



Canada's Drug and  
Health Technology Agency

# Procedures for CADTH Reimbursement Reviews

| January 2024



## Record of Updates

Version	Date	Summary of revisions
20	Jan. 25, 2024	<ul style="list-style-type: none"><li>• Revised criteria for the submission of cost-minimization analyses.</li><li>• Revised description of attendees for reconsideration meetings.</li><li>• Duration of pipeline meetings extended to 90 minutes.</li><li>• Clarification added to the confidentiality guidelines for applications received prior to January 2, 2024.</li></ul>
19	Nov. 30, 2023	<ul style="list-style-type: none"><li>• Revised confidentiality guidelines.</li><li>• Clarification of pharmacoeconomic requirements.</li></ul>
18	Sept. 28, 2023	<ul style="list-style-type: none"><li>• Clarification regarding requirements for sponsor summary of clinical evidence.</li><li>• New application requirement to include responses to requests for deviation from the pharmacoeconomic requirements within the application materials.</li><li>• Revised procedures for reconsideration meetings to include optional attendance by the participating drug programs.</li><li>• Updates to section on reassessment through the CADTH Therapeutic Review or Streamlined Drug Class Review Processes</li></ul>
17	Jun. 8, 2023	<ul style="list-style-type: none"><li>• New instructions and application templates for industry pipeline meetings.</li><li>• New information in the list of studies included in the clinical review provided to the sponsor.</li></ul>
16	Apr. 20, 2023	<ul style="list-style-type: none"><li>• New instructions for inviting CADTH to observe Health Canada meetings.</li><li>• Revised timing for calls for patient and clinician group input.</li><li>• Clarification regarding requirements for sponsor summary of clinical evidence.</li><li>• Revisions made based on recommendations from the CADTH Procedural Review Panel:<ul style="list-style-type: none"><li>○ Clarification on the objectives of CADTH's reimbursement review process.</li><li>○ Clarification on the nature of the descriptions provided for recommendation options.</li></ul></li><li>• Revised Appendix 2 to provide further clarity and guidance for those who wish to make a request for a procedural review.</li></ul>
15	Feb. 16, 2023	<ul style="list-style-type: none"><li>• Revised instructions for filing and receiving documents.</li><li>• New application requirement for RIS files with economic references.</li><li>• Revised process and updated template for ethics review.</li><li>• Clarification about biosimilar eligibility.</li><li>• Clarification within the confidentiality guidelines that correspondence between CADTH and the sponsor regarding the drug under review may be shared with authorized recipients.</li></ul>
14	Nov. 10, 2022	<ul style="list-style-type: none"><li>• Clarification of pharmacoeconomic requirements.</li></ul>
13	Sept. 1, 2022	<ul style="list-style-type: none"><li>• Clarification regarding timing for notification following withdrawal from Health Canada.</li><li>• New information will not be accepted after draft reports issued to sponsor.</li><li>• Revised naming and eligibility criteria of the Interim Plasma Protein and Related Product review process.</li></ul>
12	Mar. 31, 2022	<ul style="list-style-type: none"><li>• New clinical evidence template for sponsors.</li><li>• Clarification regarding reconsideration process.</li><li>• Clarification of pharmacoeconomic requirements.</li><li>• Revised confidentiality guidelines.</li></ul>
11	Dec. 16, 2021	<ul style="list-style-type: none"><li>• New rapid provisional funding algorithm process introduced.</li></ul>



## Procedures for CADTH Reimbursement Reviews

10	Nov. 25, 2021	<ul style="list-style-type: none"><li>• New complex review process introduced.</li><li>• New instructions for notifying CADTH when the pause-the-clock process has been implemented during the regulatory review.</li><li>• Revised process for pre-submission meetings.</li><li>• Clarifications and revisions to pharmacoeconomic requirements.</li></ul>
9	Sept. 16, 2021	<ul style="list-style-type: none"><li>• Opportunity for sponsor to review stakeholder feedback for confidential information.</li><li>• Revised process regarding new information during the reconsideration phase.</li><li>• Revisions to pharmacoeconomic requirements.</li><li>• Revised process for incorporating patient group and clinician group input into reports.</li><li>• Feasibility of adoption listed as a reimbursement condition category.</li></ul>
8	Jun. 17, 2021	<ul style="list-style-type: none"><li>• Clarification regarding requests for reconsideration filed by the drug programs.</li><li>• New application requirement for the status of the drug in other jurisdictions.</li></ul>
7	Apr. 29, 2021	<ul style="list-style-type: none"><li>• Additional details on pharmacoeconomic requirements for a cost-minimization analysis.</li><li>• Clarification regarding the drug programs to be included in the budget impact analysis.</li><li>• Clarification regarding timelines for the calls for patient and clinician group input.</li><li>• Revision to the procedural review process.</li><li>• Reformatted checklists.</li></ul>
6	Mar. 24, 2021	<ul style="list-style-type: none"><li>• Revisions to pharmacoeconomic requirements.</li></ul>
5	Feb. 25, 2021	<ul style="list-style-type: none"><li>• Revised timelines for posting clinician group input.</li></ul>
4	Jan. 14, 2021	<ul style="list-style-type: none"><li>• Revised instructions for submitting advance notification and pre-submission meeting request forms to CADTH.</li><li>• Clarification of pharmacoeconomic submission requirements.</li></ul>
3	Dec. 3, 2020	<ul style="list-style-type: none"><li>• Document renamed as <i>Procedures for CADTH Reimbursement Reviews</i>.</li><li>• Revisions to checklists and file structures for tailored reviews to reflect that the reimbursement status of comparators is no longer located as an appendix of the tailored review submission template.</li></ul>
2	Oct. 29, 2020	<ul style="list-style-type: none"><li>• Clinician groups will not be asked to review and validate the summary of input that is prepared by CADTH.</li><li>• Clarification that the reimbursement status of comparators template must be filed as a Microsoft Word document.</li></ul>
1	Sept. 30, 2020	<ul style="list-style-type: none"><li>• Original version posted.</li></ul>



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### Abbreviations

<b>BIA</b>	budget impact analysis
<b>CAPCA</b>	Canadian Association of Provincial Cancer Agencies
<b>CDEC</b>	CADTH Canadian Drug Expert Committee
<b>CDR</b>	CADTH Common Drug Review
<b>CPEC</b>	CADTH Canadian Plasma Protein Product Expert Committee
<b>DIN</b>	Drug Identification Number
<b>FWG</b>	Formulary Working Group
<b>INESSS</b>	Institut national d'excellence en santé et en services sociaux
<b>NOC</b>	Notice of Compliance
<b>NOC/c</b>	Notice of Compliance with Conditions
<b>NOD</b>	Notice of Deficiency
<b>NON</b>	Notice of Non-Compliance
<b>PAG</b>	Provincial Advisory Group
<b>pCODR</b>	CADTH pan-Canadian Oncology Drug Review
<b>pCPA</b>	pan-Canadian Pharmaceutical Alliance
<b>pERC</b>	CADTH pCODR Expert Review Committee
<b>PPRP</b>	Plasma Protein and Related Product
<b>PTBLC</b>	Provincial and Territorial Blood Liaison Committee
<b>RCT</b>	randomized controlled trial
<b>RWE</b>	real-world evidence



## 1. Introduction

### 1.1 Purpose of This Document

This document outlines the procedures for CADTH’s reimbursement review processes, including those used for oncology drugs, non-oncology drugs, and plasma protein and related products reviewed through the interim process. Selected 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](#).

CADTH may amend the *Procedures for CADTH Reimbursement Reviews* and all matters related to its drug review processes. CADTH may request stakeholder feedback for procedural changes and the drug programs will also be consulted, as required. Amendments to, and clarifications of, the *Procedures for CADTH Reimbursement Reviews* and all related documents may be effected by means of directives (called [CADTH Pharmaceutical Reviews Update](#)) issued by CADTH on an as-needed basis between revisions of these procedures. As such, this document must be read in conjunction with any relevant issues of the *CADTH Pharmaceutical Reviews Update*.

### 1.2 Procedures for Time-limited Reimbursement Recommendations

Effective September 28, 2023, CADTH has introduced a new process for time-limited reimbursement recommendations. For complete details, please consult the [CADTH Procedures for Time-limited Reimbursement Recommendations](#). If you have questions, please contact us at [requests@cadth.ca](mailto:requests@cadth.ca).

### 1.3 Overview of Reimbursement Review Process

#### 1.3.1 Drug Review Process

The objectives of CADTH’s reimbursement review processes are to reduce duplication across jurisdictions and maximize the use of limited resources. CADTH undertakes reviews of drugs and issues reimbursement recommendation and/or review reports to all federal, provincial, and territorial drug programs and cancer agencies that participate in CADTH’s review processes and Canadian Blood Services (together hereafter referred to as “drug programs”). It is important to note that CADTH’s recommendations are nonbinding to the drug programs. Each drug program makes its own reimbursement decisions based on the CADTH’s recommendation, in addition to other factors, including the plan’s mandate, jurisdictional priorities, and financial resources.

#### 1.3.2 Expert Committees

CADTH’s reimbursement recommendations are provided by appointed, national, expert review committees. Each committee is composed of individuals with expertise in drug therapy, drug evaluation, and drug utilization, as well as public members who bring a lay perspective. The current committee members are listed on the [CADTH website](#).





### 1.3.3 Advisory Committees

CADTH also has a number of jurisdictional [advisory committees](#) and working groups that provide advice to CADTH on drug policy issues. This includes the Pharmaceutical Advisory Committee, which advises CADTH on strategic issues, as well as working groups that provide advice on operational issues. The primary working groups for advising CADTH on reimbursement reviews are the Provincial Advisory Group (PAG) for oncology drugs and the Formulary Working Group (FWG) for non-oncology drugs.

## 1.4 Communications for Reimbursement Reviews

### 1.4.1 Stakeholder Inquiries

Stakeholders are asked to use [requests@cadth.ca](mailto:requests@cadth.ca) for inquiries related to CADTH’s reimbursement review processes. 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).

Consultants working on behalf of a sponsor are required to copy an official contact for the sponsor on all email correspondence with CADTH. CADTH will not respond to any email correspondence from a consultant if an official contact for the sponsor has not been copied.

**Table 1: Contacting CADTH and Filing Information**

Type of inquiry	Where to direct your inquiry
General inquiries regarding CADTH’s procedures and processes	<b>Email:</b> <a href="mailto:requests@cadth.ca">requests@cadth.ca</a> <b>Mail:</b> Central Intake CADTH 600-865 Carling Avenue Ottawa, ON K1S 5S8
Filing documents with CADTH	<a href="#">Pharmaceutical Submissions SharePoint Site</a>
Inquiries regarding an active CADTH review	By email to the designated submission coordinator contact provided in the acceptance for review letter
Inquiries regarding CADTH application fees	<b>Email:</b> <a href="mailto:accountsreceivable@cadth.ca">accountsreceivable@cadth.ca</a>

### 1.4.2 CADTH Communications

CADTH has consolidated all communications for its drug review programs into a single email newsletter that is issued once per week (typically on Thursday). The newsletter includes the following announcements and opportunities:

- calls for patient group input
- calls for clinician group input

- opportunities for feedback draft recommendations
- opportunities for feedback draft provisional algorithms
- notice of final recommendation
- notice of final provisional funding algorithm
- procedural updates and clarifications
- consultation opportunities
- other CADTH news regarding drug review programs.

## 2. Eligibility

### 2.1 Submission Eligibility

This section provides guidance regarding eligibility for the majority of submissions. In some situations, CADTH may consult with drug programs to confirm the eligibility of a drug and make a decision on a case-by-case basis. Sponsors that have questions regarding whether or not a drug is eligible for review by CADTH are asked to complete an [eligibility request form](#) and submit it to [requests@cadth.ca](mailto:requests@cadth.ca) as soon as possible. Eligibility should be determined prior to requesting a pre-submission meeting or providing advanced notification.

A sponsor or the drug programs may file an application for an eligible drug that has received or has a pending Notice of Compliance (NOC) or Notice of Compliance with conditions (NOC/c) for the indication(s) to be reviewed. In selected instances, CADTH may undertake the review of a drug for an unapproved indication in accordance with the criteria specified in section 2.4.3.

**Table 2: Eligibility for CADTH’s Reimbursement Review Processes**

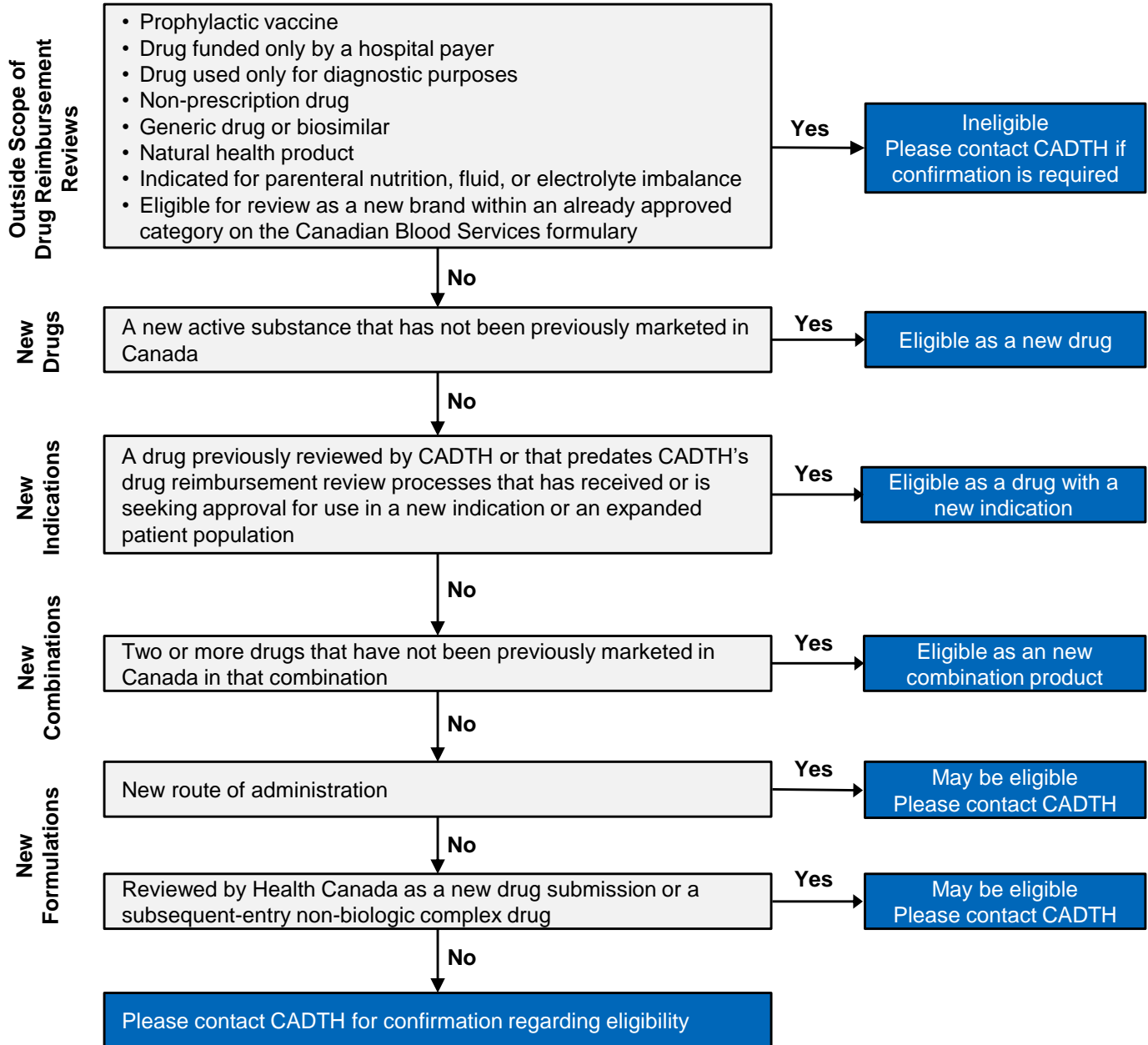
Product type	Description
<b>New drug</b>	<ul style="list-style-type: none"> <li>• A new active substance that has not been previously marketed in Canada</li> <li>• A drug consisting of a single active substance previously reviewed through one of CADTH’s reimbursement review processes only as an active substance in a combination product</li> <li>• A new salt of a marketed product</li> <li>• A drug for which eligibility for review has been confirmed by CADTH in consultation with the drug programs on a case-by-case basis</li> </ul>
<b>Drug with a new indication</b>	<ul style="list-style-type: none"> <li>• A drug previously reviewed by CADTH that has received or is seeking approval from Health Canada for use in a new indication</li> <li>• A drug marketed before the establishment of CADTH’s reimbursement review processes that has received or is seeking approval from Health Canada for use in a new indication</li> <li>• A drug previously reviewed by CADTH that has received or is seeking approval from Health Canada for use in a new age group of patients</li> </ul>
<b>New combination product</b>	<ul style="list-style-type: none"> <li>• Two or more drugs that have not been previously marketed in Canada in that combination</li> </ul>



<b>New formulation of an existing drug</b>	<ul style="list-style-type: none"><li>• New formulations of existing drugs that have a different route of administration than formulation(s) previously reviewed by CADTH</li></ul>
<b>Subsequent-entry products for non-biological complex drugs</b>	<ul style="list-style-type: none"><li>• A subsequent-entry non-biological complex drug is a medicinal product that demonstrates a high degree of similarity to an already authorized product (i.e., a reference product that has been approved for use in Canada); due to the complex nature of the product, demonstrating bioequivalence may not be possible</li></ul>

**Figure 1: Drugs Eligible for CADTH’s Reimbursement Review Processes**

Alt text: Figure summarizes eligibility criteria for review through the CADTH reimbursement review process.



### 2.1.1 New Drugs

A new drug, for CADTH’s submission purposes, typically includes one of the following:

- a new active substance that has not been previously marketed in Canada, regardless of when the NOC or NOC/c was issued



- a drug consisting of a single active substance previously reviewed through one of CADTH's reimbursement review processes only as an active substance in a combination product
- a new salt of a marketed product
- a drug for which eligibility for review has been confirmed by CADTH in consultation with the drug programs on a case-by-case basis.

### 2.1.2 New Indications

A drug with a new indication is:

- a drug previously reviewed through one of CADTH's reimbursement review processes that has received an NOC or NOC/c for a new indication
- an active substance marketed before the establishment of CADTH's reimbursement review processes that has received an NOC or NOC/c for a new indication
- a drug previously reviewed through one of CADTH's reimbursement review processes that is approved for use in a new patient population age range.

### 2.1.3 New Combination Products

A new combination product consists of 2 or more drugs that have not been previously marketed in Canada in that combination. One or more of the components may be a non-prescription drug, but at least one component must be a prescription drug.

Sponsors that are planning to file a submission for a new combination product may complete and submit a [tailored review application form](#) to CADTH ([requests@cadth.ca](mailto:requests@cadth.ca)) prior to filing the submission. CADTH will review the information and, with input from the drug programs (as needed), confirm if the application is eligible for review through the tailored review process. CADTH will typically provide a response within 10 business days of receiving the form.

### 2.1.4 New Formulations of Existing Drugs

A new drug for the purposes of a CADTH submission does not include the following variations of existing non-parenteral products containing the same active substance(s) as one or more drugs that have been previously reviewed through one of CADTH's reimbursement review processes and/or are currently being funded by the drug programs for the same indication (note: these are considered line extensions by CADTH):

- a new non-parenteral dosage form with the same route of administration, as long as the new dosage form approval is not accompanied by a change to the indicated population age range (e.g., if a drug in tablet form becomes available in capsule or oral solution dosage form)
- a new strength of the same dosage form (e.g., if a 200 mg tablet becomes available in addition to an already-marketed 100 mg tablet, and the new strength approval is not accompanied by a change to the indicated population age range, a submission for the 200 mg tablet is not required).



New parenteral products or formulations (e.g., IV, intramuscular, subcutaneous dosage forms) are not considered line extensions of one another by CADTH, as they have different routes of administration and, as a result, there may be potential differences in pharmacokinetics and pharmacodynamics, as well as differences in cost. Sponsors should submit a completed eligibility request form to [requests@cadth.ca](mailto:requests@cadth.ca) for guidance on whether a submission to CADTH is required for a new parenteral formulation.

### 2.1.5 Plasma Protein and Related Products

Submissions for new categories and/or for new products that are determined to be in some way innovative to the Canadian Blood Services formulary will be assessed by Canadian Blood Services and CADTH using the Canadian Blood Services Plasma Protein and Related Product (PPRP) selection eligibility criteria, subject to approval by the provincial and territorial governments (excluding Quebec) on the Canadian Blood Services formulary. The eligibility criteria are that the product:

- is a biological drug manufactured from human plasma or a biological drug whose active ingredient(s) are functional equivalents of the foregoing, used in the practice of Transfusion Medicine; AND
- is not carried in the health system already.

Canadian Blood Services and CADTH will initiate a review after confirmation by the Provincial and Territorial Blood Liaison Committee (PTBLC) on whether the product meets the eligibility requirements for consideration as a new category and/or a new product that is determined to be in some way innovative on the Canadian Blood Services formulary.

Canadian Blood Services will confirm with the manufacturer if the product will also be reviewed through an RFP process for PPRPs in an approved category of products.

Manufacturers with questions regarding whether or not a product is eligible for review through the interim process are asked to complete an eligibility request form and submit it to [requests@cadth.ca](mailto:requests@cadth.ca). CADTH will forward the information to Canadian Blood Services for discussion with the PTBLC. Eligibility should be determined before requesting a pre-submission meeting or providing advance notification. If it has been determined that the product does not meet the eligibility criteria as a PPRP, the sponsor can consider filing a submission through the CADTH Reimbursement Review process for a recommendation to inform reimbursement by the public drug programs.

### 2.1.6 Subsequent-Entry Products for Non-Biological Complex Drugs

A subsequent-entry non-biological complex drug is a medicinal product that demonstrates a high degree of similarity to an already authorized product (i.e., a reference product that has been approved for use in Canada). Due to the complex nature of the product, demonstrating bioequivalence may not be possible. Submissions for subsequent-entry non-biological complex drugs will typically undergo a tailored review. All sponsors should contact CADTH before filing a submission for a subsequent-entry non-biological complex drug ([requests@cadth.ca](mailto:requests@cadth.ca)).

### 2.1.7 Eligible Drugs That Have Become Genericized



As stated in section 2.1, generic drugs are not typically reviewed through CADTH's reimbursement review processes. This is usually because the branded reference product has previously been reviewed by CADTH. In the event a submission was not filed for a branded drug before the drug became genericized, CADTH will consult with the drug programs to determine if either or both manufacturers of the generic or branded product should file a submission with CADTH. Given that the context and product characteristics for these situations are likely to be unique, CADTH and the drug programs will provide guidance on a case-by-case basis as to whether a submission is required. Based on the input from the drug programs, CADTH may advise manufacturers of branded or generic products that are eligible for review through the reimbursement review process (e.g., a new drug, a drug with a new indication, or a new combination product) that a submission is not required, and that the drug programs should be contacted.

Circumstances that would likely not require a submission to be filed with CADTH may include, but are not limited to, the following:

- One or more generic versions of the drug are approved by Health Canada.
- One or more generic versions of the drug are undergoing review by Health Canada.
- The drug programs have indicated they are planning to review the generic drug(s) through their standard processes for reviewing generic drugs.
- Similar products are currently listed by the drug programs (e.g., different salts of the active substance).

A submission may be required for a generic product under the following conditions:

- Similar products are not currently listed by the drug programs (e.g., different salts of the active substance).
- The manufacturer of the branded product has confirmed that it does not intend to file the product with CADTH and does not intend to seek public reimbursement.
- The generic product was reviewed by Health Canada as a new drug submission or supplemental new drug submission.

Although CADTH may advise a manufacturer that a submission is not required, it does not preclude the manufacturer from electing to file a submission provided the product meets the eligibility criteria for a new drug, a drug with a new indication, or a new combination product. Manufacturers with questions regarding the reimbursement review processes may contact CADTH at any time ([requests@cadth.ca](mailto:requests@cadth.ca)).

### 2.1.8 Biosimilars

As stated in section 2.1, biosimilars are not typically reviewed through CADTH's reimbursement review processes. Applications are only required if the biosimilar meets other eligibility criteria (e.g., a new indication that is not approved for the reference product or a new formulation that is eligible for review). Each of those scenarios is approached on a case-by-case basis and a decision is made in consultation with the participating drug programs. Sponsors that have questions regarding whether or not a biosimilar is



eligible for review by CADTH are asked to complete an [eligibility request form](#) and submit it to [requests@cadth.ca](mailto:requests@cadth.ca).

## 2.2 Resubmission Eligibility

A resubmission is a review of any drug that has previously been reviewed by CADTH through a reimbursement review process and for which a final recommendation has been issued. Resubmission eligibility must be determined prior to requesting a pre-submission meeting or providing advanced notification to CADTH (Figure 2).

### 2.2.1 New Information

A resubmission based on new information consists of one or both of the following:

- new clinical information in support of improved efficacy or safety
- new cost information that significantly affects the cost-effectiveness of the drug.

Any new studies included in the resubmission must address the specific issues identified by the expert committee in the final recommendation document. Table 3 summarizes the supporting information that must be filed for resubmissions.

**Table 3: Summary of New Information Required for Resubmissions**

Basis of resubmission	Supporting information that must be filed
New clinical information supporting improved efficacy or safety	<ul style="list-style-type: none"><li>• One or more new studies that address specific issues identified by the expert committee in the final recommendation document</li><li>• New pharmacoeconomic evaluation</li><li>• New budget impact analysis</li></ul>
New cost information that significantly affects the cost-effectiveness of the drug	<ul style="list-style-type: none"><li>• New pharmacoeconomic evaluation</li><li>• New budget impact analysis</li></ul>

Although not always a requirement, CADTH considers new evidence from one or more randomized controlled trials (RCTs) to be the preferred form of new clinical information for resubmissions based on improved efficacy and/or safety. CADTH considers data from non-randomized studies to be particularly useful in the following situations:

- when the evaluation of important clinical end points and rare adverse events requires longer-term follow-up
- when there is uncertainty regarding the persistence of efficacy of the drug under review because of short-term clinical trials
- when an RCT is impractical because of a limited number of patients
- when it is considered unethical to conduct an RCT



- when randomized studies lack relevant comparators (e.g., an indirect comparison is conducted to evaluate the comparative efficacy and safety of the drug under review relative to appropriate comparators)
- when there is uncertainty regarding the dosage of the drug(s) under review that is used in actual clinical practice
- when the RCTs have limited external validity and additional non-randomized studies could provide meaningful insight into the effectiveness of the treatment in the target population.

### 2.2.2 Eligibility Assessment for Resubmissions and Reassessments

Prior to filing a resubmission or a reassessment, sponsors are required to have its eligibility assessed by CADTH. Sponsors must provide the following information to [requests@cadth.ca](mailto:requests@cadth.ca) for evaluation by CADTH:

- a completed [resubmission or reassessment eligibility form](#)
- **For a resubmission:** copies of one or more new studies that address specific issues identified by the expert committee in the final recommendation document
- **For a reassessment:** copies of one or more new studies that support the sponsor's request for revised reimbursement criteria.

CADTH will screen the information provided by the sponsor to determine if:

- the information provided by the sponsor represents new information
- the (one or more) new studies provided by the sponsor address specific issues identified by the expert committee in the final recommendation document or support the sponsor's request for revised reimbursement criteria.

CADTH may consult with members of the expert committee and/or clinical experts to determine if the new information filed by the sponsor meets the eligibility criteria. However, the final decision regarding whether or not a resubmission or reassessment will be eligible for review will be determined by CADTH. CADTH's assessment of eligibility will typically be completed within 10 business days. Sponsors will be notified by CADTH if additional time is required to complete the assessment.

The sponsor will be apprised in writing regarding CADTH's determination of whether or not the proposed resubmission or reassessment meets the eligibility criteria. When a sponsor has been informed by CADTH that the eligibility criteria have not been met, the sponsor may file one written request for the decision to be reconsidered by CADTH. The request must clearly outline why the sponsor disagrees with CADTH's decision. Sponsors have 10 business days to file a request after receiving notification from CADTH regarding the eligibility of their proposed resubmission or reassessment. Sponsors will only be entitled to have the eligibility decision reconsidered once.

CADTH will examine the request to determine whether the issue(s) raised change the conclusions regarding the eligibility of the resubmission or reassessment. CADTH may consult with members of the expert committee and/or clinical experts (as required). The final decision regarding whether or not a resubmission



or reassessment is eligible for review will be determined by CADTH. The reconsideration will typically be completed within 10 business days, and sponsors will be notified by CADTH if additional time is required to complete the assessment. CADTH will apprise the sponsor in writing of the final decision regarding eligibility of the resubmission. CADTH will post the results of the resubmission or reassessment eligibility assessment to its website.

CADTH will retain and dispose of documents associated with the resubmission or reassessment in accordance with the *CADTH Reimbursement Review Confidentiality Guidelines*. All completed eligibility assessments may be shared by CADTH with the federal, provincial, territorial governments (including their agencies and departments) and the pan-Canadian Pharmaceutical Alliance (pCPA) office.

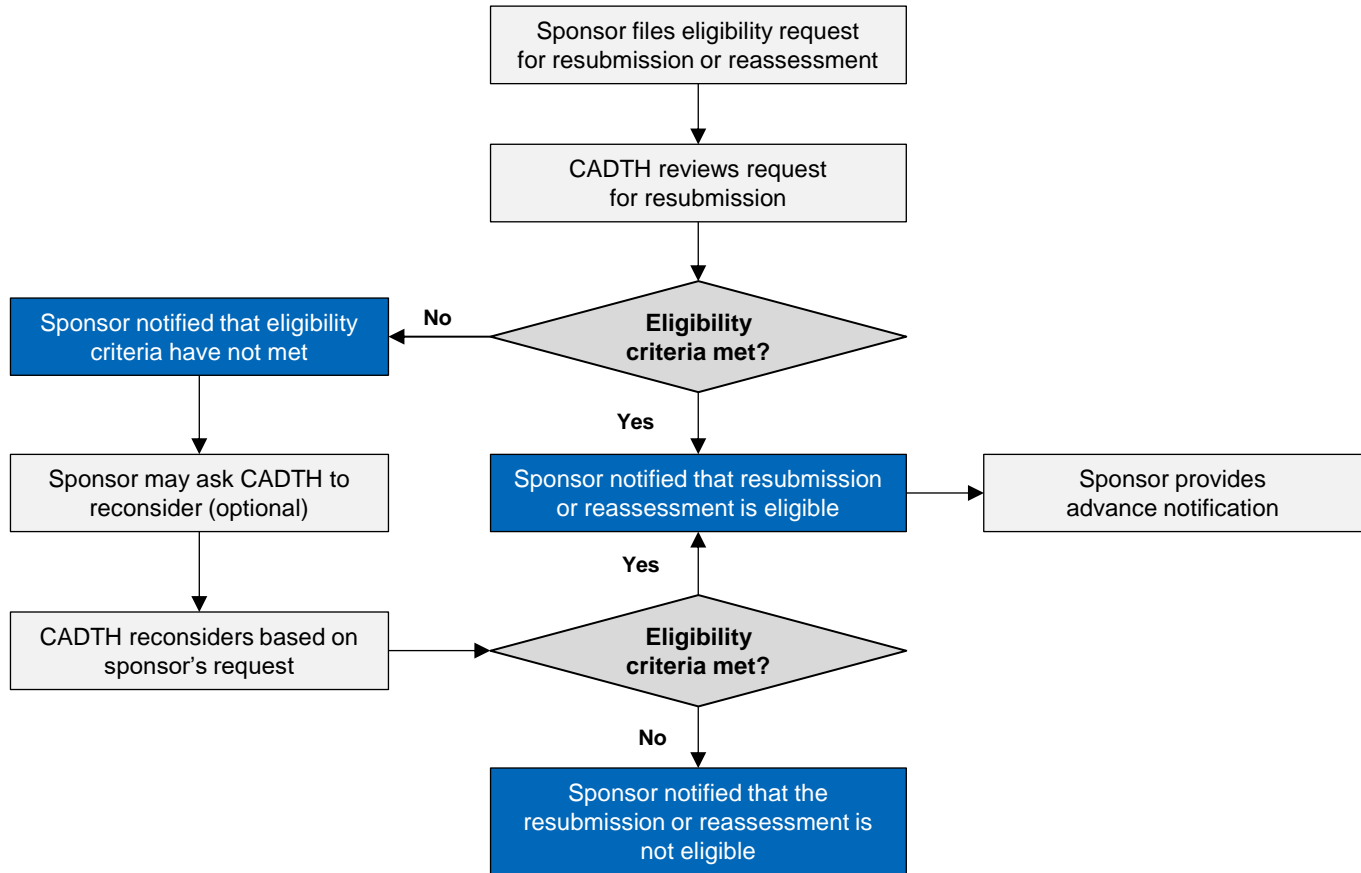
After receiving confirmation from CADTH that the proposed resubmission or reassessment is eligible for review through a reimbursement review process, sponsors are required to provide CADTH with advance notification in accordance with section 4.3.

### **2.2.3 Volume of Resubmissions and Reassessments**

To ensure fair access to CADTH's reimbursement review processes for new drug submissions, CADTH may limit the number of resubmissions and reassessments that can be made and/or initiated within a defined period of time. This decision will be made by CADTH based on the availability of resources and will be communicated to stakeholders via a [CADTH Pharmaceutical Reviews Update](#).

**Figure 2: Assessing the Eligibility of Resubmissions**

Alt text: Figure summarizes review process for evaluating resubmission and reassessment eligibility.



