFIDENTIAL INFORMATION TO BE REDACTED FROM CADTH PHARMACOECONOMIC REPORT		
Specify exact wording and page number	**Sponsor's rationale for removing information**	**CADTH response**
CONFIDENTIAL INFORMATION TO BE REDACTED FROM CADTH ETHICS REPORT		
Specify exact wording and page number	**Sponsor's rationale for removing information**	**CADTH response**

SECTION 3: TAILORED REVIEWS AND TARGETED REASSESSMENTS

CONFIDENTIAL INFORMATION TO BE REMOVED FROM CADTH REPORT		
Specify exact wording and page number	**Sponsor's rationale for removing information**	**CADTH response**

SECTION 4: EXPERT COMMITTEE RECOMMENDATION

CONFIDENTIAL INFORMATION TO BE REMOVED		
Specify exact wording and page number	**Sponsor's rationale for removing information**	**CADTH response**
ERRORS IDENTIFIED[a]		
Specify exact wording and page number	**Sponsor's rationale for removing information**	**CADTH response**

[a] Please limit this section to any errors that are identified in the document (e.g., transcription or typographical errors). Note that this does not include any issues with the presentation or interpretation of evidence.

Request for Reconsideration Template

Purpose

This template is used by sponsors when filing a request for reconsideration of a draft recommendation.

Template

SECTION 1: PRODUCT INFORMATION

Drug name	
Indication(s)	
Sponsor	
Date	

SECTION 2: RECONSIDERATION TELECONFERENCE

As part of the reconsideration process, CADTH offers the sponsor a one-hour teleconference with CADTH staff to ensure clarity around the key issues raised in the request for reconsideration. Please indicate if you are interested in participating in a teleconference:

☐ Yes, we would like to participate in a teleconference with CADTH staff.
☐ No, we do not require a teleconference with CADTH staff.

Those interested in participating in a teleconference will be contacted by CADTH regarding next steps.

SECTION 3: REQUEST FOR RECONSIDERATION

Provide the specific details of the request for reconsideration in this section of the template. The maximum length for this section is 10 pages (this total does not include the reference list).

References