### 2.3 Reassessment Eligibility

Any drug that is currently reimbursed in the Canadian public health care system could be eligible for a reassessment through one of CADTH’s processes. Reassessments could be carried out in response to a variety of potential triggers (Table 4), including:

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

**Table 4: Potential Triggers for Reassessment**

Trigger	Details
Regulatory activity	<ul style="list-style-type: none"> <li>Patent expiration or pending approval of generic formulations</li> <li>Revised indications (e.g., changes that could alter coverage but would not require a full submission)</li> <li>Conversion from NOC/c to NOC (if specified as a concern in the initial review)</li> </ul>
Reimbursement activity	<ul style="list-style-type: none"> <li>Required component of funding arrangement</li> <li>Utilization issues (e.g., perceived overuse)</li> <li>Uncertain or potentially high budget impact</li> <li>Manufacturer proposes changes to existing reimbursement criteria</li> </ul>
Questions about clinical and/or cost-effectiveness	<ul style="list-style-type: none"> <li>Emergence of new comparators</li> <li>Completion of longer-term clinical studies</li> <li>Availability of new clinical data (e.g., new RCTs or RWE studies)</li> <li>Uncertainty of the magnitude of benefit</li> </ul>
Contextual changes	<ul style="list-style-type: none"> <li>Clinical practice considerations (new Canadian guidelines that do not align with CADTH recommendation; additional therapies entering the same space that alter the treatment algorithm)</li> </ul>

NOC = Notice of Compliance; NOC/c = Notice of Compliance with conditions; RCT = randomized controlled trial; RWE = real-world evidence.

### 2.3.1 Standard Reassessments

The standard reassessment process is used when there is uncertainty regarding the comparative safety, clinical effectiveness, and/or cost-effectiveness of a single drug. The standard reassessment process requires the 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 [eligibility form](#) and copies of one or more new studies that support the requested revisions to the reimbursement criteria for the drug. CADTH will assess the information provided by the sponsor 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 4.3.

### 2.3.2 Request for Advice

CADTH will typically apply the request for advice process when jurisdictions or the pCPA raise issues regarding changes in contextual information that affect their ability to implement existing CADTH



recommendations. All requests for advice will relate to a drug that has previously been reviewed through CADTH Reimbursement Review process and for which a final recommendation has been issued.

To initiate the request for advice process, CADTH must receive a formal request from the drug programs or 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 request for advice process.

The request is provided using a CADTH template and the drug programs will set out the relevant issue(s) or question(s) that are to be addressed by CADTH and the expert committee. This information will be published on the CADTH website.

### 2.4 Market Authorization Status

Submissions can be filed prior to receiving market authorization from Health Canada (i.e., pre-NOC submissions) or after receiving market authorization from Health Canada (i.e., post-NOC submissions).

#### 2.4.1 Pre-NOC Submissions

Any submission may be filed on a pre-NOC basis up to 180 calendar days in advance of the anticipated receipt of an NOC or NOC/c. If the 180th calendar day falls on a weekend or CADTH holiday, the next business day will be used. Pre-NOC submissions may only be filed by industry sponsors (refer to section 2.5.1).

This type of submission is accepted with the agreement that some submission requirements (e.g., product monograph) may not be finalized at the time of filing; however, they are to be provided as soon as they are finalized because the draft recommendation will not be released until all required information, including a copy of the NOC or NOC/c, has been received by CADTH.

Sponsors must proactively notify CADTH regarding important changes to the indication and/or dosing information during the review of pre-NOC submissions. Sponsors will receive a request from CADTH 20 business days prior to the target date for the expert committee meeting to confirm the following:

- if there are any revisions to the anticipated date of approval by Health Canada;
- if the sponsor is anticipating or discussing revisions to the indication and/or dosing information regarding the drug under review.

Sponsors will be required to provide a written response within 3 business days of receiving the CADTH request.

#### 2.4.2 Post-NOC Submissions

A submission may be filed on a post-NOC or NOC/c basis after the drug has been granted an NOC or NOC/c by Health Canada for the indication(s) to be reviewed through the reimbursement review process.

### 2.4.3 Submissions for Unapproved Indications

Submissions may be filed for oncology drugs for new indications that are not approved or are not undergoing review by Health Canada in the following instances:

- the drug is currently marketed in Canada
- the Drug Identification 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 a 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
- the drug has the potential to address an unmet therapeutic need.

CADTH will consider this information when determining whether or not a submission may be filed for an indication that is not approved or are not undergoing review by Health Canada, and will waive the required documents that are related to regulatory review and approval for these submissions: Common Technical Document; Health Canada NOC or NOC/c; and table of Clarimails/Clarifaxes.

## 2.5 Sponsor Eligibility

### 2.5.1 Industry Sponsors

Pharmaceutical industry sponsors are typically the DIN holders for the drug being filed for review with CADTH; however, it could be another manufacturer, supplier, distributor, or other entity that has been recruited by the DIN holder.

### 2.5.2 Tumour Groups and Drug Programs

The drug programs and provincially recognized clinician-based tumour groups may file applications through CADTH's reimbursement review processes. Tumour groups will need to work with one of their jurisdictional PAG members to bring forward their intention to make an application to CADTH. PAG will assist in determining if the application would be of sufficient interest to warrant a review and recommendation from CADTH or if it could be addressed within the individual jurisdictions.

Prior to accepting a new submission from a tumour group or the drug programs, CADTH will confirm with the DIN holder that they are declining to file a submission with CADTH (i.e., in accordance with section 2.6).

It is expected that tumour groups and drug programs will not have the same access to information as the manufacturer of the drug. Therefore, CADTH may waive the following requirements or additional information for these applications if they are unavailable or not relevant: Common Technical Document; Clinical Study Reports; Health Canada NOC or NOC/c; Table of Clarimails/Clarifaxes. Sponsors from tumour groups and the drug programs will be required to include an economic evaluation in their application.



CADTH may contact the DIN holder on behalf of the tumour group and/or drug programs to determine if there is interest in providing relevant clinical and pharmacoeconomic data for the purposes of compiling the required documentation for the pending application.

In general, the review process will be the same as that used in the review of an application filed by an industry sponsor.

### 2.6 Declining to File a Submission With CADTH

The following process will be applied in situations where a manufacturer does not proactively file a submission with CADTH for an eligible product:

- Jurisdictions determine that they require a recommendation from CADTH to inform their reimbursement decisions.
- CADTH will issue a letter to the manufacturer on behalf of the Pharmaceutical Advisory Committee FWG or PAG informing it that the drug is eligible for review through CADTH's reimbursement review processes and that the drug programs would like a submission to be filed with CADTH.
- The manufacturer will have 30 business days to respond to the letter from the CADTH indicating whether or not it is planning to file a submission for the drug, as well as its anticipated timelines if it is choosing to submit.
- In the following scenarios a "CADTH is unable to recommend reimbursement as a submission was not filed by the manufacturer" statement will be issued on the CADTH website:
  - a manufacturer indicates that it is not planning to file a submission at this time
  - a manufacturer fails to respond to the FWG or PAG chair within the requested 30 business day period
  - a manufacturer indicated that a submission would be filed but did not provide advance notification with the anticipated filing date within 12 months of receiving the request from the FWG or PAG chair.
- These statements will be issued on the basis that a submission was not filed by the manufacturer and will not be discussed by CADTH's expert committees.
- The procedure will only apply to submissions and not to resubmissions.
- If CADTH has issued a statement on the basis that a submission was not filed, the manufacturer may file a submission at any point in the future in accordance with CADTH's procedures. This would result in a CADTH recommendation being issued for the drug and the previous statement being removed from the website.

- The participating jurisdictions can continue to file drug program–initiated submissions provided the requirements can be addressed (e.g., provision of an economic model and pharmacoeconomic evaluation).

### 3. Application Types

#### 3.1 Submissions

CADTH aims to conduct its reviews in the most efficient manner and applies the following review types depending on the complexity of the reimbursement review:

- A **standard review** consists of CADTH preparing a clinical report based on the sponsor’s completed summary of clinical evidence template, source documentation provided by the sponsor, and stakeholder input; and an economic report based on an appraisal of the sponsor-provided pharmacoeconomic evaluation.
- A **tailored review** consists of the CADTH conducting an appraisal of the clinical evidence and pharmacoeconomic evaluation filed by the sponsor using a CADTH-provided review template. Eligibility must be confirmed by CADTH prior to filing the submission by sending a completed tailored review application form to [requests@cadth.ca](mailto:requests@cadth.ca). CADTH will review the form and provide confirmation for the sponsor, typically within 10 business days of receiving the form.
- A **complex review** is conducted in a manner similar to a standard review but involves greater consultation with clinical experts (e.g., convening a pan-Canadian panel of specialists), greater consideration of non-randomized studies, a more detailed examination of potential implementation issues, and may include an additional review and consideration of potential ethical issues. Eligibility for review through the complex review process will be confirmed by CADTH at the time of accepting the file for review.

Drugs eligible for review through the complex review process include cell and gene therapies; drugs that are first-in-class; drugs reviewed through one of Health Canada’s expedited pathways (i.e., priority review or advance consideration under NOC/c); and drugs that have an undefined place in therapy. Eligibility of cell and gene therapies for review through the reimbursement review process must be confirmed by CADTH prior to filing the submission by sending a completed [eligibility request form](#) to [requests@cadth.ca](mailto:requests@cadth.ca). CADTH will review the form and provide confirmation for the sponsor, typically within 10 business days of receiving the form.

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

#### 3.2 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 CADTH's expert committee and are not currently reimbursed by the drug programs for the indication of interest. Eligibility must be confirmed by CADTH prior to filing the resubmission by sending a completed eligibility form to [requests@cadth.ca](mailto:requests@cadth.ca). CADTH will review the form and provide confirmation to the sponsor, typically within 10 business days of receiving the form.

The output of CADTH's review of a resubmission will be an updated recommendation document from CADTH that will supersede the document for the initial submission and any other prior resubmissions for the drug under review.

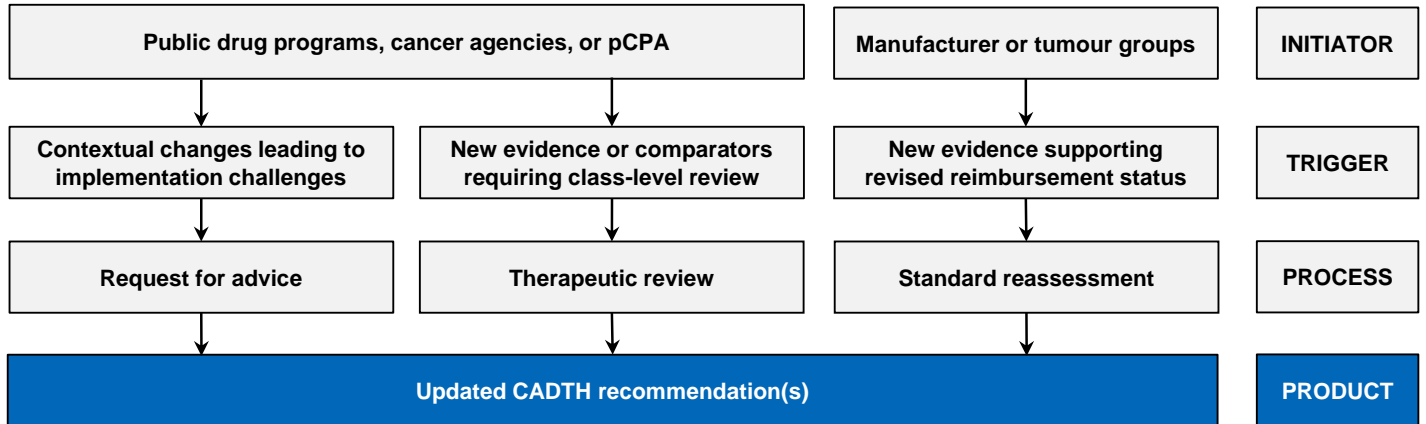
### 3.3 Reassessments

CADTH aims to conduct its reviews in the most efficient manner and applies of the following review types depending on the complexity of the reimbursement review:

- 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 drug programs for the indication(s) of interest. Eligibility must be confirmed by CADTH prior to filing by sending a completed eligibility form to [requests@cadth.ca](mailto:requests@cadth.ca). CADTH will review the form and provide confirmation for the sponsor, typically within 10 business days of receiving the form.
- A request for advice is conducted to address changes in contextual factors that may affect the ability of the drug programs 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.
- A therapeutic review is conducted where there are questions regarding the comparative safety, clinical effectiveness, and cost-effectiveness of multiple drugs.

**Figure 3: CADTH's Pharmaceutical Reassessment Processes**

Alt text: Figure summarizes CADTH reimbursement review reassessment processes.



pCPA = pan-Canadian Pharmaceutical Alliance.

**Table 5: Types of Reimbursement Reviews Conducted**

CADTH process	Eligibility	CADTH output	Eligible requestors	Typical timelines	Application fee
<b>Standard review</b>	<ul style="list-style-type: none"> <li>• Submissions for new drugs, drugs with new indications, and selected new combination products</li> </ul>	<ul style="list-style-type: none"> <li>• Reimbursement recommendation</li> <li>• CADTH review reports</li> <li>• Stakeholder input</li> </ul>	<ul style="list-style-type: none"> <li>• Industry sponsors</li> <li>• Tumour groups</li> <li>• Drug programs</li> </ul>	≤180 calendar days	Schedule A
<b>Tailored review<sup>a</sup></b>	<ul style="list-style-type: none"> <li>• Submissions for new combination products or new formulations of existing drugs that CADTH has designated as tailored reviews</li> <li>• Submissions for subsequent-entry non-biologic complex drugs</li> </ul>	<ul style="list-style-type: none"> <li>• Reimbursement recommendation</li> <li>• CADTH review reports</li> <li>• Stakeholder input</li> </ul>	<ul style="list-style-type: none"> <li>• Industry sponsors</li> <li>• Tumour groups</li> <li>• Drug programs</li> </ul>	≤180 calendar days	Schedule C
<b>Complex review</b>	<ul style="list-style-type: none"> <li>• Submissions for cell and gene therapies; products that are first-in-class; reviewed through one of Health Canada’s expedited pathways (i.e., priority review or advance consideration under NOC/c); and have an undefined place in therapy</li> </ul>	<ul style="list-style-type: none"> <li>• Reimbursement recommendation</li> <li>• CADTH review reports</li> <li>• Stakeholder input</li> </ul>	<ul style="list-style-type: none"> <li>• Industry sponsors</li> <li>• Tumour groups</li> <li>• Drug programs</li> </ul>	≤180 calendar days	Schedule E
<b>Resubmission<sup>a</sup></b>	<ul style="list-style-type: none"> <li>• Drugs that are not reimbursed and have previously been reviewed by CADTH and for which a final recommendation has been issued</li> </ul>	<ul style="list-style-type: none"> <li>• Updated reimbursement recommendation</li> <li>• CADTH review reports</li> <li>• Stakeholder input</li> </ul>	<ul style="list-style-type: none"> <li>• Industry sponsors</li> <li>• Tumour groups</li> <li>• Drug programs</li> </ul>	≤180 calendar days	Schedule A
<b>Standard reassessment<sup>a</sup></b>	<ul style="list-style-type: none"> <li>• Drugs that are currently reimbursed and there is uncertainty regarding safety, clinical effectiveness, and cost-effectiveness</li> <li>• Sponsors seeking revisions to existing reimbursement criteria on the basis of new clinical or economic evidence</li> </ul>	<ul style="list-style-type: none"> <li>• Updated reimbursement recommendation</li> <li>• CADTH review reports</li> <li>• Stakeholder input</li> </ul>	<ul style="list-style-type: none"> <li>• Industry sponsors</li> <li>• Tumour groups</li> <li>• Drug programs</li> </ul>	≤180 calendar days	Schedule A



CADTH process	Eligibility	CADTH output	Eligible requestors	Typical timelines	Application fee
<b>Request for advice</b>	<ul style="list-style-type: none"><li>Changes in contextual information that may affect the ability to implement existing CADTH recommendations</li></ul>	<ul style="list-style-type: none"><li>Updated CADTH recommendation</li><li>CADTH review report(s)</li><li>Stakeholder input</li></ul>	<ul style="list-style-type: none"><li>Drug programs</li><li>pCPA</li></ul>	90 to 150 calendar days	Not applicable
<b>Therapeutic review</b>	<ul style="list-style-type: none"><li>Uncertainty regarding the comparative safety, clinical effectiveness, and/or cost-effectiveness of multiple drugs</li></ul>	<ul style="list-style-type: none"><li>Therapeutic review recommendations</li><li>Updated reimbursement recommendations (if required)</li><li>Review reports</li><li>Stakeholder input</li></ul>	<ul style="list-style-type: none"><li>Drug programs</li><li>pCPA</li></ul>	12 months	Not applicable

pCPA = pan-Canadian Pharmaceutical Alliance.

<sup>a</sup> Eligibility must be confirmed prior to filing with CADTH.



## 4. Pre-submission Procedure

### 4.1 Pre-submission Meetings

#### 4.1.1 Purpose

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

#### 4.1.2 Timing of Pre-submission Meetings

Sponsors are limited to 1 meeting per application. Once an application has been filed with CADTH, it is no longer eligible for a pre-submission meeting. Sponsors may request a pre-submission meeting with CADTH for an application to be filed within 12 months of the meeting. To ensure maximum value from the discussion, sponsors are encouraged to schedule the pre-submission meeting at least 20 business days prior to the anticipated date the application will be filed.

#### 4.1.3 Requesting a Pre-submission Meeting

To request a pre-submission meeting, sponsors are required to complete a [pre-submission meeting request form](#) and upload it to the CADTH Pharmaceutical Submissions SharePoint site in the “Pre-Submission Meeting” folder.

#### 4.1.4 Briefing Paper and Meeting Materials

Sponsors are required to complete a [pre-submission meeting briefing paper template](#) for all pre-submission meetings. The purpose of the pre-submission briefing paper is to provide CADTH with the information required to adequately prepare for meeting. The briefing paper is intended to provide a concise summary of key issues and questions. The completed document must not exceed **12 pages for a 1-hour presubmission meeting** or **15 pages for 1.5-hour presubmission meeting** that will include discussion regarding a time-limited recommendation.

The completed template along with a draft version of the pre-submission meeting slides (in .ppt form) must be uploaded to the CADTH Pharmaceutical Submissions SharePoint site in the “Pre-Submission Meeting” folder. The briefing paper and pre-submission meeting slides must be filed with CADTH no later than 10

business days prior to the scheduled date of the meeting. Failure to provide these documents within this time frame may result in postponement of the meeting.

### 4.1.5 Attendees

Sponsors may bring consultants and/or clinical experts as representatives. CADTH recommends that a relevant Canadian health care professional participate in the pre-submission meeting. For example, a clinical specialist who has expertise on the disease and the available treatments in Canada, particularly in the case of an unmet medical need.

As the focus of the pre-submission meeting is on clarifying process and application requirements, these meetings are not open to patient group representatives. Patients' perspectives, experiences and values are integrated formally in the CADTH processes through the patient group input procedure (refer to section 6.2). Patient groups are welcome contact the CADTH patient engagement team if they have questions regarding the process ([requests@cadth.ca](mailto:requests@cadth.ca)).

Representatives from the drug programs and pCPA may attend pre-submission meetings.

### 4.1.6 Meeting Logistics and Agenda

Pre-submission meetings are scheduled for a maximum of 1 hour. All pre-submission meetings will be held via Microsoft Teams. CADTH will schedule the meeting and provide the sponsor with meeting details.

CADTH will open the meeting by welcoming participants. The remaining content of the meeting and the presenters are at the discretion of the sponsor. To ensure that the meeting is conducted efficiently, CADTH recommends that the sponsor appoint one of its team members to chair the meeting. This helps ensure that the sponsor can address all the key items within the allotted time frame. CADTH may pose questions throughout the presentation to help ensure that the issues being raised by the sponsor are clearly understood.

One member of the sponsor's team will be responsible for sharing the slide deck and advancing the slides throughout the meeting. The draft slides must be submitted to CADTH 10 business days in advance (as indicated in section 4.1.4), with the final slides submitted 1 business day in advance. This allows the CADTH team to have sufficient time to review the slides and prepare accordingly.

The sponsor is responsible for ensuring a member of the team is familiar with Microsoft Teams ahead of time and is able to share their screen to present the slide deck. CADTH strongly recommends designating another team member as a "backup" presenter in case of any technical difficulties.

CADTH will record pre-submission meetings for internal purposes. The recordings are not distributed outside of CADTH.

In the pre-submission phase, all sponsors will be required to specify whether or not the drug under review is expected to meet the time-limited recommendation eligibility criteria regarding the regulatory review status,

the evidence-generation plans, and that the sponsor is willing to comply with the reassessment process for a time-limited recommendation.

## 4.2 Pipeline Meetings

### 4.2.1 Purpose

Pipeline meetings will provide an opportunity for industry to present an overview of their forthcoming pharmaceutical and diagnostic products and pose questions to CADTH on procedural and process initiatives. Pipeline meetings are intended to be mutually beneficial for industry and CADTH; sponsors will benefit through early advice on questions regarding the preparation of their applications and CADTH will benefit through earlier notification and dialogue on new treatments.

Sponsors are encouraged to discuss emerging therapies that may pose implementation challenges and require co-ordination across the broader health care system to facilitate integration into Canadian practice. This includes novel diagnostic procedures or situations where existing diagnostic procedures could be substantially impacted. Early identification of these potential issues could allow CADTH to initiate work on implementation guidance earlier in the product life cycle to help facilitate overall health system readiness.

### 4.2.2 Frequency of Pipeline Meetings

To ensure fair access, sponsors will typically be limited to 1 pipeline meeting per 2-year period. Although CADTH's preference would be for a combined meeting, sponsors may request separate meetings for cancer and non-cancer therapeutics, if required (e.g., insufficient time due to a high volume of products in both therapeutic areas).

### 4.2.3 Requesting a Pipeline Meeting

Sponsors must register with the CADTH Pharmaceutical Submissions SharePoint site before filing a request for a pipeline meeting with CADTH. For detailed information on how to register, please consult the [Pharmaceutical Submissions SharePoint Site – Setup Guide](#). When registering for the SharePoint site, sponsors should indicate “pipeline meeting” in the reason for requesting access section of the form. Once access to the site has been given, sponsors are required to complete a pre-submission meeting request form and upload it to the assigned secure area of the CADTH Pharmaceutical Submissions SharePoint site.

### 4.2.4 Briefing Paper and Meeting Materials

Sponsors are required to complete a [Pre-submission Meeting Briefing Paper template](#) for all pipeline meetings. The purpose of the briefing paper is to provide CADTH with the information required to adequately prepare for the meeting. The briefing paper is intended to provide a concise summary of key issues and questions. The completed document must not exceed 12 pages.

The completed template along with a draft version of the meeting slides (in .ppt form) must be uploaded to the CADTH Pharmaceutical Submissions SharePoint site in the Pipeline Meeting folder. The briefing paper

and slides must be filed with CADTH no later than 10 business days before the scheduled date of the meeting. Failure to provide these documents within this time frame may result in meeting postponement.

#### **4.2.5 Attendees**

Given the purpose and scope of pipeline meetings, attendees will be limited to the sponsor and CADTH. Representatives from Institut national d'excellence en santé et en services sociaux (INESSS), the drug programs, and the pCPA may attend pipeline meetings.

#### **4.2.6 Meeting Logistics and Agenda**

Pipeline meetings are scheduled for a maximum of 1.5 hours and will be held via Microsoft Teams. CADTH will schedule the meeting and provide the sponsor with meeting details.

CADTH will open the meeting by welcoming participants. The remaining content of the meeting and the presenters are at the discretion of the sponsor. To ensure that the meeting is conducted efficiently, CADTH recommends that the sponsor appoint 1 of its team members to chair the meeting. This helps ensure that the sponsor can address all of the key items within the allotted time frame. CADTH may pose questions throughout the presentation to help ensure that the issues being raised by the sponsor are clearly understood.

A member of the sponsor's team will be responsible for sharing the slide deck and advancing the slides throughout the meeting. The draft slides must be submitted to CADTH via the assigned secure area on the Pharmaceutical Submissions SharePoint site 10 business days in advance of the meeting (as indicated in section 4.2.4), with the final slides submitted 1 business day in advance of the meeting. This allows the CADTH team sufficient time to review the slides and prepare accordingly.

The sponsor is responsible for ensuring a member of the team is familiar with Microsoft Teams ahead of time and is able to share their screen to present the slide deck. CADTH strongly recommends designating another team member as a "backup" presenter in case of any technical difficulties.

CADTH will record pipeline meetings for internal purposes. The recordings are not distributed outside of CADTH.

### **4.3 Advance Notification Procedure**

#### **4.3.1 Advance Notification Form**

##### **a) Filing the Advance Notification Form with CADTH**

Sponsors are required to provide CADTH with a minimum of 30 business days advance notice for anticipated submissions and resubmissions. All sponsors are encouraged to provide CADTH with as much notice as possible to facilitate resource planning and budgeting for the pharmaceutical review programs ( $\geq$  120 calendar days is preferred). Sponsors who provided less than 30 business days' notice will be required to revise the anticipated filing date to meet the minimum requirement. To fulfill the advance notification



requirement, sponsors must complete the [advance notification template](#) in its entirety and upload to the CADTH Pharmaceutical Submissions SharePoint site in the “Advance Notification” folder. The 30–business day notification period will be counted from the date of receipt of the advance notification template to the targeted filing date for all anticipated applications.

Information provided to CADTH as part of the advance notification process may be shared with the federal, provincial, and territorial governments, including their agencies and departments, as well as the pCPA office.

For resubmissions and reassessments, sponsors are required to receive confirmation from CADTH that the proposed resubmission is eligible for review, before providing advance notification (refer to section 2.1.7). The eligibility assessment and advance notification processes have to occur sequentially to ensure that the patient engagement process is only initiated for resubmissions and reassessments that are eligible for review by CADTH.

Sponsors who provide notification more than 30 business days before the anticipated date of filing are required to confirm the anticipated filing date 30 business days in advance (Table 6).

**Table 6: Advance Notification Process**

Advance notification process	Days prior to anticipated filing date
CADTH preferred advance notification	≥ 120 calendar days
Minimum mandatory advance notification	30 business days
Confirmation of anticipated filing date	30 business days <sup>a</sup>
Call for patient and clinician group input issued	29 business days

<sup>a</sup> Required only if more than 30 business days’ advance notice was provided.

## b) Revisions to the Anticipated Filing Date

A sponsor is required to advise CADTH of any changes in the anticipated date of filing an application by uploading a revised template to the Pharmaceutical Submissions SharePoint site as soon as possible. For changes to an anticipated filing date made before posting the pending application on the CADTH website and issuing the call for input from patient groups and clinician groups, the timelines will be adjusted based on the new anticipated filing date. For changes to an anticipated filing date made after the pending application has been posted on the CADTH website, and the call for input from patient and clinician groups has been issued, the call for input will remain open for a total of 35 business days from the date the call was issued in the weekly email update (refer to section 1.4.2). CADTH strongly discourages sponsors from revising the anticipated filing date after the mandatory 30 business day confirmation has been provided. The confirmed anticipated filing date is the basis for determining CADTH resourcing and timelines. Applications received at CADTH earlier than the confirmed anticipated filing date will be held and considered received only on the anticipated filing date.

## c) Posting Information about a Pending Application

Information regarding a pending application will be posted on the CADTH website at the time the call for patient and clinician group input is issued (i.e., 29 business days before the anticipated filing date).

#### 4.3.2 Proposed Place in Therapy for Oncology Drugs

At the time of providing advance notification to CADTH, all sponsors with pending applications for oncology drugs are required to provide CADTH with a completed [proposed place in therapy](#) template. The proposed place in therapy template will provide the following information:

- the sponsor's proposed place in therapy for the drug under review, including a clearly stated rationale for the proposed place in therapy with supporting references (as required)
- an overview of the existing treatment algorithm for the indication of interest
- a proposed algorithm showing the place in therapy for the drug or regimen under review and the potential impact on the place in therapy of the currently reimbursed treatment options.

CADTH will screen this template for completeness and will follow up with the sponsor if there is any information missing or anything that requires clarification.

During the review phase, CADTH will consider the sponsor's proposed place in therapy for the drug under review, including discussion with clinical experts and critical appraisal of relevant supporting evidence. The drug programs will review the information contained in the proposed place in the therapy when considering the potential implementation issues associated with the drug under review. This may include direction to CADTH to initiate implementation support activities to advise on the impact of reimbursing the drug under review on the existing funding algorithm within the indication (further details are available in section 13).

## 4.4 Health Canada Information Sharing

### 4.4.1 Consenting to Information Sharing

As described in [Notice to industry: Aligned reviews between Health Canada and health technology assessment organizations](#), an optional information-sharing process for submissions filed with CADTH on a pre-NOC basis has been established to permit Health Canada and CADTH to exchange information regarding the drug under review. Participation in this process could ensure that CADTH has advance notice of any issues that have the potential to impact CADTH's review of the drug (e.g., changes to the indicated patient population), which could help avoid delays in the issuance of CADTH's recommendation.

Sponsors must indicate on the advance notification form (i.e., received  $\geq$  30 business days in advance of the submission filing date) whether or not they have consented or will be consenting to participate in the information-sharing process with Health Canada.

To promote alignment of regulatory and CADTH reviews, sponsors should consent to information sharing at the time of, or prior to, submission filing with Health Canada. This may help to minimize the time between



issuance of market authorization and CADTH's recommendation. If the sponsor is unwilling to participate in the information-sharing process with Health Canada, CADTH will continue to request information directly from the sponsor.

A secure portal will be used to exchange documents between Health Canada and CADTH.

In the interest of transparency, CADTH will indicate whether or not a sponsor has consented to participate in the information-sharing process (if applicable).

### 4.4.2 Invitations to Health Canada Pre-Submission and Pipeline Meetings

CADTH welcomes opportunities to observe Health Canada pre-submission meetings, pipeline meetings, or pre-clinical trial application consultation meetings. To streamline the process and reduce the administrative burden for sponsors, we ask that industry please note the following instructions:

#### d) Sending an Initial Request to CADTH

**Where to send the initial request:** To ensure proper tracking and triage of the meeting request, please ensure that the request for CADTH attendance is sent **only** to [requests@cadth.ca](mailto:requests@cadth.ca).

**What information must be included:** To ensure appropriate attendance at the meeting, please include the following information in the initial request to CADTH:

- Meeting date and time
- Meeting location (i.e., confirmation that virtual attendance is acceptable)
- For pre-submission meetings: Drug name and the proposed indication
- For pipeline meetings: please note if the presentations will focus on a particular therapeutic area (oncology drugs)
- When the sponsor requires the list of CADTH attendees.

Review the CADTH confidentiality guidelines in Appendix 1 of the [Procedures for CADTH Reimbursement Reviews](#) to understand how sponsor-provided information is managed.

#### e) Sending the Meeting Invitations

Once CADTH has confirmed the list of attendees, please send the meeting invitation directly to the individuals identified by CADTH.

#### f) Uploading Meeting Materials

CADTH provides sponsors with a secure portal (the Pharmaceutical Submissions SharePoint site) to upload confidential meeting materials for pre-submission meetings and pipeline meetings. Please follow the instructions outlined in the [Pharmaceutical Submissions SharePoint Site Set-Up Guide](#) for details on requesting access to the site. Meeting materials must be uploaded to the CADTH Pharmaceutical

Submissions SharePoint site in the location assigned for the meeting. Sponsors should request access to the Pharmaceutical Submissions SharePoint site 10 business days prior to the intended date of uploading the meeting materials, so that CADTH can set up the secure area for the sponsor's submission. In the event that this timeline cannot be met, please contact CADTH ([support@cadth.ca](mailto:support@cadth.ca)) as soon as possible to ensure the meeting materials can be submitted without delay.

#### g) CADTH Participation in the Meetings

At meetings organized by Health Canada, CADTH will observe the presentations and discussions. Sponsors with questions regarding the reimbursement review process should contact CADTH directly and arrange a pre-submission meeting to have a detailed discussion about a pending application.

## 5. Application Requirements

This section provides details regarding the documentation that must be filed and accepted for before CADTH will initiate the review of an application.

- The clinical and pharmacoeconomic information provided by the sponsor should focus on the indication(s) to be reviewed by CADTH (unless otherwise specified).
- Sponsors must use the templates that are hyperlinked throughout this section whenever applicable (these are also available on the CADTH website).
- Checklists are available in Appendix 4 to assist sponsors in ensuring that all required documentation has been included in their application. To expedite screening and for efficient use of documents throughout the review, sponsors must organize all documents in the order described subsequently and follow the file folder format in Appendix 5.
- The requirements for submissions are summarized in Table 7 and the requirements for resubmissions and reassessments are summarized in Table 8.
- Whenever relevant, the specific requirements for a submission filed on a pre-NOC versus a post-NOC basis are delineated in the description.
- The sponsor is responsible for ensuring that appropriate copyright permissions have been obtained for copies of the articles that will be shared among CADTH, the expert committee, and the drug programs.

CADTH has developed confidentiality guidelines to protect confidential information obtained through reimbursement review processes (Appendix 1). These confidentiality guidelines ensure that appropriate steps and procedures are in place to protect confidential information, and that this information will be handled in a consistent manner. CADTH will comply with these confidentiality guidelines when handling information as part of the reimbursement review processes. A sponsor will be deemed to have consented to

the confidentiality guidelines when it files an application, or when it supplies other information to CADTH. A sponsor will maintain the confidentiality of documents shared with it by CADTH. The confidentiality guidelines will constitute an agreement between CADTH and the sponsor.

**Table 7: Submission Requirements**

Section	Specific items and criteria	CADTH review type		
		Standard	Tailored	Complex
General information	Application overview template	Required	Required	Required
	Signed cover letter	Required	Required	Required
	Executive summary template	Required	Required	Required
	Product monograph	Required	Required	Required
	Completed declaration letter template	Required	Required	Required
	Completed regulatory and HTA status template	Required	Required	Required
	Request for deviation response letter or statement that a deviation was not requested	Required	N/A	Required
Submission template	Completed tailored review submission template	N/A	Required	N/A
	Complete sponsor summary of clinical evidence template	Required	N/A	Required
	RIS file with references	Required	Not required	Required
Health Canada documentation	NOC or NOC/c and Letter of Undertaking, or a document specifying the anticipated NOC date	Required	Required	Required
	Table of Clarimails or Clarifaxes	Required	Required	Required
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 studies	Required	Required	Required
	Reference list, copies of key 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 copies of 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 population identified in the approved Health Canada indication(s) to be reviewed by CADTH	Required	Not required	Required

Section	Specific items and criteria	CADTH review type		
		Standard	Tailored	Complex
	Unlocked and fully executable economic model	Required	Not required	Required
	Economic model supporting documentation	Required	Not required	Required
	Completed checklist of economic requirements	Required	Required	Required
	RIS file with economic references	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 BIA	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 information	Submitted price per smallest dispensable unit to 4 decimal places	Required	Required	Required
	Method of distribution	Required	Required	Required
Reimbursement status	Reimbursement status of all relevant comparators	Required	Required	Required
Provisional algorithm <sup>a</sup>	Place in therapy template	Required	Not required	Required
	Reference list and copies of studies	Required	Not required	Required
Companion diagnostics	Reference list and articles highlighting clinical utility	May be required	May be required	May be required
	Disclosable price	May be required	May be required	May be required
Implementation	Completed implementation plan template	Not required	Not required	Required for cell and gene therapies
Pre-NOC letter	Letter for sending NOC or NOC/c to CADTH	Required	Required	Required

BIA = budget impact analysis; NOC = Notice of Compliance; NOC/c = Notice of Compliance with conditions.

<sup>a</sup> Required only in applications for oncology drugs.

**Table 8: Resubmission and Reassessment Requirements**

Section	Specific items and criteria	Resubmissions		Standard reassessment
		New clinical and cost	New cost only	
General information	Application overview template	Required	Required	Required
	Signed cover letter	Required	Required	Required
	Executive summary template	Required	Required	Required
	Product monograph	Required	Required	Required
	Completed declaration letter	Required	Required	Required

Section	Specific items and criteria	Resubmissions		Standard reassessment
		New clinical and cost	New cost only	
	Completed regulatory and HTA status template	Required	Required	Required
	Request for deviation response letter or statement that a deviation was not requested	Required	Required	Required
<b>Efficacy, effectiveness, and safety information</b>	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	Not required
	Clinical study reports for pivotal and/or key studies	Required	Not required	Required
	Reference list, copies of studies, and errata	Required	Not required	Required
	Reference list and copies of articles for validity of outcome measure	Required	Not required	Required
	Reference list and copies of editorial articles	Required	Not required	Required
	Table of studies	Required	Required	Required
	Indirect comparison with full technical report	May be required	May be required	May be required
<b>Submission template</b>	Complete sponsor summary of clinical evidence template	Required	May be required	Required
<b>Epidemiologic information</b>	Disease prevalence and incidence data	Required	Required	Required
	Number of patients accessing a new drug	May be required	May be required	Not required
<b>Reimbursement status</b>	Reimbursement status of all relevant comparators	Required	Required	Required
	Reimbursement status of the drug under review	Required	Required	Required
<b>Economic information</b>	New pharmacoeconomic evaluation for the full population identified in the approved Health Canada indication(s) to be reviewed by CADTH	Required	Required	Not required
	Updated pharmacoeconomic evaluation(s) addressing: population covered under current reimbursement criteria; and population covered under proposed reimbursement criteria (if applicable)	Not required	Not required	Required
	Unlocked and fully executable economic model	Required	Required	Required
	Economic model supporting documentation	Required	Required	Required
	Completed checklist of economic requirements	Required	Required	Required
	RIS file with economic references	Required	Required	Required
<b>Budget impact analysis</b>	Aggregate pan-Canadian budget impact report	Required	Required	Required
	Aggregate pan-Canadian budget impact model	Required	Required	Required
	Supporting documentation used in BIA	Required	Required	Required
<b>Pricing and distribution information</b>	Submitted price per smallest dispensable unit to 4 decimal places	Required	Required	Required
	Method of distribution	Required	Required	Required
	Place in therapy template	Required	Required	Required

Section	Specific items and criteria	Resubmissions		Standard reassessment
		New clinical and cost	New cost only	
Provisional algorithm <sup>a</sup>	Reference list and copies of studies	Required	Required	Required
Companion diagnostics	Reference list and articles highlighting clinical utility	May be required	May be required	May be required
	Disclosable price	May be required	May be required	May be required
Implementation	Updated implementation plan template	May be required	May be required	May be required

BIA = budget impact analysis.

<sup>a</sup>Required only in applications for oncology drugs.

## 5.1 General Information

### 5.1.1 Application Overview Template

A completed [application overview template](#).

### 5.1.2 Signed Cover Letter

A signed cover letter (an electronic signature is acceptable) from the sponsor, providing the following information:

- a clear description of the application being filed (e.g., new drug submission filed on a pre-NOC basis)
- the indication(s) to be reviewed by CADTH
- the requested reimbursement conditions (if applicable)
- the names and contact information (email and phone number) for the primary and backup contact(s) that CADTH can contact regarding the submission. The sponsor may designate the consultant(s) preparing the submission as primary and/or backup contact(s). Any changes in contacts should be communicated to CADTH as soon as possible.

### 5.1.3 Executive Summary

A high-level summary of the application using the executive summary template available on the CADTH website. The document must be referenced and must not exceed 5 pages for standard and tailored reviews or 6 pages for complex reviews (excluding references).

### 5.1.4 Product Monograph

Table 9 summarizes the product monograph requirements for submissions filed on a pre-NOC or post-NOC basis.



Sponsors must immediately notify CADTH, up until the time that the final recommendation is issued of any changes to the Health Canada–approved product monograph for the drug under review and provide a revised copy. Failure by the sponsor to inform CADTH of any changes to the product monograph could result in a temporary suspension of the review.

Following notification of changes to the product monograph, CADTH will assess the nature and extent of the changes and determine the timelines required for review and, if necessary, incorporate the changes into the review report(s). This could result in the review timelines being delayed, including the submission being considered at a later meeting of the expert committee or a delay in issuing the final recommendation. The sponsor will be apprised of any revisions to the anticipated timeline for the review, deferral by the expert committee, or the subsequent recommendation not reflecting the most currently available product monograph information relating to the drug under review.

**Table 9: Requirements for Filing Product Monograph With CADTH**

NOC status	Application requirements
Pre-NOC	<ul style="list-style-type: none"> <li>• At the time of filing the submission: a copy of the most recent draft product monograph showing the company, drug brand, and non-proprietary names that correspond to the anticipated NOC</li> <li>• As soon as available:               <ul style="list-style-type: none"> <li>▪ a copy of the draft product monograph initially filed with CADTH showing, in tracked changes, all of the clinical and label review changes made up to the time of the product monograph being approved by Health Canada (if there are no changes to the draft product monograph initially filed with CADTH, other than the date on the product monograph, please include a placeholder document indicating this)</li> <li>▪ a copy of the clean and dated product monograph approved by Health Canada.</li> </ul> </li> </ul>
Post-NOC	<ul style="list-style-type: none"> <li>• A copy of the most current version of the Health Canada–approved product monograph</li> </ul>

NOC = Notice of Compliance.

### 5.1.5 Declaration Letter

A letter from the holder of the NOC or NOC/c (or from the sponsor applying for an NOC, in the case of a submission filed on a pre-NOC basis), using the [declaration letter template](#), printed on company letterhead, and signed by an appropriate senior official.

### 5.1.6 Regulatory and HTA Status in Other Jurisdictions

At the time of filing of the application, a completed [template](#) summarizing the status of the drug under review at selected regulatory and Health Technology Assessment agencies. The sponsor is required to provide an updated copy of the template to reflect any changes in the status (if applicable) when the sponsor provides their comments on the draft CADTH reports. This document must be provided as a Microsoft Word document.

### 5.1.7 Request for Deviation from Pharmacoeconomic Requirements

Effective for all applications received on or after November 1, 2023, all sponsors that file a [request for deviation](#) must include a copy of the decision letter from CADTH within the General Information section of the application. Sponsors are required to include a copy of the letter from irrespective of the decision from CADTH regarding whether the deviation has been accepted. If the sponsor has not filed a request for deviation, we request that they please include a placeholder document stating that no request for deviation was filed.

Sponsors are reminded that deviations from any of the requirements within the economic evaluation section must be discussed with and accepted by CADTH in advance of filing the application. Failure to seek advanced approval of the deviation may result in an extension of the screening timelines.

## 5.2 Sponsor Submission Templates

### 5.2.1 Clinical Evidence Template for Standard and Complex Reviews

Sponsors filing a standard or complex review are required to complete the [sponsor summary of clinical evidence template](#) in accordance with the instructions provided in the template.

**Section 1:** In this section of the template the sponsor is required to summarize key background information regarding the drug under review and the condition for which the drug under review is indicated. Please ensure that statements are appropriately referenced.

**Section 2:** In this section the sponsor is required to summarize the results from a systemic literature review. The literature review must be conducted and reported in accordance with the instructions provided within this template. Data should reflect the results reported in the Clinical Study Report(s) whenever possible. The sponsor must ensure that source document, including the Clinical Study Report (if available), are included in the application materials.

**Section 3:** In this section the sponsor is required to summarize long-term extension studies. The sponsor must ensure that source document, including the Clinical Study Report (if available), are included in the application materials. If data from long-term extension studies are not available at the time of filing the application, this should be noted within this section.

**Section 4:** In this section of the template, the sponsor must summarize all indirect comparisons that have been included in the application (i.e., to support the comparative efficacy or safety and/or the assumptions in the pharmacoeconomic model). The summary does not preclude the need to provide complete technical reports for the indirect comparisons, as described in section 5 of the [Procedures for CADTH Reimbursement Reviews](#). Any sponsors that have not included one or more indirect comparisons in the application should explain within the template why an indirect comparison is not relevant for the review and/or why an indirect comparison was not feasible with the available information.

**Section 5:** This section allows the sponsor to summarize evidence from additional studies that address important gaps in the evidence presented in sections 2 to 3 of the template. Prior to completing Section 5,

sponsors must clearly identify the gaps in the evidence that has been provided in each of the preceding sections. Examples of gaps in the evidence include the following:

- Studies designed to demonstrate safety and effectiveness in important patient populations that were excluded from the clinical trials.
- Studies designed to address outcomes that require longer-term follow-up and were not investigated in the clinical trials and/or extension studies.
- Studies that address uncertainty regarding the dosage of the drug under review that is used in actual clinical practice.

It is recommended that studies presented within section 5 should be derived from a systematic literature review to minimize the risk of evidence selection bias. CADTH will consider the information provided by the sponsor in section 5 and make a case-by-case determination if the additional evidence will be included in the CADTH clinical report. The inclusion of evidence from section 5 in the CADTH clinical report will be determined solely by CADTH based on the following factors:

- the additional information may address an important gap in the pivotal and RCT evidence
- the sponsor has provided the additional information in a format that allows CADTH to complete a detailed review and appraisal of the data (e.g., in accordance with the CONSORT reporting guidelines or [Guidance for Reporting Real-World Evidence](#), as applicable).

## 5.2.2 RIS File with References for Standard and Complex Reviews

The sponsor must provide a RIS file containing the references used in the report. A RIS file is a standardized bibliographic format that enables citation management programs to exchange documents. The file should be named in accordance with the instructions in Appendix.

## 5.2.3 Submission Templates for Tailored Reviews

A completed [tailored review submission template](#).

## 5.3 Health Canada Documentation

### 5.3.1 Health Canada NOC or NOC/c

Table 10 summarizes the NOC requirements for pre-NOC and post-NOC submissions.

**Table 10: Requirements for Filing an NOC With CADTH**

NOC status	Application requirements
Pre-NOC	<ul style="list-style-type: none"> <li>• At the time of filing the submission: a placeholder document indicating the anticipated target date for receipt of an NOC or NOC/c for the indication(s) to be reviewed</li> </ul>

NOC status	Application requirements
	<ul style="list-style-type: none"> <li>A copy of the granted NOC or NOC/c for the indication(s) under review by CADTH, dated and signed by Health Canada, must be sent to CADTH as soon as it is available (i.e., on the day of, or next business day after, receipt from Health Canada)</li> <li>If the drug receives an NOC/c for the indication(s) being reviewed by CADTH: a copy of the Letter of Undertaking that outlines the confirmatory studies intended to verify the clinical benefit, including an indication of time frames, must also be provided by email to CADTH as soon as it is available</li> </ul>
Post-NOC	<ul style="list-style-type: none"> <li>A copy of the NOC or NOC/c for the indication(s) for which the drug is to be reviewed by CADTH</li> <li>If the drug in the submission has received an NOC/c for the indication(s) to be reviewed, the sponsor must provide a copy of the Letter of Undertaking that outlines the confirmatory studies intended to verify the drug's clinical benefit, including an indication of time frames</li> </ul>

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

### 5.3.2 Clarimails or Clarifaxes

Table 11 summarizes the requirements regarding Clarimails/Clarifaxes for pre-NOC and post-NOC submissions.

**Table 11: Requirements for Filing Clarimails/Clarifaxes With CADTH**

NOC status	Application requirements
Pre-NOC	<ul style="list-style-type: none"> <li>At time of filing the submission: a summary table of Clarimails/Clarifaxes relating to any clinical aspects of the Health Canada review of the drug (e.g., clinical studies or product monograph, not chemistry- and manufacturing-related topics) up to the time of filing with CADTH; including the date of each Clarimail/Clarifax, the topic for clarification, a brief summary of the response, and the date of the response must be included</li> <li>On an ongoing basis up to the point of the NOC or NOC/c being issued, the sponsor must provide CADTH with revised summary tables to reflect any additional Clarimails/Clarifaxes as aforementioned</li> </ul>
Post-NOC	<ul style="list-style-type: none"> <li>A summary table of Clarimails/Clarifaxes relating to any clinical aspects of the Health Canada review of the drug (e.g., clinical studies or product monograph, <i>not</i> chemistry- and manufacturing-related topics) up to the point of the NOC or NOC/c being issued; including the date of each Clarimail/Clarifax, the topic for clarification, a brief summary of the response, and the date of the response must be included.</li> </ul>

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

## 5.4 Efficacy, Effectiveness, and Safety Evidence

### 5.4.1 Common Technical Document

A copy of the Common Technical Document sections listed in Table 12 is required. If any of these sections of the Common Technical Document were not a requirement for filing the regulatory submission with Health Canada, a placeholder document with a statement confirming this is required.

**Table 12: Common Technical Document Module Sections**

Section	Title
2.5	Clinical Overview
2.7.1	Summary of Biopharmaceutical Studies and Associated Analytical Methods
2.7.3	Summary of Clinical Efficacy
2.7.4	Summary of Clinical Safety
5.2	Tabular Listing of All Clinical Studies

### 5.4.2 Clinical Study Reports

Clinical study reports must be provided for the pivotal trials as well as any other studies that address key clinical issues. The clinical study reports should be provided in full and include both the complete study protocol and analysis plan. If a Clinical Study Report is unavailable to the sponsor, a placeholder document with a statement confirming this is required.

### 5.4.3 Publications or Manuscripts for Key Clinical Studies

The requirements for including publications or manuscripts for key clinical studies are summarized in Table 13. For the clinical studies requirements, CADTH’s preference is for any unpublished data to be submitted in manuscript format; however, if the data are unavailable in manuscript format, the information should be provided in accordance with the CONSORT 2010 Statement Checklist, using clearly labelled sections (i.e., title, abstract, introduction, methods, results, discussion, other information).

Should an unpublished study submitted become published during the review process, the sponsor must provide a copy of the published study to CADTH using the “2. Submission Files” folder on the Pharmaceutical Submissions SharePoint site. Depending on the nature of the information, CADTH will determine the timelines required to review it and incorporate it into the review report(s). This could result in the submission being considered at a later expert committee meeting. The sponsor will be apprised of any revisions to the anticipated timelines for the review.

**Table 13: Requirements for Publications or Manuscripts for Key Clinical Studies**

Review type	Application requirements
Submission	<ul style="list-style-type: none"> <li>• Copies of the published and unpublished studies that address key clinical issues for the drug under review</li> <li>• Copies of any supplemental appendices that are associated with published studies</li> <li>• Copies of any errata related to any of the published studies provided (or a placeholder document with a statement confirming that there are no errata)</li> <li>• A reference list with all of the published and unpublished studies (including any errata) that address key clinical issues for the drug under review</li> </ul>
Resubmission based on new clinical information	<ul style="list-style-type: none"> <li>• Copies of the published and unpublished studies that address key clinical issues for the drug under review, including all new clinical information that addresses specific issues identified by the expert committee in the final recommendation document</li> <li>• Copies of any supplemental appendices that are associated with published studies</li> <li>• Copies of any errata related to any of the published studies provided (or a placeholder document with a statement confirming that there are no errata)</li> <li>• A reference list with all of the published and unpublished studies (including any errata) that address key clinical issues for the drug under review. The studies in the list must be presented as follows:               <ul style="list-style-type: none"> <li>▪ All new clinical information that addresses specific issues identified by the expert committee in the final recommendation document</li> <li>▪ Key clinical studies that were included in the initial submission and/or previous resubmissions filed with CADTH</li> </ul> </li> </ul>
Standard reassessment	<ul style="list-style-type: none"> <li>• A reference list of the published and unpublished studies included in the submission; the list should specifically identify the new clinical information that supports the sponsor’s request for the reassessment (e.g., revised reimbursement criteria)</li> <li>• Copies of any errata related to any of the published studies provided (or a placeholder document with a statement confirming that there are no errata)</li> </ul>

#### 5.4.4 Table of Studies

A tabulated list of all published and unpublished clinical studies using the [table of studies template](#) must be provided. This table may be provided as a Microsoft Word or PDF document.

Any data (e.g., pre-planned analyses of primary outcome measures) for a planned or ongoing clinical study included in the “table of studies” requirement that becomes available during CADTH’s review process must be provided as soon as possible to CADTH using the “2. Submission Files” folder on the Pharmaceutical Submissions SharePoint site. CADTH will assess the information upon receiving it and determine the timelines required to review it and incorporate it into the review report(s). This could result in the submission being considered at a later meeting of the expert committee. The sponsor will be apprised of any revisions to the anticipated timelines for the review.

#### 5.4.5 Editorials

A reference list and copies of editorials relating to published clinical studies provided in the submission (i.e., published studies included in the “clinical studies” requirement). If no editorials are available, a placeholder document with a statement confirming this must be provided.

#### **5.4.6 New Data**

A reference list and copies of new data generated since the last date that data were reported in the studies included in the Health Canada submission. If no new data are available, a placeholder document with a statement confirming this must be provided.

The clinical studies submitted to CADTH are often the same as those submitted to Health Canada, and sometimes these studies are ongoing, with data collected after submission to Health Canada. The data that become available after the study has been submitted to Health Canada are required. These data will be accepted in a variety of formats, including late draft, Clinical Study Report, synopsis, abstract, or conference proceedings.

#### **5.4.7 Validity of Outcome Measures**

A reference list and copies of references supporting the validity of primary outcome measures in clinical studies. If no references are available, a placeholder document is required with a statement confirming that a search was undertaken but no references were located.

### **5.5 Indirect Comparisons**

Sponsors are required to provide copies of any indirect comparisons that were used in their pharmacoeconomic evaluation. In addition, sponsors may elect to provide one or more indirect comparisons to provide evidence of the comparative safety and efficacy of the drug under review relative to appropriate comparators. The indirect comparisons must be provided as a separate report in the submission package.

### **5.6 Pharmacoeconomic Submission**

The pharmacoeconomic submission for a standard review, complex review, resubmission, or reassessment consists of:

- a technical report of the pharmacoeconomic evaluation
- an economic model (for a cost-utility analysis) or cost calculations (for a cost-minimization analysis)
- a technical report of the budget impact analysis (BIA)
- a budget impact model
- a completed checklist indicating that the economic requirements have been met
- any supporting material relevant to the pharmacoeconomic submission.

The technical reports of the pharmacoeconomic evaluation and BIA must be consistent with the economic model and budget impact model, respectively. In both cases, all scenario analyses presented in the technical reports must be replicable in the submitted models. Any submitted models to CADTH cannot require CADTH to agree to terms and conditions or have a legal disclaimer. Models that require the user to review and agree to terms and conditions and/or acknowledge a legal disclaimer added by the vendor or sponsor will not be accepted for review by CADTH. Any sponsors who have questions regarding the inclusion of a disclaimer should contact CADTH prior to filing the application.

The economic submission (pharmacoeconomic evaluation and model) should be undertaken in accordance with CADTH's [Guidelines for the Economic Evaluation of Health Technologies: Canada \(4th edition\)](#) and supporting documents (as referred to on the guidelines landing page) which provide guidance on best practices for undertaking economic evaluations within the health care setting in Canada.

When multiple indications and/or populations are relevant, CADTH will assess whether the review constitutes multiple submissions or may require multiple application fees. Please refer to the [Fee Schedule for CADTH Pharmaceutical Reviews](#) for details.

The specific requirements described in the sections that follow must be met when submitting to the CADTH Reimbursement Review processes. A summary is provided in Appendix 5.

The preferred approach for the pharmacoeconomic analysis is a cost-utility analysis. In some specific situations, a cost-minimization analysis could be submitted, but the sponsor is asked to review the criteria in the cost-minimization section carefully (refer to section 5.6.2).

Only 1 type of economic evaluation can be included in a submission to CADTH. For example, the following will not be accepted by CADTH:

- including more than one economic model for the review of a single indication;
- submitting both a cost-minimization analysis and cost-utility analysis for the review of a single indication.

The sponsor is required to include a completed [economic requirements checklist](#) within their application package. This checklist is required to ensure that the sponsor is undertaking a quality check of their application in order to minimize delays in the screening process. The requirements within checklist align with those described in Appendix 5.

### 5.6.1 Type of Analysis: Cost-utility Analysis

#### a) Pharmacoeconomic Evaluation: Technical Report

##### Target Population

For submissions and resubmissions:



- The base-case analysis must reflect the Health Canada–approved indication for which the drug is being submitted.
- If a sponsor is requesting reimbursement for a specific subgroup of the indicated population or there are any relevant subgroups, these must be provided as scenario analyses.
- For submissions filed on a pre-NOC basis, where the approved NOC indication differs from the anticipated indication for which the pharmacoeconomic evaluation was conducted, the review may be suspended until a revised pharmacoeconomic submission reflecting the approved indication is provided.

For reassessments, the base-case analysis must reflect the scope of the reassessment:

- If the reassessment is focused on proposed revisions to the existing reimbursement criteria for the drug under review (e.g., a proactive reassessment initiated by the sponsor), the base-case analysis must reflect the target population that would be covered under the revised reimbursement criteria that have been proposed by the sponsor.
- If the reassessment is focused on validation of the existing reimbursement criteria for the drug under review (e.g., a reactive reassessment initiated in response to a request from the drug programs), the base-case analysis must be focused on the population which is currently covered under the current reimbursement criteria.
- If there are any relevant subgroups, these must be provided as scenario analyses.

### **Comparators**

The base case must include all relevant comparators (i.e., treatments currently reimbursed by at least 1 participating drug plan for the indication under review, reimbursed treatments that are currently used off-label in Canadian practice, or treatments that have previously received a recommendation in favour of reimbursement from CADTH for the indication under review).

If the sponsor submits a different reimbursement request, all relevant comparators must be included in that scenario analysis.

CADTH may identify missing comparators during the screening phase and the application will not be accepted for review. However, in some situations, the absence of one or more relevant comparators may not be apparent until the application has been accepted for review and initiated by CADTH. In these cases, CADTH will notify the sponsor regarding the deficiency and the timelines of the review may be affected (i.e., may result in the application being reviewed at a later meeting of the expert review committee).

### **Perspective**

The base case must be from the perspective of the publicly funded health care payer.

### **Discounting**

If the time horizon is greater than 1 year, the base case must use a discount rate of 1.5% for both costs and quality-adjusted life-years.

### Effectiveness

Composite outcomes are generally not satisfactory to inform treatment effect estimates. Sponsors should base their pharmacoeconomic evaluation on relevant individual outcomes. If composite outcomes are included in the pharmacoeconomic evaluation, CADTH may request that sponsors include the individual outcomes during the review process. In this situation, CADTH will notify the sponsor regarding the deficiency and the timelines of the review may be affected (i.e., may result in the application being reviewed at a later meeting of the expert review committee).

### Costs and Resource Use

The specific drug price(s) submitted to CADTH for the lowest dispensable unit (to 4 decimal places) must be used in the sponsor's base-case analysis. The unit cost(s) must be stated transparently within the model.

All submitted forms and strengths must be included in the submitted model.

### Analysis

If more than 1 comparator is included, the results should be reported using a sequential analysis that indicates where the drug lies on the cost-effectiveness efficiency frontier.

- As referred to earlier in section 5.6, the [Guidelines for the Economic Evaluation of Health Technologies: Canada \(4th edition\)](#) and supporting documentation should be consulted for guidance on sequential and pairwise analyses.

The base-case analysis must be conducted probabilistically. The base-case analysis must be presented deterministically as well. Scenario analyses may be reported deterministically, but the pharmacoeconomic model must be programmed in such a way that allows them to be run probabilistically by CADTH.

### Reporting

The results of the sponsor's base case and scenario analysis for the reimbursement-requested population (if different from the base case) must be presented in a disaggregated manner before being aggregated.

A breakdown by costs (e.g., drug acquisition costs, administration costs, adverse event cost, health state costs), by life-years, and by quality-adjusted life-years (e.g., benefits generated in each health or event state, benefits generated during the trial period versus the extrapolation period), as relevant, must be reported based on the probabilistic results.

A suggested reporting format is presented in Appendix 4.

### Companion Diagnostics

If there is a companion diagnostic test associated with the drug under review, the pharmacoeconomic evaluation (and model) must include relevant costs and consequences for these tests in relation to the drug under review (e.g., test costs for all patients in whom the drug under review is considered, costs from diagnostic information obtained and subsequent treatment decisions, rates of true- and false-positives and true- and false-negatives, and potential consequences of the test results). The source(s) and assumption(s) of the relevant inputs should be provided as well.

#### b) Economic Model

- An unlocked version of the economic model used to inform the technical report of the pharmacoeconomic evaluation must be provided.
- The economic model must be programmed in Excel. The sponsor must contact CADTH in advance if considering alternative program software to ensure that it is acceptable and whether additional requirements will apply. The version of Excel must be clearly stated in the sponsor's technical report.
- The model must be able to function in a stand-alone environment that does not require access to a web-based platform.
- The sponsor must provide the model in its entirety, meaning CADTH must have full access to the programming code (e.g., macros, Visual Basic for Applications [VBA] code) and be able to fully execute the model based on modifications to parameters of interest. CADTH must be able to vary individual parameters, view the calculations, and run the model to generate results.

Probabilistic analysis must be stable over multiple model runs. A congruence test should be provided to identify the appropriate number of iterations required for convergence to be reached. Results from the congruence test should inform the number of simulations conducted in the base case and all scenario analyses. If the sponsor chooses to use seeding within the model, the functionality to easily revise or disable this feature must be included to allow CADTH to verify the stability of the probabilistic analysis.

The probabilistic analysis must run all interventions that are being compared against each other simultaneously or be conducted in a way that ensures the same input parameter values are considered within each simulation, and report the analysis results sequentially as relevant (per guidance in the analysis section above).

For submissions that use time-to-event (e.g., survival) data, the sponsor's model must be flexible to easily assess all parametric distributions tested by the sponsor (at minimum, distributions tested must include Weibull, Gompertz, exponential, log-normal, log-logistic, generalized gamma, and gamma, which must be provided as 1-piece distributions unless an appropriate rationale for a piecewise analysis has been provided by the sponsor. Additional methods may be used as relevant). If any of these distributions are not possible, an acceptable rationale for exclusion must be provided. The sponsor must include 1 graph for each outcome (e.g., progression-free survival, time-to-death, etc.) that is flexible to simultaneously present the observed Kaplan-Meier curves and all fitted distribution curves assessed by the sponsor for each treatment. The

graph(s) must allow CADTH to include and remove distributions and treatments to allow visual inspection of each distribution individually and comparatively as needed.

Details on how a cohort or individuals progress through the model must be transparently reported. For instance, if a Markov model is submitted, a Markov trace is required; if a model does not incorporate set cycles, event-time traces must be provided that records the sequence of events that occurred over the model's full time horizon. The computation behind the traces must not be hard-coded via VBA, but derived through formula. While a trace must be provided, if inclusion of a trace will impact the model run time such that it does not meet requirements, the trace does not need to be incorporated within the PSA.

The submitted economic model must have a reasonable run time. If the model run time for the base-case analysis and key scenario analyses exceeds 1 business day (8 hours) it will be considered by CADTH to be excessive and will not be accepted by CADTH. The run time is determined by CADTH based on CADTH computing powers.

### 5.6.2 Type of Analysis: Cost-Minimization Analysis

#### a) Pharmacoeconomic Evaluation: Technical Report

The preferred approach for the pharmacoeconomic analysis is a cost-utility analysis. However, in some specific situations, a cost-minimization analysis (CMA) may be sufficient.

A sponsor is encouraged to submit a cost-minimization analysis in situations where the following conditions are met:

1. The drug represents an additional drug in a therapeutic class in which there is already a reimbursed drug for the same indication.
2. The drug under review demonstrates similar clinical effects (i.e., has at least equivalent effectiveness and/or efficacy and be equivalently or less harmful) compared to the most appropriate comparator(s), based on:
  - 1 or more clinical studies that directly compared the drug under review to relevant comparator(s), or
  - 1 or more indirect comparisons that allow for the comparison of the drug under review to relevant comparator(s).

As comparative efficacy and safety will be assessed within the review, the appropriateness of a cost-minimization analysis cannot be confirmed by CADTH during the screening phase of the process. The decision to submit a cost-minimization analysis for the pharmacoeconomic evaluation therefore rests with the sponsor. If a sponsor elects to submit a cost-minimization analysis, it will be essential for the sponsor to have appropriate evidence to demonstrate how it has met the criteria above, and specifically that the drug and the relevant comparator(s) are comparable or equivalent in clinical effects.

The submission of a cost minimization analysis implies comparable/equivalent clinical effects; where this is not demonstrated, the sponsor should submit a cost-utility analysis.

Should sponsors elect to provide a cost-utility analysis after the initiation of a review accepted on the basis of a cost-minimization analysis, CADTH will suspend the review for as long as is required to allow the sponsor and CADTH to accommodate a change in the modelling approach. This may delay the target committee meeting date and CADTH will not be liable to refund any review fees.

If there is a companion diagnostic test associated with the drug under review that is different than those required for the comparator treatments, a cost-utility analysis must be submitted. **Target Population**

The base-case analysis must reflect the Health Canada–approved indication for which the drug is being submitted. If a sponsor is requesting reimbursement for a specific subgroup of the indicated population or there are any relevant subgroups, these must be provided as scenario analyses.

For submissions filed on a pre-NOC basis, where the approved NOC indication differs from the anticipated indication for which the pharmacoeconomic evaluation was conducted, the review may be suspended until a revised pharmacoeconomic submission reflecting the approved indication is provided.

For reassessments, the base-case analysis must reflect the scope of the reassessment:

- If the reassessment is focused on proposed revisions to the existing reimbursement criteria for the drug under review (e.g., a proactive reassessment initiated by the sponsor), the base-case analysis must reflect the target population that would be covered under the revised reimbursement criteria that have been proposed by the sponsor.
- If the reassessment is focused on validation of the existing reimbursement criteria for the drug under review (e.g., a reactive reassessment initiated in response to a request from the drug programs), the base-case analysis must be focused on the population which is currently covered under the current reimbursement criteria.
- If there are any relevant subgroups, these must be provided as scenario analyses.

## Comparators

The base case must include all relevant comparators (i.e., treatments currently reimbursed by at least 1 participating drug plan for the indication under review, treatments that are currently used off-label in Canadian practice, or treatments that have previously received a recommendation in favour of reimbursement from CADTH for the indication under review).

If the sponsor submits a different reimbursement request, all relevant comparators must be included in that scenario analysis.

CADTH may identify missing comparators during the screening phase and the application will not be accepted for review. However, in some situations, the absence of 1 or more relevant comparators may not be apparent until the application has been accepted for review and initiated by CADTH. In these cases, CADTH will notify the sponsor regarding the deficiency and that the timelines of the review may be affected (i.e., may result in the application being reviewed at a later meeting of the expert review committee).

## Perspective

The base case must be from the perspective of the publicly funded health care payer.

## Discounting

If the time horizon is greater than 1 year, the base case must use a discount rate of 1.5% for costs.

## Costs and Resource Use

The specific drug price(s) submitted to CADTH for the lowest dispensable unit (to 4 decimal places) must be used in the sponsor's base-case analysis. The unit cost(s) must be stated transparently within the model.

All submitted forms and strengths must be included in the submitted model.

## Analysis

The base-case analysis should be conducted probabilistically. A deterministic analysis may be presented if a rationale to support the absence of parameter uncertainty is provided.

## Reporting

The results of the sponsor's base case and scenario analysis for the reimbursement-requested population (if different from the base case) must be presented in a disaggregated manner before being aggregated. A breakdown by costs (e.g., drug acquisition costs, administration costs) must be reported based on the base case results (i.e., based on probabilistic [or deterministic] output, as justified within the submission).

A suggested reporting format is presented in Appendix 4.

### b) Cost Calculations

An unlocked Excel workbook containing the cost calculations used to inform the technical report of the pharmacoeconomic evaluation must be provided.

The Excel workbook must be able to function in a stand-alone environment that does not require access to a web-based platform.

If the analysis is deterministic, all analyses should be easily traceable through formulas within the Excel worksheet. CADTH should be able to fully execute the analysis based on modifications to parameters of interest. CADTH must be able to vary individual parameters and run the analysis to generate results.

If the analysis is probabilistic:

- The sponsor must provide the model in its entirety, meaning that CADTH must have full access to the programming code (e.g., macros, VBA code) and be able to fully execute the analysis based on modifications to parameters of interest. CADTH must be able to vary individual parameters and run the analysis to generate results. The results of the analysis must be traceable via formulas not hard-coded based on VBA output.
- Results must be stable over multiple model runs. A congruence test should be provided to identify the appropriate number of iterations required for convergence to be reached. If the sponsor chooses to use seeding within the model, the functionality to easily revise or disable this feature must be included to allow CADTH to verify the stability of the probabilistic analysis.
- If more than 1 comparator is included, the probabilistic analysis must run all comparators simultaneously or be conducted in a way that ensures the same input parameter values are considered within each simulation.

The submitted economic model must have a reasonable run time. If the model run time for the base-case analysis and key scenario analyses exceeds 1 business day (8 hours) it will be considered by CADTH to be excessive and will not be accepted by CADTH. The run time is determined by CADTH based on CADTH computing powers.

### 5.6.3 Budget Impact Analysis

The following information on the BIA (technical report and model) apply to all submissions to CADTH.

a) BIA: Technical Report

#### Target Population

The population(s) presented in the BIA must align with that/those reported in the economic evaluation:

- The base-case analysis must reflect the Health Canada–approved indication for which the drug is being submitted.

- If a sponsor is requesting reimbursement for a specific subgroup of the indicated population or if there are any relevant subgroups, these must be provided as scenario analyses.
- For submissions filed on a pre-NOC basis, where the approved indication differs from the anticipated indication for which the BIA was conducted, the review may be suspended until a revised BIA reflecting the approved indication is provided.

### **Perspective**

The base case must reflect a pan-Canadian (national) drug program perspective (excluding Quebec), which must be derived from the following subset of individual drug programs participating in CADTH's drug reimbursement review processes: British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador, and the Non-Insured Health Benefits Program (if applicable). No other participating drug program should be included in the analysis. If the drug is being reviewed through the plasma protein review pathway, an analysis from the Canadian Blood Services perspective must be provided.

### **Time Horizon**

When forecasting the budget impact of a new treatment, 4 years of data must be presented: a 1-year baseline period and a 3-year forecast period in the base case. The base-case analysis must report costs by year. The total budget impact must be calculated based on the 3-year forecast period. Discounting should not be applied within the BIA.

### **Costs and Resource Use**

The specific drug price(s) submitted to CADTH for the lowest dispensable unit (to 4 decimal places) must be used in the sponsor's base-case. The unit cost(s) must be stated transparently within the model. All submitted forms and strengths must be included in the submitted model.

### **Reporting**

The technical report must incorporate a decision problem, methods, assumptions, and results that align with the submitted budget impact model.

Results must be presented individually, by drug program, before being aggregated to provide pan-Canadian results for the sponsor's base case and, if applicable, scenario analysis for any patient populations identified in the sponsor's requested reimbursement criteria.

The sponsor's base case and, if applicable, scenario analysis of the reimbursement-requested population, must be deterministic. Sensitivity analyses should be undertaken to assess parameter uncertainty on the base case and, if applicable, scenario analysis of the reimbursement-requested population.



All relevant comparators included in the submitted economic evaluation must be included in the BIA. In accordance with the economic evaluation, CADTH may determine that potentially relevant comparators were excluded from the pharmacoeconomic submission.

Specific considerations, such as those listed below, may apply depending on the submission:

- The method of dose preparation, dose stability, and specifics around potential drug wastage should be addressed within the BIA. Vial sharing, if applicable, may be considered in a scenario analysis.
- If there is a companion diagnostic test associated with the drug under review, the BIA (and model) must include a scenario analysis that captures the relevant costs for the companion tests in relation to the drug under review (e.g., test costs for all patients in whom the drug under review is considered; incorporating the impact of diagnostic accuracy of the test on the budget impact). The source(s) and assumption(s) of the relevant inputs should be provided as well.
- If the drug under review replaces an existing compounded product, a scenario analysis must be presented in which the compounded product is a comparator within the analysis.
- A scenario analysis must be presented that considers a broader Canadian health care payer perspective for the following technologies:
  - cell and gene therapies (e.g., consideration of costs to the health care system associated with the introduction and implementation of the new technology)
  - drugs that are partly or solely administered in hospital (e.g., consideration of drug costs borne by the hospital system)
  - infusion therapy (e.g., consideration of the cost impact due to drug administration)
- If the full implementation is expected to extend beyond 3 years, a longer time horizon may be submitted as a scenario analysis.
- Change in market size (e.g., due to demographic change, changes in incidence, and so forth) should be considered if significant.

### b) Budget Impact Model

An unlocked version of the budget impact model used to inform the technical report of the BIA must be provided.

The budget impact model must be programmed in Excel.

The model must be able to function in a stand-alone environment that does not require access to a web-based platform.

The sponsor must provide the model in its entirety, meaning CADTH must have full access to the mathematical calculations and be able to fully execute the model based on modifications to parameters of interest. That is, calculations must not be done within the VBA code and CADTH must be able to view within formulas how patients move through the model. CADTH must be able to vary individual parameters, view the calculations, and run the model to generate results.

The BIA model must be flexible enough to be applied to the context of any individual drug program participating in CADTH's drug reimbursement review processes, which may differ with respect to the funding of comparators or the design of the program responsible for drug reimbursement. With the exception of drug prices (for which the same value should be used across all programs), input values used in the BIA should be specific to the individual drug program, where possible. When data specific to Prince Edward Island are unavailable, the inputs for Prince Edward Island are to be based on data from Nova Scotia.

A breakdown of costs by perspective (i.e., drug program and, if applicable, health care payer) must be reported within the submitted budget impact model.

Results, by year, must be reported for both the reference and new drug scenario before the budget impact is calculated (as the difference between the new drug and reference scenario).

#### **5.6.4 Supporting Material**

Details regarding information used as input parameters in the pharmacoeconomic submission must be provided in detail. The sponsor must provide:

- a user guide for the economic model to ensure clarity on how to modify input parameters and how to run the economic model for the base case and all scenario analyses; within the user guide, please note the expected model run time
- the full technical report of the indirect treatment comparison(s), if 1 or more indirect treatment comparison is used to inform model parameters in the submitted economic evaluation
- technical reports of any unpublished studies or analyses used to inform parameters or assumptions in either the pharmacoeconomic evaluation or BIA (this includes but is not limited to data from utility studies, patient registries, Clinical Study Reports, expert opinion, market research information, epidemiological data on disease incidence and/or prevalence); the technical report(s) must be easily identified (i.e., provided separately to published studies or reports), and provide details of how input parameter values were derived, including a description of the study or dataset, the analysis plan, and results of the analyses; any modification or transformation of the results for use in the economic model must be described

- supporting documentation (i.e., references), numbered according to their respective number in the reference list, used to inform the methods, assumptions, and inputs in the economic evaluation and the BIA reports and models
- CADTH requires a RIS file with all references that are used in the pharmacoeconomic evaluation technical report and BIA technical report. The preferred format is a single RIS file, but separate RIS files for the pharmacoeconomic evaluation technical report and BIA technical report will be accepted.
- a document clarifying any key source(s) and assumption(s) of the relevant inputs for the companion diagnostic (e.g., articles, studies), if there is a companion diagnostic test associated with the drug under review.

Deviations from any of the requirements within the economic evaluation section must be discussed with and accepted by CADTH in advance of filing the submission. Please submit the following [template](#) to [requests@cadth.ca](mailto:requests@cadth.ca) with complete details of the deviations from these requirements. Alternative specifications may be considered in scenario analyses.

## 5.7 Epidemiologic Information

### 5.7.1 Disease Prevalence and Incidence

Provide the prevalence and incidence of the disease(s) or condition(s) for the indication(s) to be reviewed. Include a breakdown of prevalence by participating province, territory, and First Nations populations (where available).

References must be provided for this document in the following format:

- in-text citations numbered in their order of appearance
- a numbered reference list in the JAMA Oncology format.

### 5.7.2 Patients Accessing a New Drug

The following information is required only for submissions that are filed for new drugs or a new combination product if 1 of the components is a new drug (as defined in section 2.1). For the indication(s) to be reviewed by CADTH, the number of patients in Canada currently accessing the drug to within 20 business days of filing the submission must be provided. This must include the number of patients accessing the drug through each of the different possible mechanisms (such as compassionate use, Health Canada's Special Access Program, and participation in a clinical trial). Please use the template for [patients accessing a new drug](#) to provide this information.

## 5.8 Reimbursement Status of Comparators

A completed [template](#) summarizing the reimbursement status of all appropriate comparators. The completed template must be filed as a Microsoft Word document.

## 5.9 Pricing and Distribution Information

### 5.9.1 Submitted Price

The submitted price for the drug, reported to 4 decimal places, as follows:

- price per smallest dispensable unit for all dosage forms and strengths available in Canada
- price for all packaging formats available in Canada.

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 following completion of CADTH's review process. Only 1 price (anticipated or current market price) to 4 decimal places per smallest dispensable unit is to be submitted per drug that is to be reviewed by CADTH (i.e., only 1 price for all indications undergoing review by CADTH concurrently).

CADTH does not accept confidential submitted prices for applications filed for review through its reimbursement review processes. The submitted price is disclosed in all applicable CADTH reports. The price(s) of other treatments included in the pharmacoeconomic evaluation and in the BIA (e.g., comparators, concomitant medications) are not considered to be confidential and may be disclosed in the CADTH report.

The submitted price must be used in the pharmacoeconomic evaluation and in the BIA (budget impact reports and the models used to produce the results).

### 5.9.2 Method of Distribution

Indicate within the pricing and distribution document the method of distribution to pharmacies (e.g., wholesale, direct, or other arrangements).

## 5.10 Provisional Algorithm for Oncology Drugs

### a) Proposed Place in Therapy Template

A completed [proposed place in therapy template](#) with the following information:

- the sponsor's proposed place in therapy for the drug under review, including a clearly stated rationale for the proposed place in therapy with supporting references (as required)
- an overview of the existing treatment algorithm for the indication of interest
- a proposed algorithm showing the place in therapy for the drug or regimen under review and the potential impact on the place in therapy of the currently reimbursed treatment options.

### b) Studies for Studies Addressing the Sequencing of Therapies

Where applicable, a reference list and copies of published and unpublished studies that address the sequencing of therapies in relation to the drug under review, including the search strategy for those studies.

## 5.11 Companion Diagnostics

### 5.11.1 Clinical Utility of Companion Diagnostic

If applicable, provide a reference list and copies of articles that highlight the clinical utility of the companion diagnostic(s) under review. In this context, clinical utility refers to evidence of improved health outcomes as a result of biomarker testing. If no references are provided, a statement will be required to confirm that a search has been undertaken but no references have been located.

### 5.11.2 Price of Companion Diagnostic

If applicable, the disclosable price for the companion diagnostic(s) be provided.

## 5.12 Additional Letter for Submissions Filed on a Pre-NOC Basis

Once the NOC or NOC/c has been issued, the sponsor must provide a signed letter, using the [letter for sending NOC or NOC/c to CADTH template](#), indicating any wording changes to the Health Canada–approved final product monograph, as compared with the draft product monograph filed with CADTH at the time of acceptance for review.

## 5.13 Additional Information Requests

To complete the review CADTH may request additional information from the sponsor or Health Canada. Note the sponsor's continuing responsibility to advise CADTH of any harms or safety issues that may arise during the time the submission is under review.

### 5.13.1 Economic Information

Throughout the review period, CADTH may find that the economic evaluation that has been filed by the sponsor contains limitations or that there is a lack of clarity in the pharmacoeconomic submission. In situations where there are important limitations with the economic evaluation (identified broadly as relating to model transparency, model validity, and exclusion of relevant comparators), CADTH may provide written notice to the sponsor of the limitations identified and provide a description of the specific issues. At this time, the sponsor will be given 5 business days to notify CADTH which of the following options they would like to pursue:

- The sponsor plans to address the issues raised by CADTH, in which case CADTH will temporarily suspend the review in accordance with section 10.
- The sponsor will not be addressing the limitations raised by CADTH, in which case the review will continue and the limitations will be identified in CADTH's review report.
- The sponsor would like to voluntarily withdraw from the process in accordance with section 11.

Failure to respond within 5 business or a request for an extension will result in the temporary suspension of the review in accordance with section 10.

#### **5.13.2 Health Canada Clinical Reviewer Report(s)**

CADTH may request copies of all Health Canada clinical reviewer reports (*Pharmaceutical Safety and Efficacy Assessment* or *Biologics Safety and Efficacy Assessment Report*) pertaining to the evaluation of pivotal safety and efficacy clinical trials – including those associated with any previous negative decision received during any review iteration – for the indication to be reviewed by CADTH. If the *Pharmaceutical Safety and Efficacy Assessments* or *Biologics Safety and Efficacy Assessment Reports* are unavailable from Health Canada at the time the request is received from CADTH, the sponsor should provide the reports to CADTH as soon as they are available (i.e., on the day of, or the business day after, receipt from Health Canada).

#### **5.13.3 Health Canada Clarifaxes and Clarimails**

CADTH may request copies of Clarifaxes and Clarimails and/or responses to Clarifaxes and Clarimails issued by the sponsor. These documents must be provided in searchable format (i.e., PDF or .docx).

#### **5.13.4 Clinical Study Reports and Periodic Safety Update Reports**

CADTH may request complete copies or sections of Clinical Study Reports and Periodic Safety Update Reports from the sponsor. These documents must be provided in searchable format (i.e., PDF or .docx).

## **6. Stakeholder Engagement**

CADTH follows strict processes to independently and objectively evaluate evidence. It is inappropriate and unhelpful to the process for the sponsor, individual patients, patient groups, consumer advocacy groups, individual clinicians, professional organizations, or lobbyists to directly contact expert committee members with regards to a specific drug review.

### **6.1 Sponsor Engagement**

#### **6.1.1 Communications Between CADTH and the Sponsor**

Once an application for a reimbursement review has been filed, CADTH will only address procedure and process-related matters with sponsors via email, unless otherwise defined in this document (e.g., a conference call offered during the reconsideration process). Due to the volume of requests and the need to optimize limited resources, CADTH is unable to offer conference calls to sponsors that have questions regarding the process, and encourages sponsors that have questions regarding the process to submit a written inquiry to [requests@cadth.ca](mailto:requests@cadth.ca). A written response will be provided in a timely manner. In-person meetings will not be offered.

Direct contact between a sponsor and expert committee members (in their capacity as members of CADTH's expert committees) or the CADTH review team is not permitted during the review process. Direct



approaches in any form to committee members or the CADTH review team may be viewed as introducing conflict of interest and may create an appearance of bias or unfairness. Direct contact by a sponsor with 1 or more members of the CADTH review team may result in a significant delay in the review process because additional steps may be required to obtain an unbiased recommendation on the product.

Consultants working on behalf of a sponsor are required to copy an official contact for the sponsor on all email correspondence with CADTH. CADTH will not respond to any email correspondence from a consultant if an official contact for the sponsor has not been copied.

### **6.1.2 Pre-Submission Phase**

CADTH offers pre-submission meetings to facilitate the efficient preparation and filing of applications with CADTH. The pre-submission meeting provides the opportunity for CADTH staff and the sponsor to discuss the pending application. Please consult section 4.1 for details regarding the pre-submission process and instructions on how to request a meeting with CADTH.

### **6.1.3 Review Phase**

During the review phase, CADTH may request additional information and clarification from sponsor that is required in order to complete the review. These requests will be provided in writing and CADTH encourages the sponsor to respond in a timely manner in order to avoid potential delays with the review timelines. Additional details regarding these requests are provided in section 5.13.

CADTH provides the sponsor with the opportunity to review and comment on the draft reports (i.e., clinical report, pharmacoeconomic report, and ethics report, as applicable) prior to deliberation by the expert committee. CADTH will provide responses to the commentary and revise the reports as required. Sponsors will be provided with the CADTH's responses 8 business days prior to the scheduled expert review committee meeting. Refer to section 8.3 for details on the process for the sponsor review of the draft CADTH reports.

### **6.1.4 Recommendation Phase**

Sponsors will have the opportunity to review and provide feedback on the draft recommendation (section 9.4.2), as well as to file a request for reconsideration (refer to section 9.5).

## **6.2 Patient Engagement**

### **6.2.1 Role of Patient Groups**

Patient group input provides patients' experiences and perspectives of living with a medical condition for which a drug under review is indicated, their experiences with currently available treatments, and their expectations for the drug under review. This information is used by CADTH and by the expert committees in all phases of the review, including, appraisal and interpretation of the evidence, and the development of recommendations. Table 14 provides a summary of the key milestones for patient group involvement in the reimbursement review processes.

**Table 14: Key Milestones for Patient Group Engagement**

Milestones	Description
Call for patient group input	The call for patient input is issued 29 business days before the anticipated date of filing the application and will be open for 35 business days from the date the call for input is issued in the weekly update.
Posting complete patient group input <sup>a</sup>	All patient group input will be posted on the CADTH website (this typically occurs at the same time the CADTH reports are posted).
Commentary on recommendations	Patient groups will have 10 business days to review and comment on the draft recommendations during the stakeholder feedback period.

<sup>a</sup> This will include all conflict of interest declarations.

## 6.2.2 Patient Group Input and Feedback

### a) Call for Patient Input

The call for patient input regarding a submission, resubmission, or standard reassessment is posted 29 business days in advance of the anticipated filing date (as provided in the advance notification form) or on the same day a request for advice is received by CADTH. Patient groups have a total of 35 business days (from the date the call for input is issued in the weekly update) for preparing and submitting their input.

Open calls for patient input are available via:

- the CADTH website (as a pending drug submission and an open call for patient input)
- E-Alerts to all subscribed patient groups (patient groups can subscribe to E-Alerts by using the subscribe option on the CADTH website)
- CADTH’s Twitter accounts: @CADTH\_ACMTS (English) and @ACMTS\_CADTH (French).

If a pending submission, resubmission, or standard reassessment is delayed following the issuance of the call for patient input, CADTH may re-post the call for patient input if the delay is 6 months or longer. This is undertaken for 2 reasons:

- to ensure that the patient group input reflects the current perspective from the patient group(s)
- to provide an opportunity for any additional groups to contribute to CADTH’s review process.

### b) Submitting Patient Input

Patient input is submitted to CADTH by patient groups. Individual patients or caregivers who wish to provide input are encouraged to work with a patient group that represents their condition to prepare a group submission to CADTH. CADTH will accept patient input from individual patients and caregivers only when there is no patient advocacy group representing patients with a condition for which a drug under review is indicated. Individual patients and caregivers who wish to submit input for a drug review should first contact CADTH (at [requests@cadth.ca](mailto:requests@cadth.ca)) to confirm the absence of a relevant patient group. Upon confirmation that





no relevant patient group exists, CADTH will provide interested individuals with the individual patient and caregiver template for completion. The process for providing input, and how CADTH uses and posts that input, remains the same as that for patient groups, with minor modifications, as applicable, for an individual patient or caregiver.

Patient groups are asked to use the [patient input template](#) that is posted on the CADTH website. This template has questions and prompts to help guide patients to provide the information that will be most helpful to the review team and the expert committees.

Patient groups must submit their input as a Microsoft Word document by the posted deadline date for the information to be used by CADTH.

### c) How Patient Group Input Is Used

All patient group input received for the drug under review is collated by CADTH. The complete patient group input is incorporated into the CADTH report(s). The patient group input submissions in their entirety are included in the committee brief. The public and patient members on the expert committees present the patient input at the outset of the deliberations (section 9.2), and a summary of the patient input discussion is included in the recommendation documents.

All patient input submissions are kept on file and may be referred to in future CADTH reviews of the same drug or other drugs with similar indications.

### d) Posting Patient Group Input

The names of the patient groups that provided input will be included on the CADTH website within the key milestone table for the drug under review after the call for patient input is closed.

The patient group submissions for each drug are consolidated for posting on the CADTH website. Posting will typically occur at the same time the CADTH reports are posted. The conflict of interest information will be included in the posted material.

CADTH takes reasonable precautions to remove any private information, such as names of individual patients, before posting the patient group input submissions in their entirety. However, it is the responsibility of the patient group to ensure that no private information is included in the submissions.

### e) Feedback on Draft Recommendations

All draft recommendations are posted on the CADTH website for stakeholder feedback. The feedback period begins when the draft recommendation is posted on the CADTH website. Patient groups and other stakeholders will have 10 business days to review the draft recommendation and provide feedback using the [CADTH template](#). Refer to section 9.4.2 for complete details on the procedures for stakeholder feedback.

## 6.3 Clinician Engagement

## 6.3.1 Clinician Group Input and Feedback

### a) Role of Clinician Groups

Clinician group input is used by CADTH in all phases of the review, including appraisal of evidence, and interpretation of the results. The clinician group input submissions are included in the CADTH report(s) and committee briefing materials. A summary of the clinician input is included in the recommendation documents.

Table 15 provides a summary of the key milestones for clinician group involvement in the reimbursement review processes.

**Table 15: Key Milestones for Clinician Group Engagement**

Milestones	Description
Call for clinician group input	The call for clinician group input is issued 29 business days before the anticipated date of filing the application and will be open for 35 business days from the date the call for input is issued in the weekly update.
Commentary on recommendations	Clinician groups will have 10 business days to review and comment on the draft recommendations during the stakeholder feedback period.
Posting complete clinician group input and feedback <sup>a</sup>	All clinician group input and feedback will be posted on the CADTH website.

<sup>a</sup> This will include all conflict of interest declarations

### b) Call for Clinician Input

The call for clinician input regarding a submission, resubmission, or standard reassessment is posted 29 business days in advance of the anticipated filing date (as provided in the advance notification form) or on the same day a request for advice is received by CADTH. Groups or associations of health care professionals will have a total of 35 business days (from the date the call for input is issued in the weekly update) for preparing and submitting their input. Open calls for clinician input are available via the CADTH website, E-Alerts to all subscribers, and the CADTH Twitter accounts (English: @CADTH\_ACMTS and French: @ACMTS\_CADTH).

If an application is delayed following the issuance of the call for clinician input, CADTH may re-post the call for clinician input if the delay is 6 months or longer. This is undertaken for 2 reasons:

- to ensure that the clinician input reflects the current perspective from the group(s) or association(s)
- to provide an opportunity for any additional groups to contribute to CADTH's review process.

### c) Submitting Clinician Group Input



Input from clinicians is submitted to CADTH by groups or associations of health care professionals. Individual clinicians who wish to provide input are encouraged to work with a group that represents their profession to prepare a group submission. CADTH will accept input from individual clinicians only when there is no relevant group or association that could provide input for the drug under review. Individuals who wish to submit input for a drug review should first contact CADTH (at [requests@cadth.ca](mailto:requests@cadth.ca)) to confirm the absence of a relevant group or association.

Clinicians providing input on behalf of a group or association are asked to use the [clinician input template](#) that is posted on the CADTH website. This template has questions and prompts to help guide respondents to provide the information that will be most helpful to the review team and the expert committees in their work. CADTH maintains the discretion to remove any information that may be out of scope for the review or not within the intent of the clinician input template. The input must be filed as a Microsoft Word document by the posted deadline date for the information to be used by CADTH.

### d) Posting Clinician Group Input

The information will be posted for the drug under review after the call for clinician input is closed. The clinician group submissions for each drug are consolidated in the CADTH report(s). Posting will typically occur at the time of posting the CADTH report(s). The conflict of interest information will be included in the posted material.

### e) Feedback on Draft Recommendations

All draft recommendations are posted on the CADTH website for stakeholder feedback. The feedback period begins when the draft recommendation is posted on the CADTH website. Clinician groups and other stakeholders will have 10 business days to review the draft recommendation and provide feedback using the [CADTH template](#). Refer to section 9.4.2 for complete details on the procedures for stakeholder feedback.

## 6.3.2 Clinical Experts on the Review Team

### a) Role of Clinical Experts

All CADTH review teams include at least 1 clinical specialist with expertise in the diagnosis and management of the condition for which the drug is indicated. Clinical experts are a critical part of the review team and are involved in all phases of the review process (e.g., 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, the clinical experts are invited to attend expert committee meetings to address any issues raised by the committee.

CADTH increases the number of clinical specialists 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 (refer to section 6.3.2b).

Lower complexity drugs include all tailored reviews as well as standard reviews that 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 1 to 2 clinical specialists as part of the review team but do not require a clinical panel.

Higher complexity products include cell and gene therapies as well as standard reviews for products that 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 2 to 3 clinical specialists as part of the review team and CADTH may convene a panel with additional clinical specialists.

**Table 16: Key Functions of Clinical Experts**

Phase	Role in CADTH process
<b>Review phase</b>	<ul style="list-style-type: none"> <li>• Assisting in the critical appraisal of clinical evidence</li> <li>• Interpreting the clinical relevance of the results</li> <li>• Providing guidance on the potential place in therapy</li> <li>• Reviewing and advising on the appraisal and interpretation sections of the clinical report</li> <li>• Advising on the assumptions used in the pharmacoeconomic analysis to assist in critical appraisal and to inform CADTH reanalyses</li> <li>• Advising on implementation issues raised by jurisdictions</li> </ul>
<b>Recommendation phase</b>	<ul style="list-style-type: none"> <li>• Attending expert committee meetings to address any issues raised by the committee</li> <li>• Providing input on requests for reconsideration</li> </ul>
<b>Implementation phase</b>	<ul style="list-style-type: none"> <li>• As part of an implementation advice panel, experts may advise on outstanding implementation issues and further develop and refine reimbursement conditions</li> <li>• Advising on treatment sequencing within a particular indication for oncology drugs</li> </ul>

### b) Clinical Panels

CADTH may establish clinical panels for drugs that are undergoing or have undergone an expedited review by Health Canada for the indication of interest (i.e., priority review or advance consideration under an NOC/c). CADTH will also consider requests from the drug programs to initiate a clinical panel for a drug that did not undergo an expedited review. Such considerations could be based on the perceived complexity of the drug from an implementation perspective.

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 drug’s potential place in therapy (e.g., potential reimbursement conditions).

The panels will comprise clinical experts with experience in the diagnosis and management of the condition for which the drug under review is indicated. Potential experts will be identified by CADTH, and whenever possible, CADTH will seek to obtain representation from across Canada. 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-INESSS joint engagement process, staff from INESSS as well as members of its expert committee will also attend the clinical panel meetings. Refer to section 6.3.2d for details on joint engagement with INESSS.

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 application is accepted for review by CADTH.

### c) Input From Clinical Experts

CADTH engages with the clinical experts (with or without a supplemental clinical panel) before the expert committee meeting to ensure that the committee has this information available to inform their deliberation and recommendation. The input from the clinical experts will be made available to the sponsor for review and commentary before the expert committee meeting. CADTH will aim to integrate the input of the clinical experts into the review report(s) before it is 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 input from the clinical experts 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 clinical expert input 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 experts will be reviewed and addressed by CADTH and the experts (as required). If deemed appropriate by CADTH, the review report(s) will be revised.

The input from the clinical experts will be made available to the expert committee for their deliberations on the drug under review (section 9).

### d) CADTH and INESSS Joint Engagement

CADTH and INESSS may jointly engage with clinical experts on selected drug products. Drugs will be selected jointly by CADTH and INESSS and will typically involve the following characteristics:

- similar submission timelines to CADTH and INESSS
- challenges in generating robust evidence due to the rarity of the condition



- potential for challenging implementation issues
- perceived ethical challenges for decision-makers
- high acquisition costs and/or substantial budget impact.

CADTH and INESSS will collaborate to establish the clinical panels, interact with the clinical experts on the panels, and summarize input and key information from the clinical panellists. Otherwise, the 2 agencies independently complete all other phases of their respective review process, including the deliberation and recommendation phases.

CADTH and INESSS will select drugs based on the previously noted considerations and will notify the sponsor in writing. It is important to note the following:

- The decision to consider drugs for joint engagement will be made solely at the discretion of CADTH and INESSS.
- Sponsors cannot request or apply to have a drug considered for joint engagement by CADTH and INESSS.
- Participation in the joint engagement process will not be optional for the sponsors of the drugs identified by CADTH and INESSS.
- Drugs selected for joint engagement will be identified in the review documentation posted on the CADTH and INESSS websites.

### e) Call for Clinical Experts

CADTH issues a Call for Clinical Experts for the purposes of identifying clinical experts who are interested in working with CADTH. This call will be issued at the same time the call for patient group and clinician group input is posted (i.e., 29 business days prior to the anticipated date of receipt). Those interested will be asked to register by completing a web form with contact information and details about their areas of expertise and interest. CADTH will compile a database of registered clinicians and use this information to assist in the recruitment of clinical experts.

CADTH will review the information provided by registrants and selected individuals may be contacted to discuss their potential participation in the review. In addition to the review-specific calls for clinical experts that will be issued for the reimbursement review processes, CADTH encourages any interested clinicians to register for potential involvement in future opportunities, including initiatives through the Optimal Use and Therapeutic Review processes.

The following factors are considered by CADTH when selecting clinical experts for participation in the review process:

- expertise regarding the diagnosis and management of the condition for which the drug is indicated

- conflict of interest declaration
- availability to commit to CADTH's review timelines
- regional representation (particularly for clinical panels).

## 6.4 Drug Program Engagement

### 6.4.1 Role of the Drug Programs

The drug programs provide input on each drug being reviewed through CADTH's reimbursement review processes by identifying issues that may impact their ability to implement a recommendation. This input increases the relevance of the recommendations and can potentially help avoid the need for an implementation advice panel or a request for advice later in the process by ensuring that potential implementation issues were considered during the review.

Examples of implementation considerations include, but are not limited to:

- variation in the reimbursement status and reimbursement conditions of comparator drugs across the drug programs
- potential for combination use with other available therapies
- potential for adjusting the dosage over time
- potential issues with administration or distribution mechanisms (e.g., need for specialty clinics)
- challenges with diagnostic testing requirements.

### 6.4.2 Drug Program Input

#### a) Pre-submission Phase

As described in section 4.1, representatives from the drug programs and pCPA may attend pre-submission meetings.

Once advance notification for a pending application has been received, a lead jurisdiction is assigned by CADTH using a rotational schedule of PAG members for oncology drugs and FWG members for non-oncology drugs. For drugs reviewed through the interim PPRP process, Canadian Blood Services will be the assigned as the lead jurisdiction.

CADTH will notify the drug programs regarding the pending application at the time advance notification has been received. The drug programs will be provided with the following information in the pre-submission phase:

- the advance notification form
- the sponsor's completed proposed place in therapy template (for oncology drugs)



- an updated rotational schedule for lead jurisdictions.

### b) Review Phase

CADTH will provide the drug programs with a copy of the documents filed by the sponsor. This will supplement the information provided in the pre-submission phase, most notably with the submitted price, BIA, and implementation plan (in the case of a cell or gene therapy).

The lead jurisdiction will be tasked with preparing a draft summary of potential implementation considerations for discussion and finalization with other members of the advisory committees (i.e., PAG or FWG, as applicable).

Input from the drug programs will be incorporated into the draft CADTH reports for review and comment by the sponsor (refer to section 8.3.1). Any comments related to the input from the drug programs will be made available to PAG or FWG for their consideration.

### c) Recommendation Phase

The summary of implementation issues will be presented by the lead jurisdiction (or a designate) at the expert review committee. In the event the committee has questions regarding any potential implementation issues associated with a recommendation, the committee chair may ask the lead jurisdiction (or designate) to provide clarity for the committee.

The drug programs are eligible to provide feedback and/or file a request for reconsideration of the draft recommendation (as described in section 9.4.2). The draft recommendations will typically be discussed with PAG and FWG in order to collate and finalize their feedback.



**Table 17: Key Milestones for Drug Program Engagement**

Milestones	Description
Timing of drug program input	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	Advance notification documentation followed by the complete application filed by the sponsor
Format for drug program input	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	Drug program input will be incorporated into CADTH review report(s) and posted publicly
Role at expert committee meeting	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	Clinician groups will have 10 business days to review and comment on the draft recommendations during the stakeholder feedback period; the drug programs are eligible to file a request for reconsideration
Implementation phase	Drug programs may request that an implementation advice panel be convened and participate in the process

FWG = Formulary Working Group; PAG = Provincial Advisory Group.

## 7. Application and Screening Procedure

By filing an application with CADTH, the sponsor consents to be bound by the terms and conditions specified in the *Procedures for CADTH Reimbursement Reviews*, including the *CADTH Reimbursement Review Confidentiality Guidelines* and all provisions regarding withdrawal from CADTH’s reimbursement review processes. Consent to the terms and conditions contained herein cannot be revoked by the sponsor at any time during or after the CADTH’s review processes.

### 7.1 Application Filing

The application filed by the sponsor must adhere to the content, format, and organization stipulated in the current version of the *Procedures for CADTH Reimbursement Reviews* and any applicable [CADTH Pharmaceutical Reviews Updates](#). All documents must be provided in English.

Sponsors must be registered with the CADTH Pharmaceutical Submissions SharePoint site before filing the required documents with CADTH. For detailed information on how to register, please consult the [Pharmaceutical Submissions SharePoint Site – Setup Guide](#). Please ensure that both primary and secondary contacts, as well as any submitting consultants working on an application for a reimbursement review, are registered with the Pharmaceutical Submissions SharePoint site.

Requirements must be filed using the Pharmaceutical Submissions SharePoint site. The sponsor must upload 1 copy of all requirements to the corresponding review using the Pharmaceutical Submissions



SharePoint site, per the file folder and file format specified in Appendix 6. Requirements must be filed using the Pharmaceutical Submissions SharePoint site during CADTH business hours (between 8:00 a.m. and 4:00 p.m. Eastern time). If filed outside of CADTH business hours, the next business day will be considered the date of transmittal.

CADTH sends an acknowledgement of receipt to the sponsor to confirmation that the requirements have been received. Sponsors that experience difficulties filing documents with the Pharmaceutical Submissions SharePoint site should contact CADTH by email (at [support@cadth.ca](mailto:support@cadth.ca)) for support or to arrange an alternate delivery method (e.g., by email or mailing a USB flash drive).

CADTH will provide copies of the requirements to the drug programs to ensure that they have this information prior to the targeted expert committee meetings. Sponsors are still required to provide copies of their application – including all drug program–specific requirements – to the individual drug programs (i.e., CADTH does not provide the requirements on behalf of the sponsor).

### 7.2 Application Screening

The following provisions apply to all applications filed by sponsors or drug programs.

- The Pharmaceutical Submissions SharePoint site logs the date and time that the requirements are received.
- Applications are accepted on an ongoing basis and are screened in the order they are received.
- The date of receipt is considered day zero for the purpose of calculating the 10–business day targeted time frame for initial screening of requirements.
- If the filed requirements are deficient or require revision, CADTH sends a notice to the sponsor advising what information needs to be included or revised in order to be accepted for review. Rescreening of the requirements is completed by CADTH as soon as possible after receipt but may take up to 5 business days.
- On day 10 of the screening period, CADTH sends a letter to the sponsor advising whether or not the requirements have been accepted for review.
- Following an acceptance for review, the sponsor must also provide the requirements to all of the drug programs that require copies (refer to [Contact Information and Requirements for Drug programs](#) for details).

### 7.3 Finalized Information for Submissions Filed on a Pre-NOC Basis

For submissions filed on a pre-NOC basis, some requirements will be outstanding or not finalized at the time that the submission is filed with CADTH (e.g., product monograph). The sponsor must provide all outstanding and/or finalized requirements to CADTH as soon as they are available.



CADTH will assess finalized information upon receiving it. Depending on the nature and extent of changes to the information compared with what was originally filed, CADTH will determine the timelines required to review it and incorporate it into the review report(s). This could result in the submission being considered at a later expert committee meeting. In the event the finalized information is received after the drug has been discussed by the expert committee, CADTH will review the information and determine if the draft recommendation will be issued or if the drug should be placed on the agenda for a subsequent meeting of the expert committee. The sponsor will be apprised of any revisions to the anticipated timelines. If additional supporting documentation is required, the sponsor will be apprised of the requirements.

Once CADTH has notified the sponsor that the finalized requirements have been accepted, the sponsor must ensure that the drug programs are provided with a copy of the finalized requirements.

### 7.4 Application Fees for CADTH Pharmaceutical Reviews

All applications filed by manufacturers are subject to an application fee. For details please consult the [Fee Schedule for CADTH Pharmaceutical Reviews](#).

As stated in the *Fee Schedule for CADTH Pharmaceutical Reviews*, a case-by-case assessment is made regarding the application fee when there are multiple indications included in one application. Multiple fees are assessed to ensure that the application fee accurately reflects the level of effort and resources required by CADTH to review the application. CADTH bases this decision on the following 4 factors:

- The indications are sufficiently different to require consultation with different clinical specialists.
- The indications are best addressed through separate review reports and/or expert committee recommendations.
- The indications have been studied in separate clinical development programs (e.g., separate clinical trials for each population).
- The sponsor has filed different economic analyses and budget impact analyses for each of the indications.

The final decision is made by CADTH based on the considerations noted above. It is important to note that not all the factors need to be met in order for an application to warrant multiple application fees.

Any sponsors that are uncertain about the application fees are encouraged to contact CADTH early in the pre-submission phase to seek guidance ([requests@cadth.ca](mailto:requests@cadth.ca)).

### 7.5 Ordering and Initiation of Reviews

All applications will be assigned to the work schedule on a first-come, first-served basis, as determined by the date of acceptance for review by CADTH, with the exception of requests for advice. The timing of when a request for advice will be considered at an expert committee meeting is based on the nature of the request and the amount of effort required by the review team to address the request.



Reviews are typically initiated within 10 business days of acceptance for review. Key dates (including initiation and the targeted expert committee meeting) are provided to the sponsor only once the requirements have been accepted for review. CADTH posts the targeted [meeting dates](#) on which applications may be considered if their reviews are initiated by a given date.

Prior to initiating the review of an application, CADTH will:

- provide the sponsor with the name of the contact to whom all inquiries about the application are to be directed
- determine the appropriate approach for the review and develops a work plan
- establishes a review team (refer to section 7.6).

### 7.6 CADTH Review Team

The unique composition of each review team is established based on the nature of the review and in consideration of the proposed team members' qualifications, expertise, and compliance with the CADTH Conflict of Interest Policy. With the exception of the review manager(s), the names of the review team members, including members of clinical expert panels (if applicable), will not be disclosed to the sponsor.

### 7.7 Targeted Time Frames and Tracking

#### 7.7.1 Target Timeframes

The key targeted time frames and the status of all reviews are posted on the CADTH website. Table 18 indicates the targeted time frames for key tasks within the CADTH's reimbursement review processes. Depending on the volume or complexity of the material to be reviewed by CADTH, an extension of the review time frame deadlines may be required. The sponsor will be notified of any extensions, as well as the reasons for the extensions.

**Table 18: Targeted Timelines for the Reimbursement Review Processes**

Phase of review	Key milestone	Business days
Screening	Application received	0
	Requirements screened for acceptance	10
	Review initiated	1 to 10
Review	Draft report(s) prepared and sent to sponsor for comments	53 <sup>a</sup>
	Sponsor reviews draft report(s) and provides comments	7
	CADTH's responds to comments <sup>b</sup> and revises reports (as required)	8
Draft recommendation	Committee reviews materials and prepares discussant reports	10
	Expert committee meeting	1 to 2
	Draft recommendation issued to drug programs and sponsor	8 to 10
	Sponsor identifies confidential information	2
	CADTH redacts confidential information	1
	Validation of redactions by the sponsor	1
	Draft recommendation posted on CADTH website	2
Feedback phase	Stakeholder feedback period	10
	Request for reconsideration	Variable <sup>c</sup>
Final recommendation	Final recommendation issued to drug programs and sponsor (no reconsideration)	8 to 10
	Final recommendation issued to drug programs and sponsor (after reconsideration)	8 to 10
	Sponsor requests redaction of confidential information in recommendation	2
	CADTH redacts confidential information in recommendation	1
	Validation of redactions by the sponsor	1 <sup>d</sup>
	Final recommendation copy-edited and formatted for posting	7
	Final recommendation posted on CADTH website	1
Posting CADTH reports	Sponsor identifies confidential information in reports	10
	CADTH redacts confidential information in reports	8
	Sponsor verifies redactions in clinical and economic reports	5
	CADTH reports copy-edited and formatted for posting	18
	CADTH reports posted	3

<sup>a</sup> The timing required to prepare the draft reports for a request for advice depends on the complexity of the request and the amount of effort required to address the request.

<sup>b</sup> Sponsors will be sent CADTH's responses and the revised reports 8 business days prior to the expert committee meeting.

<sup>c</sup> The time frame required to address the request for reconsideration depends on the amount of work needed to address the request, as well as the available dates for expert committee meetings.

<sup>d</sup> In the case of a disagreement expressed by the sponsor regarding redactions made in the review report(s), CADTH may require additional time to resolve the disagreement in consultation with the sponsor. This additional time could delay publication of the review report(s)

## 7.7.2 New Information Filed in the Review Phase

### a) Before Draft Reports Sent to Sponsor

During all reviews, CADTH will determine whether additional information from the sponsor is needed to complete the review. If so, CADTH will contact the sponsor. Delays in providing the requested information may result in a temporary suspension of the review due to incomplete information to conduct a thorough review (refer to section 10.1).

If a sponsor submits new information for inclusion in an ongoing review (i.e., after the requirements have been accepted and the review has been initiated), CADTH will determine the timelines required to review the new information and incorporate it into the review reports. This could result in the application being considered at a later meeting of the expert committee. The sponsor would be apprised of any revisions to the anticipated timelines for the review.

CADTH strongly discourages sponsors from filing revised economic models after an application has been accepted for review. The only exceptions are situations where CADTH has identified important limitations that prevent a robust appraisal of the sponsor's economic evaluation (i.e., in accordance with the process outlined in section 5.13.1).

#### b) After Draft Reports Sent to Sponsor

No new information can be filed after the draft review reports have been sent for sponsor review and comment. This includes, but is not limited to:

- new economic models
- new economic evaluations
- new submitted price
- new clinical studies (i.e., those not included in the initial application package)
- new data cut-offs or other analyses for studies included in the CADTH review reports
- new indirect treatment comparisons.

Any sponsors who wish to file new information after receiving the draft CADTH review reports will be required to formally withdraw and refile their application with section 11.2.

### 7.7.3 Pausing the Clock During Health Canada Review

Sponsors are required to notify CADTH once a pause-the-clock request has been accepted by Health Canada. At that time sponsors are required to provide the following information:

- The specific issues being addressed by the sponsor while the clock is paused (please note that details are not required and should not be provided to CADTH for any issues related to the quality review by Health Canada [e.g., chemistry, manufacturing, and controls]).
- The revised target timelines for the regulatory review process.



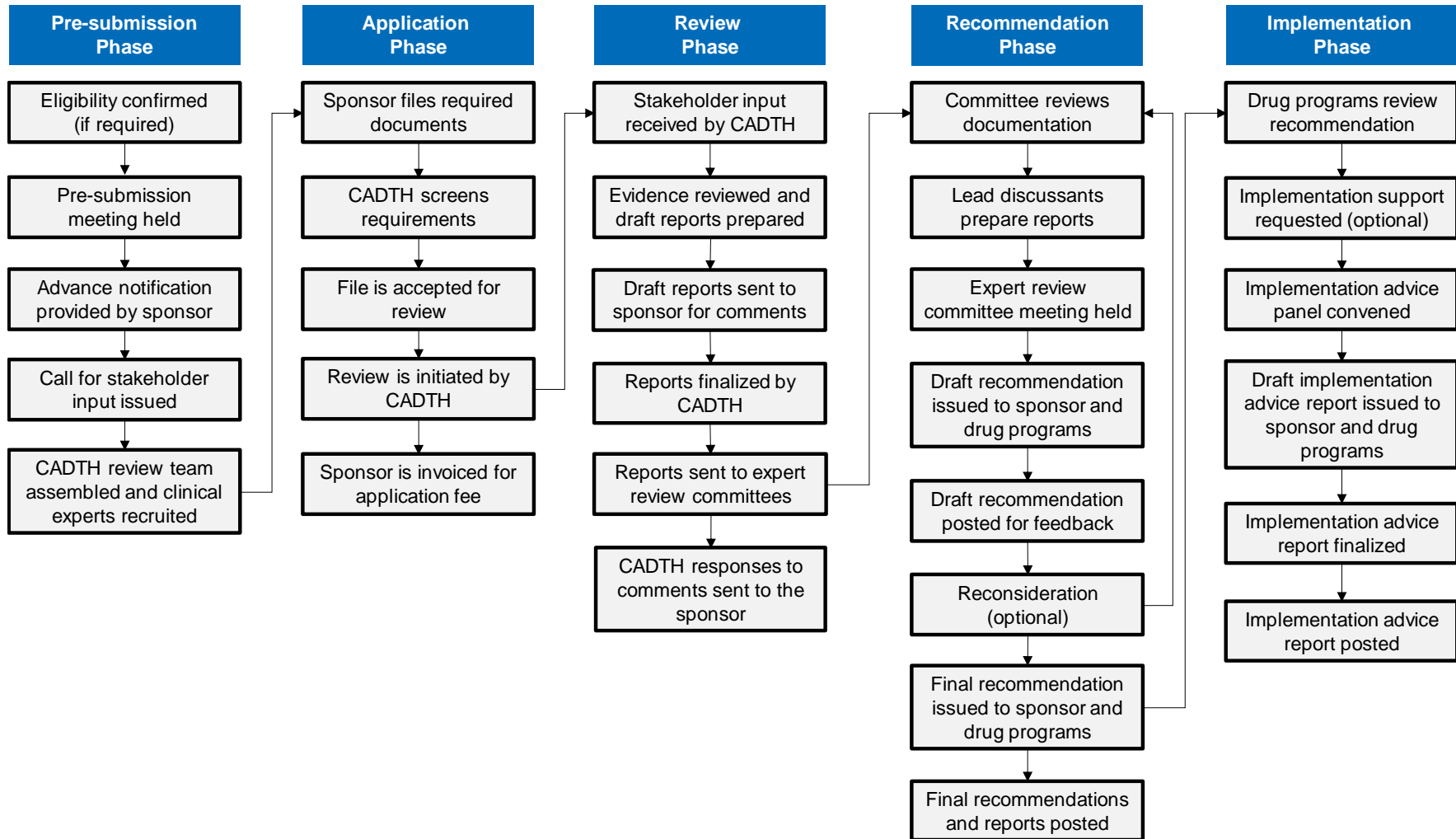
CADTH will review the issues being discussed between the sponsor and Health Canada and determine the following:

- If the issues are not anticipated to have a significant impact on the CADTH review (e.g., not anticipated to affect the indication or dosing information), CADTH may elect to continue with the review in accordance with the existing timelines.
- If CADTH believes the issues may have an impact on the CADTH review, the review may be temporarily suspended in accordance with section 10.1 pending clarification of the outstanding information.

In either of the above scenarios, CADTH may revise the target expert committee meeting date to better align with the revised regulatory review timelines.

**Figure 4: Overview of CADTH’s Reimbursement Review Processes**

Alt text: Figure shows a high-level summary of the CADTH reimbursement review process.





## 8. Review Procedure

### 8.1 Review of Submissions

#### 8.1.1 Standard Reviews

##### a) Clinical Review

CADTH prepares a clinical report based on the [sponsor summary of clinical evidence template](#), source documentation provided by the sponsor, and stakeholder input. A list of the studies and a list of the efficacy outcomes that will be included in the clinical review are sent to the sponsor for information purposes and to assist the sponsor in preparing to review and provide comments on the draft reports. CADTH summarizes and critically appraises the relevant evidence in the clinical report. Strengths and limitations with respect to both internal validity (i.e., how well the study was designed, conducted, and reported) and external validity (i.e., how well the results of the study could be applied to the target population in Canada) are documented.

Patient and clinician group input are included the clinical report. When discussing the available evidence, CADTH reflects on the input from patient and clinician groups, particularly any areas where there is an unmet therapeutic need for those living with the condition; known advantages and disadvantages of the treatments that are currently available; and any expectations regarding new therapies (including the drug under review). Refer to sections 6.2 and 6.3 for additional details on patient group and clinician group involvement, respectively.

CADTH review teams typically include at least 1 clinical expert who provides guidance and interpretation throughout the review. CADTH increases the number of clinical specialists depending on the complexity of the drug under review. In cases where the drug under review is undergoing or has undergone an expedited review by Health Canada for the indication of interest, CADTH may establish a panel of clinical experts to provide insight into the drug's potential place in therapy. Commentary in the clinical report regarding the potential place in therapy of the drug under review is provided by 1 or more clinical specialists with expertise in the diagnosis and management of the condition for which the drug is indicated. Refer to section 6.3 for additional details on clinician involvement in CADTH's review process.

The clinical report is prepared in accordance with a [template](#) and is finalized in accordance with section 8.3.

##### b) Economic Review

At the initiation of the process, CADTH economic reviewers work with the clinical reviewers to ensure that clinical information pertinent to the economic review is considered within the clinical review.

CADTH's review is conducted in line with CADTH's [Guidelines for the Economic Evaluation of Health Technologies: Canada](#). CADTH reviews the sponsor's pharmacoeconomic report and economic model, and critically appraises the sponsor's methods, inputs, and assumptions. As part of this appraisal, this entails:

- The model structure, assumptions, and inputs are validated through consultation with the CADTH clinical reviewers and clinical expert(s) involved in the review to ensure the economic model aligns with existing Canadian practice and the findings of the CADTH clinical review.
- The patient input that was received is considered, including whether or how the identified has been incorporated in the economic submission.
- The sponsor's submitted economic model is tested to confirm the reproducibility of the probabilistic results and to identify any key drivers of the model results.
- Reanalyses are conducted to address the limitations noted with the sponsor's model to provide revised results (i.e., CADTH base-case reanalysis). If reanalyses are not possible, CADTH will comment on the potential impact of such limitations to the economic findings.

The CADTH economic report will include a cost comparison table of the treatments indicated and/or used for the condition in the Canadian setting. The economic report on the cost-effectiveness of the drug is prepared in accordance with a template and is finalized in accordance with section 8.3.

### 8.1.2 Complex Reviews

#### a) Clinical Review

The clinical review processes will be completed in accordance with CADTH's standard review procedures (as described in section 8.1.1a).

#### b) Economic Review

The economic review process will be completed in accordance with CADTH's standard review procedures (as described in section 8.1.1b).

#### c) Implementation Plan Review (for Cell and Gene Therapies)

Sponsors will 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 completed implementation plan template filed by the sponsor. 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.

#### d) Ethics Review

CADTH will identify and describe ethical issues relevant to the drug's target population(s), evidentiary basis, use, implementation and outcomes. The summary of ethical issues will be incorporated into the draft review reports and the sponsor will have an opportunity to review and provide relevant commentary.

When there are multiple products with a similar mechanism of action and with indications in the same or a similar therapeutic area (e.g., CAR T-cell therapies for blood cancers), CADTH will use a summary report to identify relevant ethical considerations as opposed to conducting de novo reviews of ethical considerations for each application. The summary report will consist of an overview of ethical considerations summarized from the normative and empirical literature on CAR T-cell therapies and informed by prior completed CADTH reports of similar therapies. The report may be augmented with novel or emerging ethical considerations that are specific to the therapy, its target population, the disease state, or the evidence used to evaluate its safety, efficacy, or value. The ethics review will provide the expert committee with an overview of ethical considerations to inform its deliberations.

The ethics report is prepared in accordance with a [template](#) and is finalized in accordance with section 8.3.

### 8.1.3 Tailored Reviews

A tailored review consists of the review team conducting an appraisal of the clinical evidence and pharmacoeconomic evaluation filed by the sponsor using a CADTH-provided review template. CADTH validates and critically appraises the information provided by the sponsor in the template. Strengths and limitations with respect to both internal validity (i.e., how well the study was designed, conducted, and reported) and external validity (i.e., how well the results of the study could be applied to the target population in Canada) are documented.

CADTH includes its assessment of the submitted information and comments directly into the appropriate sections of the tailored review template. A single report that combines both the clinical and the pharmacoeconomic information is prepared by CADTH for tailored reviews (i.e., *CADTH Clinical and Pharmacoeconomic Review Report*).

Patient group input is included in the CADTH report. When discussing the available evidence, CADTH reflects on the input from patient groups, particularly any areas where there is an unmet therapeutic need for those living with the condition, known advantages and disadvantages of the treatments that are currently available, and any expectations expressed by patients regarding new therapies (including the drug under review). Refer to section 6.1 for additional details on patient engagement in CADTH's review process.

CADTH's review teams typically include at least 1 clinical expert who provides guidance and interpretation throughout the review. Commentary in the clinical report regarding the potential place in therapy of the drug under review is provided by 1 or more clinical specialists with expertise in the diagnosis and management of the condition for which the drug is indicated. Refer to section 6.3 for additional details on clinical expert involvement in CADTH's review process.

The *CADTH Clinical and Pharmacoeconomic Review Report* for a tailored review is finalized in accordance with section 8.3.

### 8.1.4 Plasma Protein Product Reviews

As described in section 6.4.2, Canadian Blood Services will be assigned as the lead jurisdiction and provide input to CADTH on all drugs reviewed through the PPRP process. The clinical and economic review processes will be completed in accordance with CADTH's standard or complex review procedures (as described in section 8.1.1).

### 8.1.5 Companion Diagnostics

For submissions that include companion diagnostics, CADTH's review process will include the following additional considerations.

#### a) Clinical Evidence

CADTH reviewers may evaluate the sponsor-provided reference list and copies of articles that highlight the clinical utility of the companion diagnostic(s) under review and may conduct a separate search of the clinical utility of the companion diagnostics. These results will be summarized in an appendix of the clinical review report.

#### b) Economic Evidence

As part of the appraisal of the sponsor-provided pharmacoeconomic evaluation, CADTH reviewers will consider the costs and consequences of any required biomarker testing that sponsors incorporate into the submitted analyses.

#### c) Patient Input

The patient input template asks patient groups to comment on their expectations and/or experiences with any required biomarker testing for the drug under review. Patient groups are asked to consider answering this question for eligible drugs that have companion diagnostics.

#### d) Clinician Input

As part of engaging expert clinicians throughout the review process, CADTH may reach out to additional experts in pathology and/or laboratory testing who would be able to comment on front-line clinical aspects of companion diagnostics (e.g., the timing of biomarker testing in the clinical care pathway, the consistency of the testing protocol with current practice, and the availability of the testing).

#### e) Jurisdictional Input

As part of soliciting implementation considerations from its participating jurisdictions, CADTH will also seek insights into the enablers and barriers related to any required biomarker testing.

## 8.2 Review of Resubmissions and Reassessments

### 8.2.1 Resubmissions and Standard Reassessments

CADTH will determine the length of time required to conduct the review of a resubmission or reassessment based primarily on the following considerations:

- the volume and complexity of the new clinical information to be reviewed
- the complexity of the economic model (e.g., model run time)
- the extent of revisions to the economic model relative to the initial submission (e.g., changes in model structure and/or assumptions)
- the date of filing the application relative to the target meeting date (e.g., filing earlier in the range provides greater opportunities for CADTH to target an earlier expert committee meeting)
- the volume of reviews being conducted concurrently by CADTH
- whether or not the drug underwent an expedited review by Health Canada.

The sponsor will be notified of the review timelines, including the target expert committee meeting date.

At the outset of the review, CADTH evaluates the information provided by the sponsor and relevant documents from the initial submission and any previous resubmissions. CADTH determines the appropriate approach to assess the new information and determines if a new systematic review is required. In general, the review of a resubmission or reassessment is conducted in accordance with the procedure used for a standard review (refer to section 8.1.1). The CADTH clinical and/or economic report(s) are finalized in accordance with section 8.3.

### **8.2.2 Requests for Advice**

Drug programs may file a request for advice through CADTH's reimbursement review processes regarding a previous final recommendation from CADTH. The request for advice must be provided to CADTH in a signed letter that clearly describes the issues of interest to the drug programs.

CADTH determines the appropriate approach for completing the requests for advice and develops a work plan for its review within 10 business days of receipt. The date on which CADTH receives the request for advice is considered day zero for the purpose of calculating the time frame for determining the approach for the request. CADTH may seek direction from the members of expert committees on how to proceed with the completing the request for advice.

The manufacturer(s) of the drug(s) (i.e., DIN holder) in question is apprised about the review and the reasons for the review and is invited to comment or provide information within 10 business days.

CADTH establishes a protocol for the review and may conduct 1 or more literature searches to identify relevant information. The studies and materials identified through the literature search, as well as any information or data provided by the manufacturer(s), are supplied to the review team to consider as part of the review.



Stakeholder input from patient groups and clinician groups input is summarized and discussed in CADTH's report. Refer to sections 6.2 and 6.3 for additional details on patient and clinician engagement, respectively.

The CADTH review report is finalized in accordance with section 8.3.

### 8.2.3 Reassessment Through the CADTH Therapeutic Review or Streamlined Drug Class Review Processes

As stated in the, one of the outputs from a CADTH Therapeutic Review or a CADTH Streamlined Drug Class Review may be revised recommendations for drugs that have previously been reviewed through the reimbursement review processes. Please refer to the following documents for complete details:

- [CADTH Therapeutic Review Framework and Process](#)
- [Procedures for CADTH Streamlined Drug Class Reviews](#)

## 8.3 CADTH Review Report(s)

CADTH forwards the draft review report(s) to the sponsor for comments and identification of confidential information, and to the drug programs for their information.

### 8.3.1 Sponsor Review of Draft Reports

The sponsor has 7 business days following receipt of the draft review report(s) to review and submit written comments about the report(s) to CADTH. This will be the sponsor's only opportunity to provide comments.

The sponsor's combined comments on the draft review report(s) must be filed using the [template](#) provided by CADTH, and must not exceed the page limitations provided in the template instructions:

- 10 pages for commentary on draft reports for standard and tailored reviews
- 11 pages for commentary on draft reports for cell and gene therapy reviews (10 pages is allotted for commentary on the clinical and economic reports and one additional page is allotted for commentary on the draft ethics report). This process will also apply to complex reviews filed on or after January 4, 2022.

The page limits include any figures, tables, and so forth, but do not include the list of references. The formatting of the template (e.g., page margins, table column widths) must not be altered. If the template filed by the sponsor exceeds the page limits, it will not be accepted by CADTH. The sponsor will be asked to refile its comments in accordance with the instructions. This could result in the review timelines being delayed, including the drug being considered at a later meeting of the expert committee. If CADTH is prevented from achieving the performance metric because of such a delay, sponsors will not be eligible for a partial refund.

As described in section 7.7.2, no new economic model may be filed after the draft review reports have been sent for sponsor review and comment. Any sponsor who wishes to file a revised economic model after



receiving the draft CADTH review reports will be required to formally withdraw and refile their application in accordance with section 11.2.

The sponsor may waive the opportunity to provide comments by indicating “not applicable” on the comments template.

The sponsor’s comments should be presented clearly and succinctly in point form, whenever possible. The issue(s) should be clearly stated, and specific reference must be made to the part of the report under discussion. References should be appropriately cited in the comments document provided by the sponsor.

The draft review report(s) are revised by CADTH, as required, based on the sponsor’s comments and are included in the committee brief. The review team has 7 business days to address the comments provided by the sponsor.

CADTH’s responses and the revised reports are sent to the sponsor 8 business days prior to the targeted expert committee meeting. The responses and reports are provided to the sponsor for information only. CADTH’s responses are incorporated into the committee brief (refer to section 9.2.1) and are shared with drug programs.

In the case of a submission filed on a pre-NOC basis, CADTH may revise the review report(s) to reflect the final product monograph or other finalized information provided by the sponsor as a result of the NOC or NOC/c being granted.

### **8.3.2 Identification of Confidential Information**

CADTH will post the review report(s) for all submissions, resubmissions, and reassessments. Sponsors are responsible for identifying and requesting the redaction of any confidential information supplied by the sponsor that was used by CADTH in the preparation of the review report(s) before these documents are posted. CADTH also provides an opportunity for the sponsor to review the feedback from the drug programs on the draft recommendation to ensure that it does not contain any confidential information. This is offered, as the drug programs may consider the unredacted draft recommendation when providing their input to CADTH.

Content identified as confidential information is expected to be kept to a minimum. It is not acceptable to mark an entire paragraph or section as confidential.

CADTH forwards the final review report(s) and stakeholder feedback to the sponsor at the same time the final recommendation is issued. The sponsor has 10 business days following receipt of the review report(s) and stakeholder feedback to identify confidential information and submit a request for redaction (refer to Table 19). This will be the sponsor’s only opportunity to request redactions from CADTH’s review report(s) and stakeholder feedback. Sponsors must identify any confidential information in the report(s) by providing:

- a completed [identification of confidential information form](#)
- a copy of the CADTH report(s) with confidential information highlighted in yellow.

- a copy of the stakeholder feedback document, with confidential information highlighted in yellow.

The sponsor may waive the opportunity to request redactions by indicating “not applicable” on the identification of confidential information form or by confirming via email.

All requests for redaction must be accompanied by a clearly stated rationale. CADTH will redact confidential information from review report(s) and/or stakeholder feedback based on the identification of confidential information form completed by the sponsor. Redactions will be made in accordance with the *CADTH Reimbursement Review Confidentiality Guidelines*.

The redaction form with CADTH’s response will be sent back to the sponsor with a copy of the redacted report(s) and stakeholder feedback (if applicable) for verification. The sponsor has 5 business days to review and confirm the redactions. In the case of a disagreement expressed by the sponsor regarding redactions made, CADTH may require additional time to resolve the disagreement in consultation with the sponsor. This additional time could delay publication of the review report(s) and/or stakeholder feedback.

CADTH may elect to update a previously posted review report should the redacted information become available in the public domain.

**Table 19: Time Allotted for Reviewing and Redacting CADTH Review Report(s)**

Key milestone	Description and timing	Business days
<b>Sponsor identifies redactions</b>	Sponsors are sent the final review report(s) and stakeholder feedback for identification of confidential information. The sponsor has 10 business days to submit the identification of confidential information form to request redactions.	10
<b>CADTH redactions</b>	CADTH redacts confidential information in accordance with the <i>CADTH Reimbursement Review Confidentiality Guidelines</i> .	8 <sup>a</sup>
<b>Sponsor verifies redactions</b>	Sponsors are sent the final redacted and unredacted review report(s) and/or stakeholder (if applicable) to review and confirm the redactions.	5

<sup>a</sup> This is a target of 8 business days. Extensions may be required depending on the nature, complexity, and clarity of the redaction requests.

## 9. Recommendation Procedure

### 9.1 CADTH Expert Committees

CADTH currently has the following drug expert committees that provide drug-related recommendations and advice to the drug programs:

- The CADTH Canadian Drug Expert Committee (CDEC) is used for drugs that are non-oncology drugs reviewed through the reimbursement review process.
- The Canadian Plasma Protein Product Expert Committee (CPEC) is a subcommittee of CDEC that is used for products that are reviewed through the interim PPRP process.



- The CADTH pan-Canadian Oncology Drug Review Expert committee (pERC) is used for oncology drugs that are reviewed through the reimbursement review process.

The expert committees' recommendations and advice are provided to CADTH to inform the publicly funded drug programs and a range of stakeholders.

The expert review committees are established in accordance with the terms of reference for the [Canadian Drug Expert Committee](#) and [pCODR Expert Review Committee](#). All expert committee members must comply with the [Conflict of Interest Policy](#) and the [Code of Conduct Agreement](#).

## 9.2 Expert Committee Meetings

### 9.2.1 Meeting Preparation

#### a) Meeting Agenda

The expert committee meeting agenda is set by CADTH and the committee chair.

#### b) Committee Briefing Materials

CADTH compiles and distributes the committee brief to all members of the expert committees and the drug programs 10 business days before the next scheduled meeting. The committee members are responsible for reviewing the briefing materials for all drugs under consideration at the meeting. Materials contained in the committee brief for each drug under review include, but are not limited to the following:

- patient group input
- clinician group input
- drug program input
- CADTH review report(s)
- sponsor's comments on the draft CADTH reports and CADTH's responses
- reimbursement status for the drug under review and its relevant comparators
- a summary of all CADTH recommendations issued with the same or a similar indication as the drug under review
- a summary of regulatory decisions and HTA recommendations for the drug under review in other jurisdictions
- additional information, such as
  - reference material (for CADTH's review report[s])
  - a sponsor-provided executive summary and table of studies.

In addition to the materials in the committee brief, the committee has access to the complete package of requirements filed by the sponsor. CADTH therapeutic review and optimal use reports may be included in the committee briefing materials when available and relevant.

In the case of a request for advice, the CADTH report(s) related to the application(s) for which the request for advice is made will be included in the committee brief.

### 9.2.2 Attendance

In addition to the expert committee members, the following people may attend a committee meeting in accordance with the terms of reference for the expert committees:

- Health ministry officials appointed by participating jurisdictions may attend as observers and may contribute information on practical considerations as described in the decision-making framework, but do not have the right to vote.
- Representatives of the pCPA office may attend as observers and may ask clarification questions as needed, but do not have the right to vote.
- Relevant CADTH staff and external reviewers contracted by CADTH may actively participate in the presentation of information. The staff role includes provision of administrative and secretariat support. CADTH staff and external reviewers do not have the right to vote.
- External experts (including clinical specialists) attend the expert committee meetings upon invitation from CADTH. These clinical experts provide input regarding the drug under review, address questions from the committee, and may assist in establishing and refining reimbursement conditions. They do not vote on the recommendation.

Sponsors, patients, and others (except as previously described) are not entitled to attend any expert committee meeting, either as observers or to make an oral presentation or submission.

### 9.2.3 Meeting Minutes

Minutes of committee deliberations will be taken so that there is a record of attendance at the meeting, of the recommendations made, and of the decisions and actions.

## 9.3 Deliberative Framework and Processes

As communicated in the [Proposed Alignment of CADTH Drug Reimbursement Review Processes](#) consultation, CADTH is currently undertaking a review of the deliberative processes used by its expert committees. The time frame for consulting on the proposed aligned deliberative process and framework for CADTH's reimbursement reviews has been adjusted due to the COVID-19 pandemic and additional details will be announced at a later date. The current deliberative frameworks and processes used by CADTH's expert committees can be found in the [Procedures for the CADTH pan-Canadian Oncology Drug Review](#) for oncology

drugs and the [Procedures for the CADTH Common Drug Review and Interim Plasma Protein Product Review](#) for non-oncology drugs.

### 9.3.1 Recommendations Framework

#### a) Recommendation Options

The expert committees may recommend one of the following options for a drug under review: that a drug be reimbursed, that a drug be reimbursed with conditions, or that a drug not be reimbursed (Table 20). Please note that the scenarios described within the table are meant to be illustrative and are not exhaustive.

**Table 20: Description of Recommendations**

Category	Description
Reimburse	The drug under review demonstrates comparable or added clinical benefit <u>and</u> acceptable cost or cost-effectiveness relative to one or more appropriate comparators <sup>a</sup> 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: <ul style="list-style-type: none"> <li>• The drug under review demonstrates comparable or added clinical benefit <u>and</u> acceptable cost or 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.</li> <li>• The drug under review demonstrates comparable clinical benefit <u>and</u> acceptable cost or cost-effectiveness relative to one or more appropriate comparators.<sup>a</sup> In such cases, a condition may include that the drug be listed in a similar manner to one or more appropriate comparators.<sup>a</sup></li> <li>• The drug under review demonstrates comparable or added clinical benefit, <u>but</u> the cost or cost-effectiveness relative to one or more appropriate comparators<sup>a</sup> is unacceptable. In such cases, a condition may include a reduced price.</li> <li>• 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 or cost-effectiveness relative to one or more appropriate comparators<sup>a</sup> is unacceptable, a condition may include a reduced price.</li> </ul>
Do not reimburse	There is insufficient evidence identified to recommend reimbursement. Scenarios that typically fit this recommendation category include: <ul style="list-style-type: none"> <li>• The drug under review does not demonstrate comparable clinical benefit relative to one or more appropriate comparators.<sup>a</sup></li> <li>• The drug under review demonstrates inferior clinical outcomes or significant clinical harm relative to one or more appropriate comparators.<sup>a</sup></li> </ul>

Note: Scenarios described in this table are meant to be illustrative and are not exhaustive. Existing treatment options may include best supportive care and non-pharmaceutical health technologies or procedures.

<sup>a</sup> 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, considering input from jurisdictions and clinical experts.

### b) Reimbursement Conditions

The CADTH drug expert committees may specify that a recommendation in favour of reimbursement is contingent upon one or more conditions being satisfied. These conditions commonly include initiation criteria, renewal criteria, discontinuation criteria, prescribing criteria, and conditions related to the price of the drug.

Table 21 provides some examples of reimbursement conditions that are commonly included in CADTH recommendations. The examples cited are intended to serve as illustrations only to help guide the reader to better understand some of the factors that CADTH’s drug expert committees will assess as part of their deliberations in formulating a reimbursement recommendation and are by no means exhaustive or impose any procedural obligations that would constitute grounds for a procedural review.

**Table 21: Examples of Commonly Used Reimbursement Conditions**

Reimbursement conditions	Description
<b>Initiation criteria</b>	Provides guidance on the appropriate reimbursement criteria for initiating treatment with the drug under review. Commonly used patient characteristics include: <ul style="list-style-type: none"> <li>• severity of the condition</li> <li>• treatment history (e.g., inability to use, intolerance, or inadequate response to appropriate comparator[s])</li> <li>• comorbidities</li> <li>• subtypes of the condition (e.g., based on genotypic and/or phenotypic characteristics).</li> </ul>
<b>Renewal criteria</b>	Provides guidance on how and when patients who are receiving the drug should be assessed to determine if they are benefiting from the treatment. Commonly used criteria include: <ul style="list-style-type: none"> <li>• minimum treatment response for continuation of therapy</li> <li>• type and timing of the clinical assessment(s) that should be used to evaluate the response to treatment.</li> </ul>
<b>Discontinuation criteria</b>	Provides guidance on when reimbursement of the drug under review should be discontinued. These conditions can be used to identify the drug in patients who are longer responding and/or benefiting from treatment. Commonly used criteria include: <ul style="list-style-type: none"> <li>• need for an invasive intervention (e.g., organ transplant or ventilation)</li> <li>• initiation of a different therapy for the condition</li> <li>• disease progression.</li> </ul>
<b>Prescribing criteria</b>	Provides guidance on the appropriate setting for the treatment. Commonly used criteria include: <ul style="list-style-type: none"> <li>• that prescribing and/or administration should be limited to clinicians or health care teams with a particular area of expertise</li> <li>• restrictions on dosage strength and frequency of administration</li> <li>• restrictions on combination use with other drugs.</li> </ul>

<b>Pricing conditions</b>	<p>Provides guidance on cost considerations for the drug under review. Commonly used criteria include:</p> <ul style="list-style-type: none"> <li>• a reduction in price (i.e., cost-effectiveness must be improved)</li> <li>• that the cost of the drug under review not exceed the cost of appropriate comparator(s)</li> <li>• that the cost of the drug under review should provide cost savings compared with appropriate comparator(s).</li> </ul>
<b>Feasibility of Adoption into the Health System</b>	<p>Provides an assessment of the ease with which the drug can be adopted into the overall health care and cancer care systems. Feasibility of adoption may be noted in the following scenarios:</p> <ul style="list-style-type: none"> <li>• Economic feasibility may be noted when there are concerns regarding the affordability of the drug under review based on the budget impact assessment.</li> <li>• Organizational feasibility may be noted when there are concerns regarding the ability of the health system to adopt the drug under review based on an assessment of health system enablers and barriers to implementation, as identified by the participating drug programs, inclusive of all elements: operational, capital, human resources, legislative, and regulatory requirements.</li> </ul>

### c) Considerations for Significant Unmet Need

In exceptional cases where there is uncertain clinical and pharmacoeconomic evidence, the CADTH drug expert committees may issue a recommendation to reimburse with conditions, due to practical challenges in conducting robust clinical trials and pharmacoeconomic evaluations and in the presence of significant unmet medical need. In these situations, although there is uncertainty with the clinical evidence, the available evidence must reasonably suggest that the drug under review could substantially reduce morbidity and/or mortality associated with the disease. Significant unmet clinical need is identified on a population or subpopulation basis (i.e., not on an individual basis) through CADTH’s drug review processes.

Please note that the scenario examples noted in Table 22 are intended to serve as illustrations only to help guide the reader to better understand some of the factors that CADTH’s drug expert committees will assess as part of their deliberation in formulating a reimbursement recommendation, and are by no means exhaustive or impose any procedural obligations that would constitute grounds for a procedural review.

Please also note that the rarity of the condition will not be the sole consideration for defining significant unmet need. The condition must also be identifiable with reasonable diagnostic precision.

**Table 22: Considerations for Significant Unmet Need and Uncertainty of Clinical Benefit**

Consideration	Description
<b>Considerations for significant unmet need</b>	
<b>Rarity of condition</b>	<ul style="list-style-type: none"> <li>The drug under review is approved by Health Canada for the treatment of a rare disease. Specifically, the condition for which the drug is indicated has the following characteristics:               <ul style="list-style-type: none"> <li>is life-threatening, seriously debilitating, or both serious and chronic in nature</li> <li>affects a relatively small number of patients (incidence of fewer than 5 in 10,000, but typically closer to 1 in 100,000)</li> <li>is often genetically based, onset at birth or early childhood, and leads to a shortened lifespan</li> <li>places a heavy burden on caregivers and the health care system</li> <li>is difficult to study because of the small patient population.</li> </ul> </li> </ul>
<b>Population</b>	<ul style="list-style-type: none"> <li>Need is identified on a population or subpopulation basis and not on an individual basis.</li> </ul>
<b>Absence of alternatives</b>	<ul style="list-style-type: none"> <li>There is an absence of clinically effective drug or non-drug alternative treatments.</li> <li>Substantial morbidity and mortality exist despite the available drug or non-drug alternative treatments.</li> </ul>
<b>Factors that contribute to uncertainty of clinical benefit</b>	
<b>Clinical data</b>	<ul style="list-style-type: none"> <li>Limited number of clinical studies</li> <li>Small sample sizes (e.g., due to rare disease that affects a relatively small number of patients [incidence of fewer than 5 in 10,000, but typically closer to 1 in 100,000])</li> <li>Absence of comparator groups</li> <li>Alternative or adaptive trial designs for rare diseases</li> <li>Short study durations or follow-up</li> <li>Inability to distinguish disease severity in heterogeneous manifested rare diseases</li> <li>Limited to surrogate end points</li> <li>Insufficient evidence on meaningful clinical end points</li> <li>Greater uncertainty in statistical analyses</li> </ul>

### 9.3.2 Drafting Recommendations

The committee must make a recommendation or defer if additional clarification is needed.

#### a) Submissions and Resubmissions

Based on the deliberation of the available evidence, the committee members choose one of the recommendation options described in section 9.3.1, provide reasons for the recommendation, and implementation guidance (when applicable). The reasons for the recommendation will represent the key considerations and rationale used by the committee in formulating the recommendation. CADTH staff may

be tasked with preparing the draft reasons for the recommendation, for approval by the committee members.

#### b) Reassessments

The committee may address reassessments by one of the following approaches:

- providing a revised recommendation that would supersede a previous final recommendation (e.g., changes to the recommendation category and/or reimbursement conditions)
- upholding the existing recommendation and providing additional context and/or clarifications that address the reassessment in an updated recommendation document.

In both scenarios noted above, a draft recommendation will be released (as described in section 9.4). The recommendation document would include standardized disclaimers that indicate that the new recommendation supersedes the previous recommendation that was issued at the conclusion of the initial CADTH review of the drug.

### 9.3.3 Voting on Recommendations

The committee members vote on the recommendation in the following manner.

- Only committee members may vote.
- All members must vote unless there is a declared conflict of interest that precludes a member from voting.
- The committee members vote anonymously on the recommendation.
- The reasons for the recommendation are drafted and discussed before committee members vote on a recommendation.
- The committee chair validates the voting results and announces if the motion is carried. Results of the vote are determined based upon a simple majority of the voting members.
- The committee chair votes only in the case of a split vote.

### 9.3.4 Deferring a Recommendation

If the committee needs additional information from CADTH, the sponsor, or external experts, the matter will be deferred to a subsequent meeting of the expert committee, pending the collection of such information.

## 9.4 Draft Recommendations

### 9.4.1 Issuing the Draft Recommendation

In the case of a submission that was filed on a pre-NOC basis, the draft recommendation will not be released until CADTH has received a copy of all the required information, including a copy of the NOC or NOC/c. CADTH will review the information and determine if the draft recommendation will be issued or if the drug



should be placed on the agenda of a subsequent meeting of the expert committee. The sponsor will be apprised of any revisions to the anticipated timelines.

The draft recommendation will be sent to the sponsor and drug programs 8 to 10 business days following the expert committee meeting at which the recommendation was made.

Before a recommendation is posted on the CADTH website, sponsors are responsible for identifying and requesting the redaction of any confidential information supplied by the sponsor that has been included in the draft recommendation. If the sponsor requests that confidential information be redacted from the draft recommendation, CADTH will redact the confidential information in accordance with the *CADTH Reimbursement Review Confidentiality Guidelines*. Pursuant to the *CADTH Reimbursement Review Confidentiality Guidelines*, CADTH will indicate that confidential information was used to make the reimbursement recommendation, and that the sponsor requested that this information be kept confidential.

Sponsors are asked to identify any confidential information in the draft recommendation using the [identification of confidential information template](#) provided by CADTH. All requests for redactions must be accompanied by a clearly stated rationale. Sponsors must submit the completed form to CADTH via the “5. CADTH Review Reports and Recommendations” folder on the Pharmaceutical Submissions SharePoint site by the date and time specified in the notice of the draft recommendation (typically 4:00 p.m. Eastern Time 2 business days after the draft recommendation was issued to the sponsor and drug programs).

If the sponsor expresses disagreement regarding redactions made in the draft recommendation, CADTH may require additional time to resolve the disagreement in consultation with the sponsor. This additional time could delay the timeline for posting the draft recommendation.

**Table 23: Target Timelines for Issuing and Posting Draft Recommendations**

Key milestones	Description
Issuance to sponsor and drug programs	CADTH issues the draft recommendation 8 to 10 business days after the expert review committee meeting
Sponsor identifies confidential information	Sponsor has 2 business days to identify any confidential information in the draft recommendation using the CADTH template
CADTH redacts confidential information	CADTH will redact information 1 business day after receipt of the completed template from the sponsor
Sponsor validates redactions	Sponsor has 1 business day to validate the redactions in the recommendation after receipt from CADTH
Posting on CADTH’s website	The draft recommendation will be posted on the day of the next scheduled issuance of CADTH’s weekly drug program updates
Stakeholder feedback period	The stakeholder feedback period will be 10 business days after the draft recommendation is posted on the CADTH website

### 9.4.2 Feedback on the Draft Recommendation



All draft recommendations are posted on the CADTH website for stakeholder feedback. The feedback period begins when the draft recommendation is posted on the CADTH website. The intent of the feedback period is to allow time for the sponsor, drug programs, and other stakeholders to comment on the draft recommendation and provide feedback before it is finalized and posted.

The sponsor, the manufacturer of the drug under review (if not the sponsor), the drug programs, patient groups, and clinician group(s) may provide feedback on the draft recommendation. Stakeholders will have 10 business days to review the draft recommendation and provide feedback (the day the recommendation is posted is considered day zero). Sponsors, patient groups, and clinician groups must provide feedback using the [CADTH template](#); feedback must be disclosable and will be posted on the CADTH website. Feedback from the participating drug programs is provided using a dedicated feedback form. Prior to posting, CADTH provides an opportunity for the sponsor to review the feedback from the drug programs to ensure that it does not contain any confidential information. This is offered as an additional measure in the event the drug programs have considered confidential information within the unredacted draft recommendation when providing their input to CADTH (section 8.3.2).

During the feedback period, the sponsor and/or the drug programs may make a request for reconsideration (section 9.5).

**Table 24: Stakeholders Eligible to Provide Feedback on Draft Recommendations**

Source	Scope of feedback
Sponsor	<ul style="list-style-type: none"> <li>Provide feedback on the draft recommendation</li> <li>File a request for reconsideration of the draft recommendation</li> </ul>
Manufacturer (if not the sponsor)	<ul style="list-style-type: none"> <li>Provide feedback on the draft recommendation</li> <li>File a request for reconsideration of the draft recommendation</li> </ul>
Drug programs	<ul style="list-style-type: none"> <li>Provide feedback on the draft recommendation</li> <li>File a request for reconsideration of the draft recommendation</li> </ul>
Patient group(s)	<ul style="list-style-type: none"> <li>Provide feedback on the draft recommendation</li> </ul>
Clinician group(s)	<ul style="list-style-type: none"> <li>Provide feedback on the draft recommendation</li> </ul>

## 9.5 Request for Reconsideration

### 9.5.1 Eligibility

The sponsor of a drug that is the subject of a draft recommendation and the drug programs may file a request for reconsideration of the recommendation during the feedback period. The sponsor and drug programs are entitled to have the draft recommendation reconsidered one time (this does not include situations where a revised draft recommendation has been issued after a request for reconsideration).

A request for reconsideration can be made only on the grounds that the recommendation is not supported by the evidence that had been submitted or the evidence identified in the CADTH review report(s). A request for reconsideration cannot be made solely because the sponsor or drug programs disagree with the

recommendation. The request for reconsideration must identify the aspect(s) of the draft recommendation with which the sponsor or drug programs disagree.

The sponsor and drug programs may only file a request for reconsideration during the feedback period. CADTH notifies stakeholders regarding the receipt of the request for reconsideration.

### 9.5.2 Reconsideration Options

As shown in Table 25, reconsideration requests are stratified depending on the focus, complexity, and effort required by CADTH to address the request. There are 3 categories:

- **Major revisions:** Requests for major revisions will typically be focused on the recommendation category (e.g., do not reimburse) or involve revisions 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 addressed in the initiation criteria).
- **Minor revisions:** Requests for minor revisions will typically be focused on any of the following: 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; or reasons for recommendation. Requests for minor revisions that would alter the patient population (e.g., expand the population or the criteria related to the identification of appropriate patients) will not be accepted and the request will have to be refiled as a request for major revisions.
- **Editorial revisions:** 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.

These categories have been developed to provide additional flexibility before the recommendation is finalized.

**Table 25: Reconsideration Options**

	Major revisions	Minor revisions	Editorial revisions
<b>Criteria</b>	Reconsideration requests that are focused on the 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: 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; 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.
<b>Deliberation</b>	All requests for major revisions to the recommendation will be addressed through discussion and deliberation with the full expert committee with additional support from clinical experts.	The majority of requests for minor revisions will be addressed through discussion and deliberation with a subpanel of the expert review committee with additional support from clinical experts, as required.	CADTH staff and the expert committee chair will address the majority of requests for editorial revisions. Other committee members may be consulted, as required.
<b>Outcomes</b>	Should the recommendation be substantially revised following deliberation on the reconsideration request, CADTH will issue another draft recommendation for stakeholder feedback. A final recommendation will be issued if the committee upheld the existing recommendation or made only minor revisions to the recommendation.	To expedite the review timelines, CADTH will not issue another draft recommendation following deliberations on a request for minor revisions. A final recommendation will 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.
<b>Timelines</b>	Requests for major revisions to a recommendation will typically require 2 to 3 months to address.	Requests for minor revisions to a recommendation will typically require 1 month to address.	A final recommendation will be issued in accordance with standard timelines (i.e., typically no delays).
<b>Eligibility</b>	Due the resources required to address these requests and the implications for timelines, only those stakeholders that will be directly involved in the negotiations for the drug under review are 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.



<b>Patient and clinician groups</b>	The committee will consider feedback on the recommendation from clinicians and patient groups in the deliberations for the reconsideration request.	Patient and clinician groups may request editorial revisions.
<b>Fee schedule</b>	Requests filed by sponsors will be subject to a schedule D application fee.	Not applicable.

### 9.5.3 Filing a Request for Reconsideration

#### a) Request for Major or Minor Revisions

A request for major or minor revisions is filed by the sponsor using the [reconsideration request template](#) and by the participating drug programs using a dedicated feedback form. The completed template must be received by CADTH during the stakeholder feedback period.

#### b) Request for Editorial Revisions

Requests for editorial revisions may be filed by any eligible stakeholder using the [stakeholder feedback template](#). Editorial revisions should not be filed using the request for reconsideration template.

### 9.5.4 Patient and Clinician Group Feedback

Reconsiderations result in a significant extension of the overall review timelines (typically 2 to 3 months) and have important resource implications for CADTH, as well as for sponsors. As such, only those stakeholders that will be directly involved in the negotiations for the drug under review are permitted to file requests for reconsideration (i.e., the sponsor and the drug programs). This helps 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.

Clinician groups and patient groups still play an important role in the reconsideration process as their feedback on the draft recommendation will be considered by the committee members in their deliberations for the reconsideration request.

### 9.5.5 Examination of Request for Reconsideration by CADTH

#### a) Assessment and Timelines

CADTH will examine, within 5 business days, each request for reconsideration to determine whether the issue(s) raised can be resolved in discussions with the sponsor and/or drug programs. It may be that the issue(s) can be clarified, and the sponsor will accept the recommendation. To minimize the overall timelines for the review, CADTH aims to resolve requests for reconsideration in the most efficient manner. In some cases, requests for reconsideration may be resolved through editorial revisions to the recommendation document. In such cases, CADTH may contact the sponsor and/or drug programs for confirmation that the editorial revisions are acceptable, and that the reconsideration process will not be required to resolve the issues.

If CADTH is unable to address the issue(s), the request for reconsideration is accepted and will be forwarded to the expert committee (details in section 9.5.7). When a request for reconsideration is accepted, the sponsor is offered an optional 1-hour meeting with CADTH to ensure clarity around the key issues raised in their request for reconsideration so that these can be clearly presented by CADTH to the expert committee members (details in section 9.5.6). In the event the request for reconsideration is not accepted, CADTH will finalize and issue the recommendation in accordance with section 9.6. The recommendation will be typically issued 5 business days after the decision not to accept the request for reconsideration has been communicated to the sponsor.

CADTH will not accept requests for reconsideration that are focused on the rationale for the pricing condition(s) that have been included in the recommendation (e.g., reasons noting a particular reduction in price could be required for the drug under review to be considered cost-effective relative to an appropriate comparator). CADTH will not accept these requests for reconsideration as they are related to the findings of the CADTH economic report as opposed to the committee's recommendation. As stated in section 9.5.1, a request for reconsideration can be made only on the grounds that the recommendation is not supported by the evidence that had been submitted or the evidence identified in the CADTH review report(s). A request for reconsideration cannot be made solely because a sponsor or the participating drug programs disagree with the recommendation.

When the draft recommendation is issued, sponsors have already been provided with an opportunity to review and comment on the CADTH economic report. The stakeholder feedback period and reconsideration process are not intended to provide additional opportunities for the sponsor to comment on issues that have been or should have been highlighted in the sponsor's comments on the draft CADTH report(s). The sponsor's comments on the draft CADTH economic report are provided to the expert committee members in accordance with section 9.2.1. The refiling of commentary on the CADTH economic report through the request for reconsideration process is not an efficient use of resources and the requests will not be accepted by CADTH.

#### b) New Information

CADTH may allow sponsors to provide new information during the reconsideration process in selected circumstances. The decision to allow new information during the reconsideration will be made solely by CADTH based on the following considerations:

- the application was accepted through the complex review process (effective for applications targeting the October 2022 expert committee meetings)
- the new information has been provided to try and address an important clear gap in the evidence that has been identified by the CADTH expert committee
- the sponsor confirms in writing that the new information was not available during the review phase of the CADTH Reimbursement Review process (i.e., it could not have been included in the

initial application without substantially delaying the overall review process and was not available at the time of providing comments on the draft CADTH reports)

- the expert committee has concluded that the drug under review has the potential to address an important unmet medical need
- the drug under review was reviewed by Health Canada through an expedited review pathway (e.g., priority review)
- the sponsor provides the new information in a format that allows CADTH to complete a detailed review and appraisal of the data (e.g., in accordance with the CONSORT reporting guidelines).

As the inclusion of new information during the reconsideration process cannot reasonably be anticipated by CADTH, the timelines for managing these situations will be established on a case-by-case basis. Any sponsors who feel they have new information that may address an important gap in the evidence that has been identified by the CADTH expert committee should identify the new information within the reconsideration request template when submitting the request.

#### c) Timelines for Expert Committee Meeting

CADTH will notify the sponsor of the target expert committee meeting date for the reconsideration. CADTH considers the following factors when establishing the timelines for reviewing a request for reconsideration:

- the grounds and complexity of the request for reconsideration
- the time required by CADTH to examine the grounds for the request and determine whether or not the request will be accepted (e.g., depending on the complexity of the request this can take up to 5 business days)
- whether or not the sponsor would like to participate in the 1-hour meeting offered by CADTH to discuss the request for reconsideration
- the time required to prepare documentation from the reconsideration meeting with CADTH for inclusion in the committee brief (e.g., meeting minutes)
- the deadline for the reconsideration committee brief to be delivered to all members and the drug programs (i.e., typically at least 10 business days before the scheduled expert committee meeting).

### 9.5.6 Reconsideration Meeting

#### a) Purpose

The reconsideration meeting provides the sponsor an opportunity to elaborate on the issues that were raised in their request for reconsideration that was filed with CADTH. These meetings are not offered for a situation where the request for reconsideration has been filed by the participating drug programs. In such cases, CADTH provides the complete written request for reconsideration to the sponsor and provides an



opportunity for direct input and commentary on the request. CADTH cannot facilitate a meeting between the sponsor and representatives of the public drug programs.

### b) Attendance

The sponsor is free to select its attendees; however, CADTH recommends that sponsors ensure that at least one person on the call is familiar with the clinical and economic details of the drug under review, including the appraisal, interpretation, and reanalyses reported in CADTH's reports and the draft recommendation.

Sponsors are welcome to invite clinicians and/or patients to participate in the web conference, provided they have agreed to maintain the confidentiality of the proceedings, including any CADTH documents that have not been posted publicly. Attendance will be capped at a maximum of 1 clinician and/or 1 patient representative at each meeting.

Key CADTH staff will attend the meeting (e.g., program directors and review team members). The names of the review team members are not disclosed to the sponsor, except for the review manager(s). CADTH will extend an invitation to observe the reconsideration meeting to members of the Formulary Working Group or Provincial Advisory Group (as applicable); however, their attendance for these meetings will be optional. At the sponsor's request, CADTH may extend an invitation to INESSS to observe the reconsideration meeting. In these situations, CADTH will extend the invitation to INESSS; however, their participation is optional. Sponsors must communicate if they would like INESSS to be invited to the meeting in section 1 of the [reconsideration request template](#).

### c) Meeting Logistics and Agenda

Reconsideration meetings are only offered via web conference and can be a maximum of 1 hour. In-person meetings are not offered for reconsideration meetings. CADTH will provide the meeting information prior to the meeting and may record the call for internal purposes.

CADTH will open the meeting by welcoming participants and stating the purpose of the reconsideration meeting. The remaining content of the meeting and the presenters are at the discretion of the sponsor. To ensure that the teleconference is conducted efficiently, CADTH recommends that the sponsor appoint one of its team members to chair the call. This helps ensure that the sponsor is able to address all of the key items within the allotted time frame. CADTH may pose questions throughout the presentation to help ensure that the issues being raised by the sponsor are clearly understood. If providing a presentation, sponsors must limit the number of slides to 30 or less.

### d) Summary of the Discussion

The sponsor is required to prepare a draft summary of the discussion using the template provided by CADTH. The summary must not exceed 2 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). Expert committee members will be provided with the meeting materials and the summary of the meeting.

### 9.5.7 Requests for Reconsideration Filed by the Drug Programs

CADTH provides an opportunity for sponsors to comment on requests for reconsideration that are filed by the public drug programs. Sponsors will be notified regarding the request for reconsideration once it has been accepted by CADTH and receive a copy of the request for reconsideration. At that time, the sponsor has the opportunity to provide written commentary on the request that has been filed by the drug programs. Commentary should be filed using section 2 of the request for reconsideration [template](#) within 5 business days of receiving notification from CADTH (as directed in the correspondence). The completed template will not be posted on the CADTH website.

### 9.5.8 Addressing the Reconsideration Request

#### a) Request for Major Revisions

CADTH prepares the committee briefing materials to address the reconsideration request, including but not limited to:

- the request for reconsideration
- the feedback from patient groups on the draft recommendation
- the feedback from clinician groups on the draft recommendation
- the draft expert committee recommendation
- a copy of the original committee brief for the drug that is the subject of the request for reconsideration
- a summary of input on the request for reconsideration from the following (as applicable): clinical experts, CADTH review team, the drug programs (if request is filed by the sponsor), the sponsor (if the request is filed by the drug programs)
- a summary of CADTH's reconsideration meeting with the sponsor (if applicable).

The reconsideration brief is delivered to all members of the expert committee members and the drug programs at least 10 business days before the scheduled expert committee meeting.

If the expert committee needs clarification from the CADTH review team or the sponsor, or advice from external experts, in order to address the request for reconsideration, the matter will be sent back to CADTH staff to collect such clarification or advice. Consideration of the drug under review will be moved forward to the next expert committee meeting, pending the collection of the necessary information. No one attending the expert committee meeting may introduce new information.



The expert committee will consider all recommendation categories as described in section 9.3 irrespective of the category of recommendation used for the original draft recommendation issued to the drug programs and the sponsor. The expert committee will determine if the original recommendation should be upheld or changed.

CADTH will issue either a final recommendation or a revised draft recommendation to the sponsor and drug programs 8 to 10 business days following the expert committee meeting.

CADTH will issue a revised draft recommendation in situations where the committee's recommendation has been substantially revised following a request for reconsideration. Specifically, this process will apply in the following circumstances:

- an initial draft recommendation stating that a drug should not be reimbursed was revised to state that the drug should be reimbursed with or without conditions.
- an initial draft recommendation stating that a drug should be reimbursed with or without conditions was revised to state that the drug should not be reimbursed.

CADTH will issue a final recommendation in situations where the draft recommendation has been upheld or has only undergone modifications to the recommended reimbursement criteria, reasons for recommendation, or other changes regarding the description in the recommendation document. When a revised draft recommendation is issued, the options available to the drug programs and sponsor in the additional feedback period will be the same as those currently described in the section 9.5.2.

The procedure for issuing a final recommendation following a request for reconsideration is described in section 9.6.

### b) Request for Minor Revisions

CADTH will convene a panel of expert committee members to review the minor reconsideration request filed by the sponsor and/or drug programs. The panel will typically be composed of the expert committee chair, lead discussants, and patient and public members, with additional support from clinical experts, as required. As with full expert committee meetings, the drug programs may observe the deliberations and provide insight into any potential implementation issues with recommendation.

The panel will be provided with briefing materials to address the reconsideration request, including but not limited to:

- the request for reconsideration
- the feedback from patient groups on the draft recommendation
- the feedback from clinician groups on the draft recommendation
- the draft expert committee recommendation

- a copy of the original committee brief for the drug that is the subject of the request for reconsideration
- a summary of input on the request for reconsideration from the following (as applicable): clinical experts, CADTH review team, the drug programs (if request is filed by the sponsor), the sponsor (if the request is filed by the drug programs)
- a summary of CADTH's reconsideration meeting with the sponsor (if applicable).

The expert committee subpanel will focus their deliberations on the issues raised in the request for minor revisions and will not consider all of the recommendation categories described in section 9.3. The final decision on whether to revise or uphold the recommendation will be made based on consensus and will be documented by CADTH. In the event the subpanel determines that the issues raised in the reconsideration request require deliberation by the full expert committee, the sponsor will be notified and provided with an opportunity to refile the request as a major reconsideration or withdraw the reconsideration and accept the recommendation.

CADTH will issue the final recommendation 8 to 10 business days after the expert committee subpanel has reached a decision on whether to modify to uphold the recommendation. The procedure for issuing a final recommendation following a request for reconsideration is described in section 9.6.

## 9.6 Final Recommendations

### 9.6.1 Issuing the Final Recommendation

CADTH will issue the final recommendation in the following circumstances:

- If neither the sponsor nor the drug programs file a request for reconsideration during the feedback period within the specified time, the final recommendation will be issued 8 to 10 business days after the stakeholder feedback period has ended.
- In the case of a request for reconsideration based on major revisions, the final recommendation will be issued 8 to 10 business days after the expert committee meeting where the draft recommendation has been upheld or has only undergone modifications to the recommended reimbursement criteria, reasons for recommendation, or other changes regarding the description in the recommendation document.
- In the case of a request for reconsideration based on minor revisions, the final recommendation will be issued 8 to 10 business days after the expert committee subpanel has reached a decision on whether to modify or uphold the recommendation.
- In the case of a request for reconsideration that is not accepted, the final recommendation will be typically issued 5 business days after the decision not to accept the request for reconsideration has been communicated to the sponsor.



When a final recommendation is issued, CADTH will send a notice of the final recommendation and a copy of the final recommendation to the sponsor and the drug programs.

### 9.6.2 Posting the Final Recommendation

All final recommendations are posted on the CADTH website. Sponsors are responsible for identifying and requesting the redaction of any confidential information supplied by the sponsor that has been included in the final recommendation before this document is posted.

Sponsors are asked to identify any confidential information they have supplied in the final recommendation using the [identification of confidential information form](#). All requests for redaction must be accompanied by a clearly stated rationale. Sponsors must submit the completed form to CADTH via “5. CADTH Review Reports and Recommendations” folder on the Pharmaceutical Submissions SharePoint site by the date and time specified in the notice of the final recommendation by end of business day (4:00 p.m. Eastern time) 2 business days after the final recommendation was issued.

If the sponsor requests that confidential information be redacted from the final recommendation, CADTH will redact the confidential information in accordance with the *CADTH Reimbursement Review Confidentiality Guidelines* (typically one business day after receiving the identification of confidential information form from the sponsor). Pursuant to the *CADTH Reimbursement Review Confidentiality Guidelines*, CADTH will indicate that confidential information was used to make the reimbursement recommendation, and that the sponsor requested that this information be kept confidential.

CADTH will distribute responses to the redaction requests for validation by the sponsor. The sponsor will have one business day to validate the redactions. In the case of a disagreement expressed by the sponsor regarding redactions made in the final recommendation, CADTH may require additional time to resolve the disagreement in consultation with the sponsor. This additional time could delay the timeline for posting the final recommendation.

**Table 26: Target Timelines for Issuing and Posting Final Recommendations**

Key milestones	Description
Final recommendation issued to sponsor and drug programs	<b>No reconsideration:</b> The final recommendation is issued 8 to 10 business days after the end of the stakeholder feedback period.
	<b>Following reconsideration:</b> The final recommendation is issued 8 to 10 business days after the expert committee meeting where the recommendation was upheld following a request for reconsideration.
Sponsor identifies confidential information	The sponsor has 2 business days to identify any confidential information in the final recommendation using the CADTH template.
CADTH redacts confidential information	CADTH will redact information one business day after receipt of the completed template from the sponsor.

<b>Sponsor validates redactions</b>	The sponsor has 1 business day to validate redactions in the recommendation after receipt from CADTH.
<b>Posting on CADTH's website</b>	The final recommendation will be posted on the CADTH website 7 business days after the redactions have been validated by the sponsor.

## 10. Temporary Suspension of a Review

### 10.1 Suspension Due to Incomplete Information

In the event that CADTH is unable to conduct a thorough review and/or an appraisal due to incomplete information, CADTH, in its sole discretion, may temporarily suspend a review in the following manner:

- CADTH may temporarily suspend a review pending receipt and acceptance of all required information.
- CADTH will advise the sponsor in writing that the review has been temporarily suspended. CADTH will indicate what information is required to re-initiate the review process.
- The CADTH review report(s) will not be sent to the sponsor for comment and the application will not be placed on the agenda for the expert committee until the review team is satisfied that the sponsor has provided all the required information.
- Once the issue is resolved, depending on the availability of resources, the review will resume at the stage where it was suspended. The sponsor will be advised, in writing, when the review process resumes, along with the anticipated target dates for the remaining steps of the review process.
- A review may be temporarily suspended at any stage up until the review process has been completed.
- A review that has been suspended is tracked on CADTH's website.

### 10.2 Suspension Following an NOD or NON

For submissions filed on a pre-NOC basis that receive an NOD or NON from Health Canada, CADTH will allow the review of certain submissions to be temporarily suspended while resolution of the NOD or NON is discussed with Health Canada. In order to be eligible for suspension rather than withdrawal, sponsors must have consented to the information-sharing process between CADTH and Health Canada. CADTH will also consider the following factors when determining if suspension is an option, including but not limited to:

- Health Canada's rationale for the NOD or NON (e.g., clinical versus quality issues)
- the anticipated timelines for addressing the issues raised by Health Canada.

The decision to allow a suspension rather than a mandatory withdrawal will be made solely at the discretion of CADTH on a case-by-case basis. If CADTH determines that a temporary suspension is not appropriate, the submission will have to be withdrawn (in accordance with section 11.1).

For drugs that undergo temporary suspension as a result of an NOD or NON, the following information would be required in order for CADTH to lift the suspension:

- a brief summary of the issue and how the sponsor has or is planning to resolve the issue (please note that details are not required and should not be provided to CADTH for any issues related to the quality review by Health Canada [e.g., chemistry, manufacturing, and controls])
- any new clinical data filed with Health Canada to address the issue
- advance notification of a minimum of 6 weeks from the sponsor when the issue is likely to be resolved and the anticipated date that an NOC or NOC/c may be issued by Health Canada.

Depending on the availability of resources, CADTH will resume the review at the stage where it was suspended. The sponsor will be advised, in writing, when the review process resumes, along with the anticipated target dates for the remaining steps of the review process.

### 10.3 Suspension for Other Reasons

In the event that questions or issues outside of the regular review process arise (for example, but not limited to, legal issues) regarding the drug under review, CADTH, in its sole discretion, may temporarily suspend the review in the following manner:

- CADTH will advise the sponsor in writing that the review has been temporarily suspended. CADTH will indicate the anticipated duration of the suspension period. As it deems necessary, CADTH has the discretion to extend the temporary suspension.
- CADTH's decision to temporarily suspend a review that was filed on a pre-NOC basis is made independently of Health Canada's review of that drug.
- Once the issue is resolved, depending upon the availability of resources, the review will resume at the stage where it was suspended. The sponsor will be advised by CADTH, in writing, when the review process resumes, along with the anticipated target dates for the remaining steps of the review process.
- The review may be temporarily suspended for reasons outside of the regular review process during any stage of the review process.
- A review that has been suspended is tracked on the CADTH website.

## 11. Withdrawal From the Reimbursement Review Processes

### 11.1 Withdrawal Procedure

An application will be withdrawn from the CADTH's reimbursement review processes if:

- the sponsor voluntarily requests withdrawal from the CADTH process
- the sponsor has withdrawn from the Health Canada review process
- Health Canada has withdrawn market authorization
- Health Canada has issued a Notice of Deficiency – Withdrawal or Notice of Non-Compliance.
- Health Canada has issued a Notice of Non-Compliance or Notice of Deficiency and the sponsor has not or will not consent to the information-sharing process
- CADTH determines that temporary suspension following the issuance of an Notice of Deficiency or Notice of Non-Compliance is not appropriate.

A sponsor may request voluntary withdrawal from the CADTH's reimbursement review process at any time up until 4:00 p.m. Eastern time 3 business days before the target expert committee meeting is scheduled. Voluntary withdrawal will not be permitted after this time.

In all cases where marketing authorization has been withdrawn or will not be issued by Health Canada, the sponsor must advise CADTH, in writing, within **1 business day**. CADTH appreciates that sponsors may need to manage communications regarding withdrawn files; as a result, when requested, delayed posting of the withdrawn status on the CADTH website can be accommodated. Please ensure that such requests are clearly stated within the correspondence to CADTH.

All requests for withdrawal from the reimbursement review process must be provided in writing and contain the following information:

- name and signature of the sponsor
- reason for the withdrawal (please note that the reason will not be posted on the CADTH website)
- if market authorization was withdrawn, the date on which market authorization was withdrawn.

CADTH will stop the review immediately upon being notified of a withdrawal or non-issuance of market authorization. CADTH will advise the sponsor and drug programs that the review has been withdrawn. The CADTH website will be updated to state that the application has been withdrawn.

Sponsors that withdraw from the reimbursement review process may be entitled to receive a partial refund of the application fees in accordance with the [Fee Schedule for CADTH Pharmaceutical Reviews](#).

CADTH will retain and/or dispose of materials associated with the withdrawn application (as described in section 16).

## 11.2 Refiling With CADTH After Withdrawal

The sponsor is required to refile a complete application in accordance with section 5. The refiled application must include a list of the changes made as compared with the initial application that was withdrawn. All updated documents (not limited to new information – e.g., an updated product monograph) must be provided.

In the case of a withdrawn submission for a drug that was previously filed on a pre-NOC basis and that has subsequently received market authorization from Health Canada (NOC or NOC/c), the sponsor is required to file the submission on a post-NOC basis.

CADTH will determine the appropriate approach for conducting the review of an application that has been withdrawn and refiled based on where the previous review was stopped and the amount of new information.

## 12. Implementation Advice for a Recommendation

### 12.1 Purpose and Eligibility

After a final recommendation has been issued, CADTH provides implementation support for the drug programs, pCPA, and Canadian Association of Provincial Cancer Agencies (CAPCA) to assist in developing and refining reimbursement conditions for certain drug products. This support is distinct from CADTH's reimbursement review processes and is offered for the purposes of assisting jurisdictions in implementing recommendations from CADTH and/or making reimbursement policy decisions.

At the request of the drug programs, CADTH may initiate work on an implementation advice report to address any outstanding issues that the expert committee was unable to due to limitations with the available evidence or the need for additional consultation with subject matter experts. Examples of when implementation advice is required may include, but are not limited to, the following:

- The expert 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 conditions 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 the expert committee has issued a recommendation in favour of reimbursement and will not generally be initiated in situations where the expert committee has recommended that the drug under review not be reimbursed by the drug programs.

## 12.2 Implementation Advice Panels

CADTH may convene panels of clinical experts to address the implementation issues noted by the drug programs and/or the expert review committee. These panels will only be established at the request of the drug programs that participate in CADTH's reimbursement review processes.

CADTH will establish a panel consisting of clinical specialists 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 specialists 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 drug being considered. In accordance with the current policies used by CADTH, the identities of the clinical experts who participate in the panels will remain confidential.

CADTH will apply its current conflict of interest policy and all panellists will be required to provide completed conflict of interest declarations.

The attendance at clinical panel meetings will be limited to the clinical specialists, key CADTH staff (i.e., review team members), and representatives from CAPCA, pCPA, and/or the drug programs. The manufacturer will not be able to attend the panel meetings at this time. Representatives from INESSS and/or INESSS' expert committee members may also attend the implementation panel meetings.

## 12.3 Stakeholder Engagement

### a) Drug Manufacturers

The manufacturer of the drug that is the subject of the implementation advice report will be notified by CADTH once the process has been initiated and will be included in the process as described in section 12.4.

### b) Patient and Clinician Group Engagement

The clinical panellists will be provided with copies of the input received from patient groups and clinician groups during the call for patient input and it will be incorporated into the reimbursement review process, along with the summary of input that was prepared by CADTH.

Similar to the process used in expert committee deliberations, a summary of the patient input will be provided at the outset of the deliberations. This will focus on the perspectives and issues of patients and/or their caregivers related to the condition for which the drug under review is indicated; the impact and unmet needs of current therapy; the treatment outcomes of greatest importance; and the expectations for the drug under review, as identified in the input submitted by patient groups. This information will provide important context for clinical panel's deliberations.

### c) Drug Program Engagement





To help ensure that the issues are clearly addressed by the implementation advice panel and to help expedite the overall process, CAPCA, pCPA, and the drug programs will have the opportunity to participate in panel meetings and comment on the draft implementation advice report.

### 12.4 Implementation Advice Report

Once the request for implementation advice has been received, CADTH notifies the sponsor of the drug under review and convenes a panel of clinical experts.

The sponsor will have 10 business days to provide written input to CADTH regarding the implementation issues. This input must be shared using the [template](#) provided by CADTH and must not contain any confidential information (all information included in the template will be considered disclosable by CADTH).

Following receipt of written input, CADTH will consult with clinical experts and draft an implementation advice report that addresses the issues raised by the public drug programs. The draft implementation advice report is provided to the sponsor, drug programs, CAPCA, and/or pCPA for review and comment.

The sponsor will have 5 business days to provide their comments. This input must be provided using a template provided by CADTH and must not contain any confidential information (all information included will be considered disclosable by CADTH).

CADTH will review and discuss the feedback from the sponsor and drug programs with the expert panel and the guidance report will be revised as required.

CADTH will prepare responses to the sponsor's comments, which will be provided to the sponsor at the same time as the final implementation advice report. The final report from this process will be posted on the CADTH website. There will be no confidential information included in the implementation advice report. Sponsors will not have the opportunity to request any redactions.

## 13. Provisional Funding Algorithm for Oncology Drugs

### 13.1 Purpose and Eligibility

The provisional funding algorithm process is used to provide advice when the drug programs have indicated that there is need to establish an appropriate place in therapy for the drug under review relative to alternative treatments that are currently reimbursed by the drug programs, including the impact on the appropriate sequencing of treatments for the purposes of reimbursement (e.g., should reimbursing the drug under review result in a shift or a displacement of other available treatments). This support is distinct from the CADTH Reimbursement Review process and is offered for the purposes of assisting jurisdictions in implementing recommendations from CADTH and/or making reimbursement policy decisions.

CADTH will initiate the development of a provisional funding algorithm in the following instances:

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

The creation of a new provisional funding algorithm or update of an existing provisional funding algorithm is typically initiated following the issuance of a new pERC recommendation when there are potential implications regarding the funding sequence of drugs within a therapeutic area. CADTH will only initiate work on a provisional funding algorithm at the request of PAG. Drug manufacturers are not currently able to request that CADTH initiate work on a provisional funding algorithm.

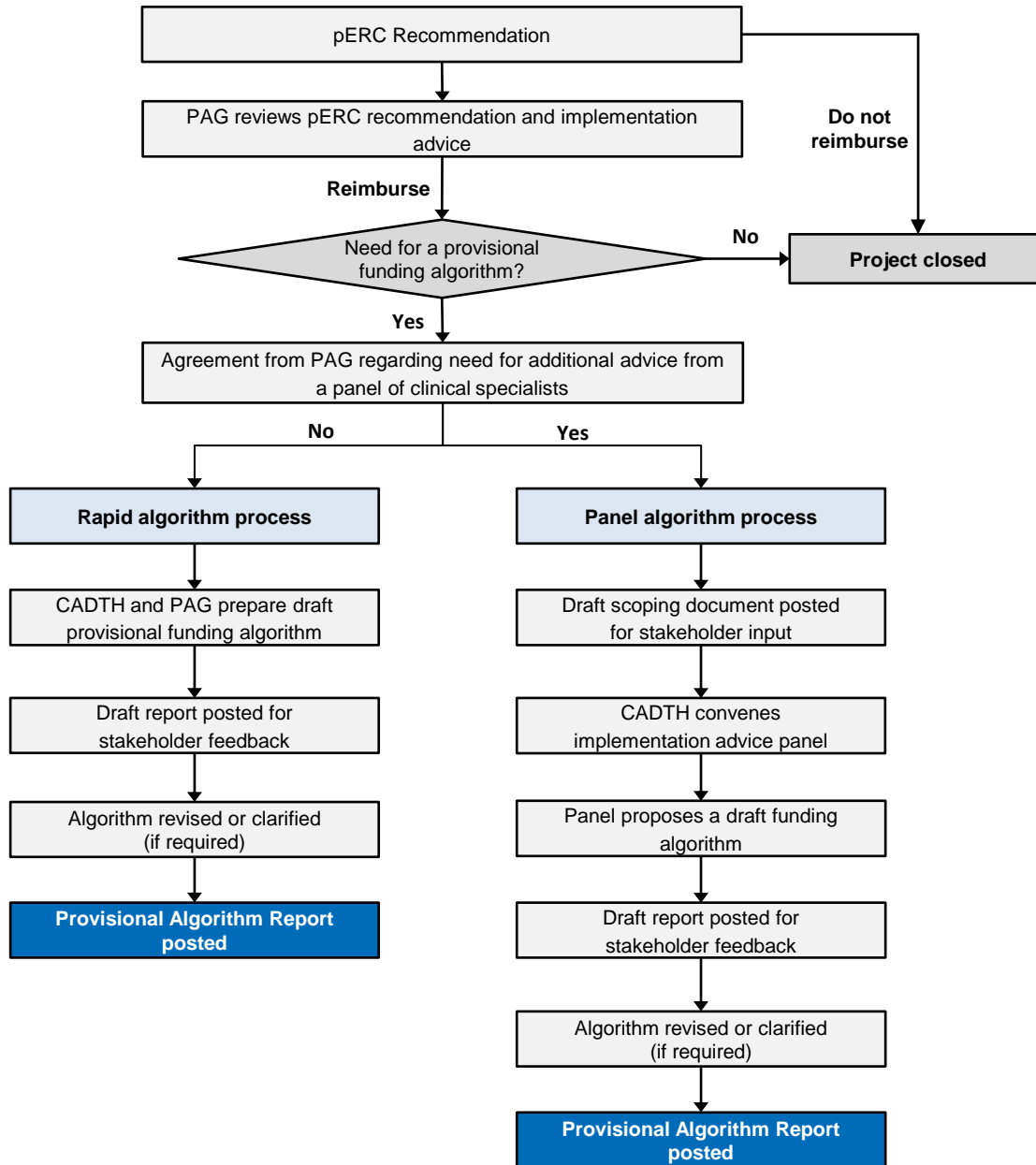
### 13.2 CADTH Algorithm Processes

CADTH aims to conduct its reviews in the most efficient manner and applies the following processes depending on the complexity of the algorithm:

- A **panel algorithm** is undertaken when the advice of clinical specialists is required to adapt an existing funding algorithm or establish a completely new provisional funding algorithm. Panel algorithms will typically be initiated when 1 or more drugs may be impacted by the implementation of a new drug (e.g., shifting existing drugs to different lines of therapy). Panel algorithms are typically completed within 3 months of receiving the request from PAG. Refer to section 13.4 for complete details.
- A **rapid algorithm** is undertaken when pERC recommendations can be directly incorporated into an algorithm without supplemental advice from clinical specialists. The rapid algorithm process will typically be initiated in situations where the new drug will not alter the current sequence of drugs within an existing funding algorithm (e.g., a follow-on drug within an existing line of therapy or a completely new line with no comparators). Rapid algorithms are typically completed within 2 months of receiving the request from PAG. Refer to section 13.5 for complete details.

**Figure 5: CADTH Provisional Funding Algorithm Processes**

Alt text: Figure shows a high-level summary of the CADTH provisional funding algorithm processes.



CAPCA = Canadian Association of Provincial Cancer Agencies; PAG = Provincial Advisory Group; pERC = CADTH pan-Canadian Oncology Drug Review Expert Review Committee.

### 13.3 Targeted Time Frames and Tracking

The key targeted time frames and the status of all reviews are posted on the CADTH website. Table 27 indicates the targeted time frames for key tasks within CADTH provisional funding algorithm processes. The actual timelines may vary depending on the scheduling of PAG meetings.

**Table 27: Targeted Timelines for the Provisional Funding Algorithm Processes**

Phase of review	Key milestones	Business days	
		Panel Algorithm	Rapid Algorithm
Project initiation	Request received	0	0
	Lead jurisdiction identified, review team assembled, notification of impacted drug manufacturers	4	4
Scoping phase	Draft scoping document	6	N/A
	Post-scoping document for stakeholder input	1	
	Stakeholder input period	10	
Draft algorithm report	Panel preparation and meeting	5	10
	Draft provisional algorithm report prepared	17	
	Post draft provisional funding algorithm report for stakeholder feedback	1	
Feedback phase	Stakeholder feedback period	5	5
Final report	Review and consideration of stakeholder feedback	7 <sup>a</sup>	7 <sup>a</sup>
	Finalize provisional funding algorithm report	9 <sup>b</sup>	9
	Final report copy-edited and formatted for posting	4	4
	Final report posted on CADTH website	1	1

N/A = Not Applicable.

<sup>a</sup> The actual timelines may depend on the scheduling of Provincial Advisory Group meetings.

<sup>b</sup> The time frame will be extended if there is the need for an additional panel meeting.

## 13.4 Panel Algorithms

### 13.4.1 Stakeholder Engagement

#### a) Industry Engagement

All manufacturers (i.e., DIN holders) whose products may be directly impacted by the provisional algorithm may provide input into the review being conducted by CADTH. For drug manufacturers other than the 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 post a scoping document with the following information:

- that CADTH will be developing a provisional algorithm for the indication of interest
- the drugs that may be impacted by CADTH's report.

Upon notification that the algorithm is being developed by CADTH, all manufacturers with products that fall within 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 shared using the template provided by CADTH and must not contain any confidential information (as all information included in the template will be considered disclosable by CADTH). Once CADTH has drafted the provisional algorithm report, the manufacturer(s) will be provided with an opportunity to review and provide comments (as described in section 13.4.3).

#### 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. Once CADTH has drafted the provisional algorithm report, the drug programs(s) will be provided with an opportunity to review and provide comments (as described in section 13.4.3).

The CAPCA Board of Directors offers important input and guidance in the development of provisional funding algorithms. Using information assembled by CADTH and CAPCA, the CAPCA Board of Directors assesses a number of factors when considering endorsement of a provisional funding algorithm:

- the ability for the provisional funding algorithm to address relevant implementation issues identified through the CADTH review process;
- alignment of the proposed funding algorithm with existing public payor algorithms;
- system sustainability considerations including affordability and potential budget impact.

#### c) Patient and Clinician Group Engagement

Upon notification that a provisional algorithm is being developed by CADTH, relevant patient and clinician groups will have 10 business days to provide written input to CADTH regarding their perspective on the provisional algorithm. This input must be provided using the CADTH template and must not contain any confidential information (as all information included in the template will be considered disclosable by CADTH). Once CADTH has drafted the provisional algorithm report, patient and clinician groups will be provided with an opportunity to review and provide comments (as described in section 13.4.3).

### 13.4.2 Implementation Panel and Deliberative Process

CADTH will convene clinical panels to advise on provisional algorithms. The panellists 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 panellists will be required to comply with CADTH's Conflict of Interest Policy.

Panellists 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 the reimbursement review process that triggered the need for the algorithm review, and the input from 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.

#### **13.4.3 Provisional Funding Algorithm Reports**

##### **a) Scoping Document and Call for Input**

CADTH will notify all stakeholders that an implementation advice panel is being convened to discuss the sequencing of treatments for a particular indication. CADTH will post a document detailing the scope of the implementation advice panel and will communicate that the call for stakeholder input is open. All stakeholders 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). No requests for extensions will be granted by CADTH. This input must be provided using the CADTH template and must not contain any confidential information (all information included in the template will be considered disclosable by CADTH).

##### **b) Draft Provisional Algorithm Report**

CADTH will post the draft provisional algorithm report for stakeholder feedback. The call for feedback will be open for 5 business days. No requests for extensions will be granted by CADTH. Comments must be provided using a template provided by CADTH and must not contain any confidential information (all information included will be considered disclosable by CADTH).

CADTH will review and discuss the stakeholder feedback with the chair of the implementation advice panel, who will determine if there is a need to reconvene the panel for additional meeting(s) to discuss and revise the algorithm report.

#### c) Final Provisional Algorithm Report

The final report from this process will be posted on the CADTH website. There will be no confidential information included in the implementation advice report; as such, manufacturers and other stakeholders will not have the opportunity to request any redactions.

## 13.5 Rapid Algorithms

### 13.5.1 Stakeholder Engagement

#### a) Industry Engagement

At the outset of the review, CADTH will attempt to notify all manufacturers (i.e., DIN holders) whose products may be directly impacted by the provisional funding algorithm that the review is being undertaken. For drug manufacturers other than the 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).

Once CADTH has drafted the provisional algorithm report, all manufacturers (i.e., DIN holders) whose products may be directly impacted by the provisional funding algorithm will be provided with an opportunity to review and provide comments (as described in section 13.4.3).

#### b) Drug Program Engagement

The participating drug programs will be engaged throughout all phases of the provisional funding 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. Once CADTH has drafted the provisional funding algorithm report, the drug programs(s) will be provided with an opportunity to review and provide comments (as described in section 13.4.3).

The CAPCA Board of Directors offers important input and guidance in the development of provisional funding algorithms. Using information assembled by CADTH and CAPCA, the CAPCA Board of Directors assesses a number of factors when considering the endorsement of a provisional funding algorithm:

- the ability for the provisional funding algorithm to address relevant implementation issues identified through the CADTH review process
- alignment of the proposed funding algorithm with existing public payor algorithms
- system sustainability considerations including affordability and potential budget impact.

### c) Patient and Clinician Group Engagement

CADTH will notify all stakeholders that a rapid algorithm is being prepared through publication of the project details on the CADTH website. To expedite the process, CADTH will not draft a scoping document or seek initial stakeholder input in the rapid algorithm process. Once CADTH has drafted the provisional algorithm report, patient and clinician groups will be provided with an opportunity to review and provide comments (as described in section 13.4.3).

### 13.5.2 Development of the Algorithm

CADTH, in consultation with PAG, will draft an algorithm using the following sources of information:

- prior pERC recommendations on all drugs that are to be considered in the algorithm
- prior CADTH implementation advice and provisional funding algorithms in the same therapeutic area
- drug reimbursement criteria implemented by jurisdictions at the pan-Canadian level following decisions made by consensus.

Evidence not previously reviewed by CADTH will not be considered in the development of rapid algorithms. CADTH will provide both a pictorial and descriptive representation of the algorithm in a brief report.

### 13.5.3 Provisional Funding Algorithm Reports

#### a) Draft Provisional Algorithm Report

CADTH will post the draft provisional algorithm report for stakeholder feedback. The call for feedback will be open for 5 business days. No requests for extensions will be granted by CADTH. Comments must be provided using a template provided by CADTH and must not contain any confidential information (all information included will be considered disclosable by CADTH).

CADTH will review and discuss the stakeholder feedback with PAG. PAG will determine if there is a need to revise the algorithm based on the feedback that was received.

#### b) Final Provisional Algorithm Report

The final report from the rapid algorithm process will be posted on the CADTH website. There will be no confidential information included in the report; as such, manufacturers and other stakeholders will not have the opportunity to request any redactions.



### 14. Other Implementation Support Activities

CADTH routinely gathers information from the drug programs regarding the implementation of recommendations. Any issues or challenges are brought forward for discussion with the drug programs, pCPA, and/or CAPCA. Implementation challenges can often be addressed directly by these organizations; however, in some situations, it may be necessary to obtain additional information and guidance from CADTH. This can include filing a request for advice or obtaining decision-making support from CADTH's other services (e.g., Rapid Response or Optimal Use).

### 15. Request for Procedural Review

Implementing a procedural review mechanism is an important cornerstone for ensuring an accountable and ethical review process that aligns with CADTH's foundational values for decision-making. The grounds for a procedural review relate only to whether or not CADTH failed to act in accordance with its procedures in conducting the reimbursement 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 a reconsideration). This procedure 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. Unsubstantiated allegations of general unfairness (for example, the alleged inability to understand a conclusion or the applicant simply disagrees with the views or conclusions in the final recommendation) will not be accepted as valid grounds for a procedural review. Please refer to Appendix 2 for detailed procedural review process requirements.

### 16. Document Management

CADTH's reimbursement review processes are complete when all relevant CADTH documents have been posted on the CADTH website (e.g., recommendation, CADTH review report[s], and patient group input). CADTH then undertakes the steps detailed in the *CADTH Reimbursement Review Confidentiality Guidelines* regarding the retrieval, disposal, and archiving of files associated with the review. This document management procedure is also followed for a withdrawn application.

## Appendix 1: Confidentiality Guidelines

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

Together with the *Procedures for CADTH Reimbursement Reviews*, the confidentiality guidelines provide clarity to CADTH and sponsors on how to appropriately protect and disclose information, allowing for a reimbursement review process that is transparent and accountable. CADTH complies with these confidentiality guidelines when handling confidential information related to the reimbursement review processes. By filing an application or by supplying other information to CADTH for a filed application, each sponsor consents to complying with the requirements of these confidentiality guidelines and establishes an agreement between CADTH and the sponsor on its application.

### A. Definition of Confidential Information

Sponsor-supplied information that will be treated by CADTH as confidential includes proprietary scientific, technical, or commercial information about a manufacturer's business or a manufacturer's product received through the exchange of information as part of CADTH's reimbursement review processes, but does not include information that:

- is or becomes available to the general public other than as a result of a breach of the procedures contained herein (note that information available to the general public includes but is not limited to published articles, drug prices, product monographs, clinical study information available from regulatory agency reports, other Health Technology Assessment agency reports and recommendations, and [www.clinicaltrials.gov](http://www.clinicaltrials.gov))
- a third party (who is not under any obligation as to confidentiality or non-disclosure) rightfully discloses to any authorized recipient (as described in these guidelines) without restriction as to its use or disclosure
- is provided to an authorized recipient (as described in these guidelines) without restriction as to its use, and the authorized recipient may disclose in accordance with its respective statutory requirements
- information that is identified as not redactable in Table 28 for applications received on or after January 2, 2024 or Table 30 for applications received prior to January 2, 2024.

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

For applications received on or after January 2, 2024, Table 28 provides sponsors with guidance regarding what information that has been included in an application will and will not be considered redactable by CADTH. Please note that the list provided in Table 28 is intended as general guidance and exceptions may be considered on a case-by-case basis (in favour or against the redaction of information included in the CADTH reported). Table 29 outlines minimum reporting requirements for situations where redaction may be permissible.

**Table 28: Guidance on Information That is and is Not Redactable (Applications Received on or after January 2, 2024)**

Item	Redactable	Rationale
<b>General Information</b>		
Changes to the indication during the review of a submission filed on a pre-NOC basis.	Not redacted	The indication and/or sponsor's requested reimbursement conditions will not be considered confidential by CADTH once this information has been posted on the CADTH website (e.g., at the time of issuing the call for stakeholder input). If the indication and/or sponsor's requested reimbursement conditions are revised during the review of a submission filed on a pre-NOC basis, the originally filed information will not be considered confidential by CADTH once it has been published on the CADTH website.
Changes to the dosing, dosage forms, or dosage strengths during the review of a submission filed on a pre-NOC basis.	Redactable	Changes relating to the recommended dosing, dosage forms, or dosage strengths (e.g., strengths filed for review on a pre-NOC basis, but not approved by Health Canada) may be considered redactable if the information is not publicly available.
<b>Clinical Data</b>		
Methods used to conduct a study or to analyze data from a study.	Not redacted	Methods information is required to understand how model inputs are derived.
Clinical data that are available in the public domain.	Not redacted	Information that is publicly available is not considered confidential information by CADTH.
Clinical data not yet in the public domain but either: <ul style="list-style-type: none"> <li>awaiting publication, including in a journal</li> <li>OR</li> <li>will be released into the public domain by regulatory authorities</li> </ul>	Not redacted	To avoid redaction of data that will subsequently be available and when publishing in committee papers will not jeopardise publication elsewhere. The International Committee of Medical Journal Editors (ICMJE) recommendations on overlapping publications state that it 'does not consider results or data contained in assessment reports published by health technology assessment agencies, medical regulators, medical device regulators, or other regulatory agencies to be duplicate publication'.

<p>Clinical data that has not been made publicly available and for which there is no plan for the data to become publicly available.</p>	<p>Redactable, except for minimum reporting requirements.</p>	<p>In recognition that there will be unpublished clinical data that will be confidential.</p> <p>However, to allow transparent reporting of decision making, CADTH has outlined minimum reporting requirements for data which is likely to be fundamental to committee decision making (see Table 29).</p> <p>Clinical data should be treated as clinical data without a publication plan if:</p> <ul style="list-style-type: none"> <li>• there is clinical data awaiting first public presentation at a congress that is scheduled to take place after documentation from CADTH would be released to the public, and</li> <li>• this data is not awaiting publication in a journal or within marketing authorisation documentation.</li> </ul>
<p>Data from real-world evidence studies that has not been made publicly available and for which there is no plan for the data to become publicly available.</p>	<p>Redactable (if collected by company then minimum summary information should be provided).</p> <p>The confidentiality requirements of third-party sources of data will be adhered to.</p>	<p>See the above rationale for clinical data that has not been made publicly available and for which there is no publication plan.</p>
<p>Company's indirect comparison that has not been made publicly available and for which there is no plan for the data to become publicly available</p>	<p>Redactable, except for minimum summary information.</p>	<p>Assessing the benefit of a technology compared with its comparators and the uncertainty around these comparisons is fundamental to committee decision making. CADTH has outlined the minimum reporting requirements for indirect comparisons outcomes to allow transparent reporting of committee decision making (see Table 29).</p>

Critical appraisal of clinical studies and indirect comparisons (for example, of the validity of methodology and assessment of bias and uncertainty).	Not redacted	Critical appraisal is not considered to be confidential information and will not be redacted. This applies to critical appraisals carried out by both the sponsor and CADTH.
Data derived from clinical opinion.	Not redacted	Clinical opinion may vary, and it is vital to have transparent discussion. This includes the outcome of expert elicitation. Clinical expert opinion is not considered to be confidential information and will not be redacted.
References	Not redacted	Referencing is required to understand where inputs and assumptions are derived and does not predicate inputs that are considered confidential.
<b>Pharmacoeconomic Evaluation</b>		
Description of methods used to conduct the economic evaluation.	Not redacted	Methods of economic evaluations are not considered confidential, as they are required to understand what was submitted.
Weighted distribution of comparator and/or subsequent treatments.	Not redacted	<p>Methods of economic evaluations are not considered confidential. The definition of the comparator is critical to understand the results of the economic model.</p> <ul style="list-style-type: none"> <li>• Where distributions/data are based on public sources of information or expert opinion, this information will not be redacted.</li> <li>• If the input(s) is based on clinical trial information that is not publicly available, then this information is redactable.</li> <li>• If the input(s) is based on alternate data source (e.g., claims data), AND no supporting reference is provided, the input(s) are not redactable. Evidence of the use of commercial in confidence information must be provided to CADTH (i.e., a detailed technical report outlining the data used and methods to derive the inputs) to be considered redactable.</li> </ul>
Clinical inputs that are in the public domain.	Not redacted	Information that is publicly available is not considered confidential information by CADTH.
Data from clinical studies that are not in the public domain.	Redactable	If the data are from clinical studies and the results are not in the public domain, then this information is redactable.



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Data that are not in the public domain but are derived from expert opinion or sponsor assumptions (e.g., the data are not from unpublished clinical studies).	Not redacted	If the input(s) is based on expert opinion or assumption, then it is not considered redactable. Any information that is listed as “assumption” or “data on file” will not be redacted unless a detailed technical report has been provided for this information to indicate the derivation methods of the input(s).
Submitted price for the drug under review.	Not redacted	CADTH does not accept confidential submitted prices for applications filed for review through its reimbursement review processes. The submitted price is disclosed in all applicable CADTH reports.
Prices for comparators and companion diagnostic testing (if applicable).	Not redacted	CADTH does not accept confidential submitted prices for applications filed for review through its reimbursement review processes. The prices of comparators and/or companion diagnostic testing are disclosed in all applicable CADTH reports.
Results in the sponsor’s economic evaluation (e.g., ICER, total or incremental LYs, total or incremental QALYs, total or incremental costs).	Not redacted	Results from the sponsor’s economic evaluation are not considered to be confidential and will not be redacted. There may be rare situations where reporting of results may result in the ability to back-calculate confidential information exactly (e.g., when deterministic results are used). The burden of proof is on the sponsor to demonstrate how this can be done (to be included with the request for redaction).
CADTH critical appraisal of the sponsor’s economic evaluation.	Not redacted	CADTH appraisal of the methods and data used in the sponsor’s pharmacoeconomic evaluation is not redacted.
CADTH reanalyses of the economic evaluation (e.g., ICER, total or incremental LYs, total or incremental QALYs, total or incremental costs).	Not redacted	Results of the economic model, including CADTH reanalyses, are not considered to be confidential and will not be redacted.
Model output (e.g., disaggregated health state, cost category results, health state distribution over time, etc.).	Not redacted	Results of the model, sponsor’s results and CADTH reanalyses are not redacted. There may be exception situations where reporting of results may result in the ability to back-calculate confidential information exactly (when deterministic results are used). The burden of proof is on the sponsor to demonstrate how this can be done (to be included with the request for redaction).
Assumptions which are not based on empirical data.	Not redacted	The expert committee’s discussion on validity of assumptions needs to be described transparently.
References	Not redacted	Referencing is required to understand where inputs and assumptions are derived and does not predicate inputs that are considered confidential.

<b>Budget Impact Analysis</b>		
Description of design of the budget impact analysis.	Not redacted	A description of the methods is required to understand the model.
Estimates for population size, market share, displacement of comparators, and resource assumptions that are based on published information.	Not redacted	Information that is publicly available is not considered confidential information by CADTH.
Estimates for population size, market share, displacement of comparators, and resource assumptions that are based on unpublished information from the following sources: <ul style="list-style-type: none"> <li>• Expert opinion</li> <li>• Assumption that is not supported by evidence (e.g., where no reference is provided, or stated as data on file with no reference provided).</li> </ul>	Not redacted	Methods of budget impact analyses are not considered confidential. They are required to understand what is being conducted and measured.
Estimates for population size, market share, displacement of comparators, and resource assumptions that are based on unpublished information from market research obtained from a third party that cannot be publicly disclosed due to licensing agreements. This is exclusive of expert opinion.	Redactable	CADTH considers information from these sources as confidential information and will redact when requested by the sponsor. However, to be considered redactable the sponsor must provide CADTH with evidence that the information is commercial in confidence information (e.g., a detailed technical report outlining the data used and methods used to derive the inputs)

Sponsor's estimated budget impact (yearly and 3-year total).	Not redacted	Results from the sponsor's budget impact analysis are not considered to be confidential and will not be redacted. There may be rare situations where reporting of results may result in the ability to back-calculate confidential information exactly (e.g., when deterministic results are used). The burden of proof is on the sponsor to demonstrate how this can be done (to be included with the request for redaction).
CADTH critical appraisal of the budget impact analysis.	Not redacted	CADTH critical appraisal of the methods and data used in the pharmacoeconomic submission is not redacted.
CADTH estimated budget impact (yearly and 3-year total).	Not redacted	CADTH reanalyses are not considered to be confidential and will not be redacted.
Data which is commercially sensitive or allows back-calculation of data which is commercially sensitive.	May be redactable	Please see guidance on how this may be applied in Table 29.
References	Not redacted	Referencing is required to understand where inputs and assumptions are derived and does not predicate inputs that are considered confidential.
<b>Time-Limited Recommendations</b>		
Evidence-generation requirements for conditional regulatory approvals (i.e., NOC/c) described within the Qualifying Notice from Health Canada.	Not redacted	This information is required to ensure that stakeholders, including patients, understand: <ul style="list-style-type: none"> <li>• the rationale for the time-limited recommendation</li> <li>• the type of evidence that will be generated to address the uncertainty the time frame for generating and submitted the evidence.</li> </ul>

The purpose of Table 29 is to outline the information which is fundamental to the expert committee decision making and the minimum reporting requirements that are needed to ensure the reimbursement review process is transparent for stakeholders.

- **Standard reporting requirements:** These refer to information that will not be redacted whenever possible.
- **Minimum reporting requirements:** These should be used when there is a demonstrated risk to the company of releasing data specified in the standard reporting column. When these minimum reporting requirements list a descriptive summary of the data, this should be presented in addition to the data which is highlighted as confidential by the sponsor.



**Table 29: Standard Reporting and Minimum Reporting Requirements**

Standard reporting requirements	Minimum reporting requirements
<p>Baseline and patient characteristics of trial populations that will be subject to disclosure by Health Canada.</p>	<p>This data for the whole trial population should be reported in full because it is expected to be published within marketing authorization documentation.</p>
<p>Baseline and patient characteristics of all subgroups that are relevant to the sponsor’s requested reimbursement criteria: This includes:</p> <ul style="list-style-type: none"> <li>• Data for the population covered by the marketing authorization, if the trial population is broader than that covered by the marketing authorization.</li> <li>• The subgroup for whom the sponsor is positioning the technology if this population is narrower than that covered by the full indication approved or under review by Health Canada.</li> </ul>	<p>For the subgroups, a description of any imbalances between treatment arms or differences between the subgroups and whole trial population should be provided.</p>
<p>Primary outcomes (including for that are relevant to the sponsor’s requested reimbursement criteria, if relevant) at the data cut included in the economic model.</p>	<p>Primary outcomes at the data cut which inform the regulatory submission should be reported because they are typically published within marketing authorization documentation (e.g., Product Monograph; Summary Basis for Decision; Regulatory Decision Summary).</p>
<p>Relative treatment effect and measure of precision such as 95% confidence interval.</p>	<p>If data from a later data cut than what informed the marketing authorization are used in the economic model and is marked as confidential, then the unredacted data cut informing the marketing authorization should also be presented alongside the later data cut.</p> <p>Commentary should be provided on similarities or differences between the point estimates and confidence intervals from publicly available versus confidential data cuts.</p> <p>For subgroup data that will not be reported within marketing authorization documentation, an accompanying description of the direction of treatment effect and how the point estimate and measure of precision compare with the data for the whole population should be provided alongside the confidential information.</p>

<p>Kaplan–Meier data (including extrapolations), if relevant.</p>	<p>If Kaplan–Meier data from a later data cut than what informed the marketing authorization are used in the model and is marked as confidential, then the unredacted data cut informing the marketing authorization should also be presented alongside the later data cut.</p> <p>For overall survival extrapolation, the proportions of people alive at a range of time intervals over the time horizon should be provided to enable discussion of plausibility of this modelled outcome.</p>
<p>Secondary outcomes at the data cut that inform the modelling.</p>	<p>Follow the principles for the primary outcomes.</p>
<p>Adverse events including death.</p>	<p>The equivalent data to that reported in marketing authorization documentation is expected.</p>
<p>Indirect treatment comparison:</p> <ul style="list-style-type: none"> <li>• an overview of the methodological approach, including any matching of data or adjustments</li> <li>• number of patients included in studies</li> <li>• patient characteristics from included studies</li> <li>• commentary on potential heterogeneity or sources of bias</li> <li>• outcomes (for example, comparative efficacy) with measure of precision such as 95% credible interval, if relevant.</li> </ul>	<p>All methodology and critical appraisal should be reported.</p> <p>If there is a demonstrated reason why numerical outcomes are confidential then an accompanying statement of direction of treatment effect and commentary on the measure of precision should be provided. For example, the width of the credible intervals and if the credible intervals cross parity.</p> <p>For adjusted outcomes, an accompanying description of how these outcomes differ from unadjusted outcomes should be provided.</p>
<p>Utility values (by health state, intervention utility increments or decrements, and disutility for adverse events) which are used in the model.</p>	<p>Quality of life data collected in the trial may be redactable.</p>

**Table 30: Guidance on Information That is Redactable and Not Redactable (Applications received Prior to January 2, 2024)**

Item	Redactable	Rationale
<b>General Information</b>		
Changes to the indication during the review of a submission filed on a pre-NOC basis.	Not redacted	The indication and/or sponsor’s requested reimbursement conditions will not be considered confidential by CADTH once this information has been posted on the CADTH website (e.g., at the time of issuing the call for stakeholder input). If the indication and/or sponsor’s requested reimbursement conditions are revised during the review of a submission filed on a pre-NOC basis, the originally filed information will not be considered confidential by CADTH once it has been published on the CADTH website.
Changes to the dosing, dosage forms, or dosage strengths during the review of a submission filed on a pre-NOC basis.	Redactable	Changes relating to the recommended dosing, dosage forms, or dosage strengths (e.g., strengths filed for review on a pre-NOC basis, but not approved by Health Canada) may be considered redactable if the information is not publicly available.
<b>Clinical Report</b>		
Clinical data that are available in the public domain.	Not redacted	Information that is publicly available is not considered confidential information by CADTH.
Clinical data that have not been made publicly available	Redactable	If the data are from clinical studies and the results are not in the public domain, then this information is redactable.
Sponsor’s indirect comparison that has not been made publicly available	Redactable	If the results are not in the public domain, then this information is redactable.
CADTH critical appraisal of clinical studies and indirect comparisons	Not redacted	CADTH critical appraisal is not considered to be confidential information and will not be redacted.
Clinical expert opinion	Not redacted	Clinical expert opinion is not considered to be confidential information and will not be redacted.
References	Not redacted	Referencing is required to understand where inputs and assumptions are derived and does not predicate inputs that are considered confidential.
<b>Pharmacoeconomic Evaluation</b>		
Description of methods used to conduct the economic evaluation	Not redacted	Methods of economic evaluations are not considered confidential, as they are required to understand what was submitted.

Weighted distribution of comparator and/or subsequent treatments	Not redacted	<p>Methods of economic evaluations are not considered confidential. The definition of the comparator is critical to understand the results of the economic model.</p> <ul style="list-style-type: none"> <li>• Where distributions/data are based on public sources of information or expert opinion, this information will not be redacted.</li> <li>• If the input(s) is based on clinical trial information that is not publicly available, then this information is redactable.</li> <li>• If the input(s) is based on alternate data source (e.g., claims data), AND no supporting reference is provided, the input(s) are not redactable. Evidence of the use of commercial in confidence information must be provided to CADTH (i.e., a detailed technical report outlining the data used and methods to derive the inputs) to be considered redactable.</li> </ul>
Clinical inputs that are in the public domain	Not redacted	Information that is publicly available is not considered confidential information by CADTH.
Data from clinical studies that are not in the public domain	Redactable	If the data are from clinical studies and the results are not in the public domain, then this information is redactable.
Data that are not in the public domain, but are derived from expert opinion or sponsor assumptions (e.g., the data are not from unpublished clinical studies)	Not redacted	If the input(s) is based on expert opinion or assumption, then it is not considered redactable. Any information that is listed as “assumption” or “data on file” will not be redacted unless a detailed technical report has been provided for this information to indicate the derivation methods of the input(s).
Submitted price for the drug under review	Not redacted	CADTH does not accept confidential submitted prices for applications filed for review through its reimbursement review processes. The submitted price is disclosed in all applicable CADTH reports.
Prices for comparators and companion diagnostic testing (if applicable)	Not redacted	CADTH does not accept confidential submitted prices for applications filed for review through its reimbursement review processes. The prices of comparators and/or companion diagnostic testing are disclosed in all applicable CADTH reports.
Results in the sponsor’s economic evaluation (e.g., ICER, total or incremental LYs, total or incremental QALYs, total or incremental costs)	Not redacted	Results from the sponsor’s economic evaluation are not considered to be confidential and will not be redacted. There may be rare situations where reporting of results may result in the ability to back-calculate confidential information exactly (e.g., when deterministic results are used). The burden of proof is on the sponsor to demonstrate how this can be done (to be included with the request for redaction).
CADTH critical appraisal of the sponsor’s economic evaluation	Not redacted	CADTH appraisal of the methods and data used in the sponsor’s pharmacoeconomic evaluation is not redacted.

CADTH reanalyses of the economic evaluation (e.g., ICER, total or incremental LYs, total or incremental QALYs, total or incremental costs)	Not redacted	Results of the economic model, including CADTH reanalyses, are not considered to be confidential and will not be redacted.
Model output (e.g., disaggregated health state, cost category results, health state distribution over time)	Not redacted	Results of the model, sponsor's results and CADTH reanalyses are not redacted. There may be exception situations where reporting of results may result in the ability to back-calculate confidential information exactly (when deterministic results are used). The burden of proof is on the sponsor to demonstrate how this can be done (to be included with the request for redaction).
References	Not redacted	Referencing is required to understand where inputs and assumptions are derived and does not predicate inputs that are considered confidential.
<b>Budget Impact Analysis</b>		
Description of design of the budget impact analysis	Not redacted	A description of the methods is required to understand the model.
Estimates for population size, market share, displacement of comparators, and resource assumptions that are based on published information	Not redacted	Information that is publicly available is not considered confidential information by CADTH.
Estimates for population size, market share, displacement of comparators, and resource assumptions that are based on unpublished information from the following sources: <ul style="list-style-type: none"> <li>Expert opinion</li> <li>Assumption that is not supported by evidence (e.g., where no reference is provided, or stated as data on file with no reference provided)</li> </ul>	Not redacted	Methods of budget impact analyses are not considered confidential. They are required to understand what is being conducted and measured.

Estimates for population size, market share, displacement of comparators, and resource assumptions that are based on unpublished information from market research obtained from a third party that cannot be publicly disclosed due to licensing agreements. This is exclusive of expert opinion.	Redactable	CADTH considers information from these sources as confidential information and will redact when requested by the sponsor. However, to be considered redactable the sponsor must provide CADTH with evidence that the information is commercial in confidence information (e.g., a detailed technical report outlining the data used and methods used to derive the inputs)
Sponsor's estimated budget impact (yearly and 3-year total)	Not redacted	Results from the sponsor's budget impact analysis are not considered to be confidential and will not be redacted. There may be rare situations where reporting of results may result in the ability to back-calculate confidential information exactly (e.g., when deterministic results are used). The burden of proof is on the sponsor to demonstrate how this can be done (to be included with the request for redaction).
CADTH critical appraisal of the budget impact analysis	Not redacted	CADTH critical appraisal of the methods and data used in the pharmacoeconomic submission is not redacted.
CADTH estimated budget impact (yearly and 3-year total)	Not redacted	CADTH reanalyses are not considered to be confidential and will not be redacted.
References	Not redacted	Referencing is required to understand where inputs and assumptions are derived and does not predicate inputs that are considered confidential.

## 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 reimbursement review processes that has been designated confidential.

CADTH will not disclose confidential information in and related to an application 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 reimbursement review processes.

### 2. Responsibilities of Sponsors

Information identified as confidential information within an application 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) for its confidentiality 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 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 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 does not accept confidential submitted prices for applications filed for review through the reimbursement review processes. The submitted price is disclosed in all applicable CADTH reports, as well as the recommendation documents posted on the CADTH website. The outputs of economic models (e.g., incremental cost-effectiveness ratios) are not considered confidential and will not be redacted. Please refer to Table 28 and Table 29 which provides sponsors with guidance regarding what information that has been



included in an application will and will not be considered redactable by CADTH (or Table 30 for applications received prior to January 2, 2024).

CADTH staff members are required, as a condition of employment, to comply with CADTH's confidentiality requirements, code of conduct, and conflict of interest policy. All 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 authorized recipients include, but are not limited to:

- advance notification and pre-submission meeting materials provided by the sponsor
- the sponsor's submission, resubmission, or reassessment information
- information provided by a sponsor for a drug plan submission or a request for advice
- redacted and unredacted CADTH review report(s)
- the sponsor's comments about CADTH's review report(s)
- CADTH's responses to the sponsor's comments about draft review report(s)
- the redacted and unredacted draft recommendation
- the redacted and unredacted final recommendation
- correspondence between CADTH and the sponsor regarding the drug under review
- committee briefing materials.

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)
- the draft recommendation (until posted on the CADTH website)
- the final recommendation (until posted on the CADTH website).

The documents that CADTH may post on its website include:

- a tracking document indicating the status of the review, including for 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 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.
- When disagreement is 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 the request to identify confidential information for redaction by the deadlines specified by CADTH, CADTH may proceed with posting the review report(s), draft recommendation, and/or final recommendation in accordance with the *Procedures for CADTH 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 undertake 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 will be destroyed.

## Appendix 2: Procedural Review

### A. Purpose

The purpose of this section is to define the steps CADTH will take to determine whether the established process outlined in the Procedures for CADTH Reimbursement Reviews was followed in the development of the final recommendation issued by a CADTH expert committee for a pharmaceutical review. This section provides guidance for those who wish to make a request 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 a request for a procedural review; refer to paragraph C1 for further information on eligibility requirements.

If a request for procedural review is filed and accepted, CADTH will publish a notice on its website indicating a procedural review is underway and notify the drug programs and the pCPA.

### 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). Such examples may include omitting an eligible stakeholder input, deviating from the published steps without providing notice, failing to manage expert committee conflict of interest declaration in accordance with CADTH's conflict of interest policy, or the expert committee exceeds the scope of its mandate.

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). This procedure 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. Unsubstantiated allegations of general unfairness, for example the alleged inability to understand a conclusion or the applicant simply disagrees with the views or conclusions in the final recommendation, will not be accepted as a valid ground for a procedural review.

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. For example, it would not be unfair if the expert committee considered the relevant dataset 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 filed application dossier, 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.

If the issues identified are not resolved at the case conference stage, the adjudication of a procedural review request will be conducted by a procedural review panel (“panel”) that will comprise individuals independent of the program directly responsible for the development of the final recommendation; refer to paragraph C6 for the composition of the panel. The panel will not re-adjudicate matters on which it has already provided a ruling. For clarity, matters that have been adjudicated by the panel are identified in the [procedural review request form](#).

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. Parties are strongly encouraged to discuss their concerns about perceived deviations from the procedure with the CADTH Pharmaceutical Reviews Directorate prior to filing a request for a procedural review by contacting CADTH at [requests@cadth.ca](mailto:requests@cadth.ca).

## C. Procedure

### 1. Eligible Parties – Who Can File?

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 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
- Formulary Working Group or Provincial Advisory Group members that engaged in the drug review reimbursement process.

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 1 request per final recommendation review at issue within the 20-business day period. In cases where a request may be made by more than 1 eligible party and they are accepted for the same final recommendation review at issue, CADTH will conduct the requests jointly for the purpose of the procedural review proceeding.

### 2. Requests for Formal Procedural Reviews – How to File?

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).



Formal request for a procedural review must be made in writing using the designated [procedural review request form](#) and must be received by CADTH within 20 business days of the final recommendation in question being posted on the CADTH website.

The completed [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 must be submitted to [requests@cadth.ca](mailto:requests@cadth.ca).

### **3. Receipt of Request(s) for Procedural Reviews**

Upon receipt of the CADTH Procedural Review Request form, CADTH will acknowledge receipt of the request.

### **4. Screening the Procedural Review Request Form**

Upon receipt of the prescribed request form, CADTH will screen and assess the request for the following requirements:

- applicant eligibility (i.e., the applicant is an eligible party as described in paragraph C1),
- completeness of the form and supporting document(s) is provided within the prescribed 20 business days, and
- the ground for a procedural review is met in accordance with the definition as set out in paragraph B.

If these conditions are met, CADTH will notify the applicant 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 participating drug programs if the procedural review has been accepted.

### **5. Case Conference With CADTH**

If a request for procedural review is accepted, the applicant(s) will be given an opportunity to conference with CADTH. The purpose of the conference will be to narrow down or resolve the issue(s) in the procedural review request, including identifying those on which the panel has previously ruled, and identifying the steps required to rectify the situation. If the parties do not settle the issue and come to a mutual agreement within 5 business days, CADTH will convene a panel to review the remaining issue(s) in dispute and the procedural review process steps and timelines will apply.

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 7 business days from the date that the request is accepted.

The applicant(s) may bring up to 4 representatives knowledgeable about the issue(s) to the meeting. Legal representation is not permitted at this meeting.

## **6. Procedural Review Panel and Proceeding**

The mandate and responsibilities of the panel are set out in a CADTH Charter. The panel will have responsibility for adjudicating procedural reviews that are not resolved at case conference, and will only address such issues as remain unresolved between the parties. The panel will not re-adjudicate matters on which it has already provided a ruling, as identified in the procedural review request form.

A panel will comprise the following members selected by CADTH:

- Past expert committee member
- Patient member
- A representative independent from CADTH who is knowledgeable of the Canadian drug approval process

The panel will aim to invite the applicant(s) to make a brief presentation within 30 business days of the conference date deadline, if an agreement cannot be reached during the conference period, 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 remain unresolved between the parties and to respond to questions from the panel. Where there are multiple eligible applicants, the maximum allowable time will not exceed 120 minutes and will be divided equally among the applicants in the joint proceeding meeting. Each requesting organization may bring up to 4 representatives knowledgeable about the issue at hand to the meeting. No legal representation is permitted at the meeting.

The meeting will be conducted via web/teleconference and will not be open to the public. The meeting will 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.

## 7. Making Decisions on Procedural Reviews and Targeted Timelines

The panel has sole and absolute discretion for determining whether the established process was or was not 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 1 procedural review per final recommendation will be undertaken (i.e., no additional procedural review requests may be filed against the same recommendation at issue).

## 8. Outcomes of Decision on Procedural Reviews

The panel may issue the following decision:

- No change to the existing specific review at issue and the CADTH final recommendation will be upheld; or
- Steps in the review process for the specific review at issue must be revisited and/or the review 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 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.

No further procedural review request will be permitted against the final recommendation at issue.

## 9. Communicating Decisions on Procedural Reviews and Posting on CADTH Website

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.

## Appendix 3: List of Templates

These templates are to be used whenever applicable (also available on CADTH website).

### Templates for Pre-submission Phase

- [CADTH pharmaceutical submission SharePoint access request form](#)
- [Submission eligibility form](#)
- [Resubmission eligibility form](#)
- [Pre-submission meeting request form](#)
- [Pre-submission meeting briefing paper template](#)
- [Advance notification form](#)
- [Proposed place in therapy template](#)
- [Tailored review application form](#)
- [Request for deviation from pharmacoeconomic requirements form](#)

### Templates for Requirements

- [Application overview template](#)
- [Declaration letter template](#)
- [Executive summary template](#)
- [Table of studies template](#)
- [Reimbursement status of comparators template](#)
- [Regulatory and HTA status template](#)
- [Patients accessing new drugs template](#)
- [Letter for sending NOC to CADTH template](#)
- [Checklist for economic requirements](#)
- [Implementation plan for a cell or gene therapy](#)
- [Sponsor summary of clinical evidence template](#)
- [Tailored review submission template](#)

### Templates for Stakeholder Input

- [Patient group input template](#)
- [Clinician group input template](#)
- [Drug program input template](#)
- [Industry input template \(non-sponsored reimbursement reviews\)](#)
- [Sponsor comments on draft reports template](#)
- [Stakeholder feedback on draft recommendation](#)
- [Reconsideration request template](#)
- [Identification of confidential information template](#)
- [Procedural review request template](#)
- [Stakeholder input on scope of a provisional funding algorithm](#)
- [Stakeholder feedback on a draft provisional funding algorithm](#)
- [Stakeholder input on implementation advice request](#)
- [Stakeholder feedback on draft implementation advice](#)



## Appendix 4: Suggested Reporting Format for Economics

**Table 31: Disaggregated Clinical Outcomes and Costs for a Cost-Utility Analysis**

Parameter	Drug under review	Comparator #1	Comparator #2 (add as required)
<b>Discounted life-years</b>			
Total LYs			
By health state			
Health state 1			
Health state 2			
<b>Discounted QALYs</b>			
Total QALYs			
By health state			
Health state 1			
Health state 2			
Incremental QALYs generated within trial period			
Incremental QALYs generated after trial period			
<b>Discounted costs</b>			
Total costs			
Drug			
Administration			
Other resource costs			
Health state or event			
Add others (as required)			

QALY = quality-adjusted life-years; LY = life-years.

**Table 32: Presentation of Sequential Incremental Cost-Utility Ratio for a Cost-Utility Analysis**

Treatment	Cost	QALYs	Incremental cost per QALY gained	
			Versus reference	Sequential ICUR
Reference (Intervention A)				
Intervention B				
Intervention C				

ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-years.

**Table 33: Disaggregated Costs for a Cost-Minimization Analysis**

Parameter	Drug under review	Comparator #1	Comparator #2 (add as required)
<b>Discounted costs</b>			
Total costs			
Drug			
Administration			
Other resource costs			
Health state or event			
Add others (as required)			



## Appendix 5: Checklists for Preparing Applications

Sponsors may use the checklists used by CADTH, as provided in this appendix, to help ensure that all required documents have been included in their application to CADTH.

1. Clinical and Administrative Requirements
  - A. Submission for a standard review or complex review
  - B. Submission for a tailored review
  - C. Resubmission
  - D. Reassessment
2. Pharmacoeconomic requirements
3. Budget impact requirements

## 1A. Clinical and Administrative Requirements: Submission for a Standard or Complex Review

Requirement	Specific items and criteria	Included
<b>General information</b>		
<b>Application overview</b>	<ul style="list-style-type: none"> <li>Completed application overview template</li> </ul>	<input type="checkbox"/>
<b>Signed cover letter</b>	<ul style="list-style-type: none"> <li>Clear description of application being filed</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>The indication(s) to be reviewed by CADTH</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Requested reimbursement conditions, if applicable</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Names and contact information for primary and backup contacts</li> </ul>	<input type="checkbox"/>
<b>Executive summary</b>	<ul style="list-style-type: none"> <li>Completed executive summary template for a submission</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Maximum 5 pages for standard review or 6 pages for complex review (excluding references)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Document is referenced</li> </ul>	<input type="checkbox"/>
<b>Product monograph</b>	<p><b>Submission filed on a pre-NOC basis:</b></p> <ul style="list-style-type: none"> <li>At the time of filing: A copy of the most recent draft product monograph</li> <li>After NOC or NOC/c is issued:               <ul style="list-style-type: none"> <li>Draft product monograph with tracked changes up to time of Health Canada approval</li> <li>Clean and dated version of Health Canada–approved product monograph</li> </ul> </li> </ul>	<input type="checkbox"/>
	<p><b>Submission filed on a post-NOC basis:</b></p> <ul style="list-style-type: none"> <li>A copy of the most current version of the Health Canada–approved product monograph</li> </ul>	<input type="checkbox"/>
	<p><b>Declaration letter</b></p> <ul style="list-style-type: none"> <li>Completed declaration letter template</li> </ul>	<input type="checkbox"/>
<b>Regulatory and HTA Status</b>	<ul style="list-style-type: none"> <li>At the time of filing: a completed template summarizing the status at selected regulatory and Health Technology Assessment agencies as a Microsoft Word document</li> <li>At the time of filing comments on the draft reports: updated copy of the template as a Microsoft Word document</li> </ul>	<input type="checkbox"/>
<b>Request for deviation</b>	<ul style="list-style-type: none"> <li>Request for deviation response letter or statement that a deviation was not requested (applications received on or after November 1, 2023)</li> </ul>	<input type="checkbox"/>
<b>Sponsor Clinical Evidence Template</b>		
<b>Submission template</b>	<ul style="list-style-type: none"> <li>Complete sponsor summary of clinical evidence template</li> </ul>	<input type="checkbox"/>
<b>RIS file with references</b>	<ul style="list-style-type: none"> <li>RIS file with the references that have been cited in the sponsor summary of clinical evidence template</li> </ul>	<input type="checkbox"/>
<b>Health Canada documentation</b>		

Requirement	Specific items and criteria	Included
<b>Notice of Compliance</b>	<b>Submissions filed on a pre-NOC basis:</b> <ul style="list-style-type: none"> <li>At the time of filing: A placeholder document indicating the anticipated NOC date for the indication(s) to be reviewed by CADTH</li> <li>After NOC or NOC/c is issued: <ul style="list-style-type: none"> <li>Copy of NOC or NOC/c granted for the indication(s) under review</li> <li>Letter of Undertaking (only if NOC/c granted)</li> </ul> </li> </ul>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
	<b>Submission filed on a post-NOC basis:</b> <ul style="list-style-type: none"> <li>Copy of NOC or NOC/c granted for the indication(s) under review</li> <li>Letter of Undertaking (only if NOC/c granted)</li> </ul>	<input type="checkbox"/> <input type="checkbox"/>
<b>Clarimails/Clarifaxes</b>	<b>Submissions filed on a pre-NOC basis:</b> <ul style="list-style-type: none"> <li>At time of filing: Summary table of clinical Clarimails/Clarifaxes up to time of filing</li> <li>Ongoing basis until issuance of NOC or NOC/c: Revised Clarimail/Clarifax summary table(s)</li> </ul>	<input type="checkbox"/> <input type="checkbox"/>
	<b>Submission filed on a post-NOC basis:</b> <ul style="list-style-type: none"> <li>Summary table of any clinical Clarimails/Clarifaxes up to issuance of NOC or NOC/c</li> </ul>	<input type="checkbox"/>
<b>Efficacy, effectiveness, and safety Information</b>		
<b>Common technical document</b>	• Section 2.5	<input type="checkbox"/>
	• Section 2.7.1	<input type="checkbox"/>
	• Section 2.7.3	<input type="checkbox"/>
	• Section 2.7.4	<input type="checkbox"/>
	• Section 5.2	<input type="checkbox"/>
	• Or a statement indicating which section(s) were not required by Health Canada	<input type="checkbox"/>
<b>Clinical studies and errata</b>	• Reference list of key clinical studies (published and unpublished) and any errata	<input type="checkbox"/>
	• Copies of studies addressing key clinical issues	<input type="checkbox"/>
	• Copies of any errata (or a document stating that none found)	<input type="checkbox"/>
<b>Clinical study reports</b>	• Clinical study reports for pivotal studies and other studies that address key clinical issues	<input type="checkbox"/>
<b>Table of studies</b>	• Completed table of studies template (Microsoft Word or PDF document)	<input type="checkbox"/>
<b>Editorials</b>	• Reference list of editorial articles (or document stating none found)	<input type="checkbox"/>
	• Copies of editorial articles	<input type="checkbox"/>
<b>New data</b>	• Reference list of new data (or statement that none are available)	<input type="checkbox"/>
	• Copies of new data available	<input type="checkbox"/>
<b>Validity of outcome measures</b>	• Reference list (or statement that none are available)	<input type="checkbox"/>
	• Copies of validity of outcome measure references available	<input type="checkbox"/>
<b>Indirect comparison</b>	• Copies of any indirect comparisons used in pharmacoeconomic evaluation	<input type="checkbox"/>

Requirement	Specific items and criteria	Included
	<ul style="list-style-type: none"> <li>• Technical report</li> </ul>	<input type="checkbox"/>
<b>Epidemiologic information</b>		
<b>Disease prevalence and incidence</b>	<ul style="list-style-type: none"> <li>• Disease prevalence and incidence with specified breakdown (if available)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Document is referenced</li> </ul>	<input type="checkbox"/>
<b>Number of patients accessing a new drug</b>	<ul style="list-style-type: none"> <li>• Number of patients accessing the new drug up to within 20 business days of filing the submission (Note: this requirement is only for a new drug submission or a new combination product submission if one of the components is a new drug.)</li> <li>• Use the number of patients accessing new drug template</li> </ul>	<input type="checkbox"/>
<b>Reimbursement status of comparators</b>		
<b>Reimbursement status of comparators</b>	<ul style="list-style-type: none"> <li>• A completed template summarizing the reimbursement status of all appropriate comparators as a Microsoft Word document</li> </ul>	<input type="checkbox"/>
<b>Pricing and distribution information</b>		
<b>Price and distribution method</b>	<ul style="list-style-type: none"> <li>• Submitted unit pricing to four decimal places</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Method of distribution</li> </ul>	<input type="checkbox"/>
<b>Implementation plan</b>	<ul style="list-style-type: none"> <li>• Completed implementation plan template (only for cell and gene therapies)</li> </ul>	<input type="checkbox"/>
<b>Provisional algorithm for oncology drugs</b>		
<b>Provisional algorithm (only for oncology drugs)</b>	<ul style="list-style-type: none"> <li>• Place in therapy template</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• A reference list (or statement that none are available)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Copies of studies that address sequencing of therapies</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Copy of the search strategy for sequencing of therapies</li> </ul>	<input type="checkbox"/>
<b>Companion diagnostic (if applicable)</b>		
<b>Companion diagnostics</b>	<ul style="list-style-type: none"> <li>• Reference list</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Copies of articles that highlight the clinical utility of the companion diagnostic(s)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Disclosable price for the companion diagnostic(s)</li> </ul>	<input type="checkbox"/>
<b>Additional letter for submissions filed on Pre-NOC basis</b>		
<b>Letter for sending NOC or NOC/c to CADTH</b>	<p><b>After NOC or NOC/c is issued:</b> A signed letter indicating whether any wording changes to the Health Canada–approved final product monograph result in revisions to the clinical or pharmacoeconomic information filed on a pre-NOC basis (used the provided letter template)</p>	<input type="checkbox"/>

## 1B. Clinical and Administrative Requirements: Submission for a Tailored Review

Requirement	Specific items and criteria	Included
<b>General information</b>		
<b>Application overview</b>	<ul style="list-style-type: none"> <li>• Completed application overview template</li> </ul>	<input type="checkbox"/>
<b>Signed cover letter</b>	<ul style="list-style-type: none"> <li>• Clear description of application being filed</li> </ul>	<input type="checkbox"/>

Requirement	Specific items and criteria	Included
	<ul style="list-style-type: none"> <li>The indication(s) to be reviewed by CADTH</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Requested reimbursement conditions, if applicable</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Names and contact information for primary and backup contacts</li> </ul>	<input type="checkbox"/>
<b>Executive summary</b>	<ul style="list-style-type: none"> <li>Completed executive summary template for a submission</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Maximum 5 pages (excluding references)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Document is referenced</li> </ul>	<input type="checkbox"/>
<b>Product monograph</b>	<p><b>Submission filed on a pre-NOC basis:</b></p> <ul style="list-style-type: none"> <li>At the time of filing: A copy of the most recent draft product monograph</li> <li>After NOC or NOC/c is issued: <ul style="list-style-type: none"> <li>Draft product monograph with tracked changes up to Health Canada approval</li> <li>Clean and dated version of Health Canada–approved product monograph</li> </ul> </li> </ul>	<input type="checkbox"/>
	<p><b>Submission filed on a post-NOC basis:</b></p> <ul style="list-style-type: none"> <li>A copy of the most current version of the Health Canada–approved product monograph</li> </ul>	<input type="checkbox"/>
<b>Declaration letter</b>	<ul style="list-style-type: none"> <li>Completed declaration letter template</li> </ul>	<input type="checkbox"/>
<b>Regulatory and HTA Status</b>	<ul style="list-style-type: none"> <li>At the time of filing: a completed template summarizing the status at selected regulatory and Health Technology Assessment agencies as a Microsoft Word document</li> <li>At the time of filing comments on the draft reports: updated copy of the template as a Microsoft Word document</li> </ul>	<input type="checkbox"/>
<b>Sponsor Clinical and Economic Summary Template</b>		
<b>Tailored review template</b>	<ul style="list-style-type: none"> <li>Completed CADTH tailored review template</li> </ul>	<input type="checkbox"/>
<b>Health Canada documentation</b>		
<b>NOC</b>	<p><b>Submissions filed on a pre-NOC basis:</b></p> <ul style="list-style-type: none"> <li>At the time of filing: A placeholder document indicating the anticipated NOC date for the indication(s) to be reviewed by CADTH</li> <li>After NOC or NOC/c is issued: <ul style="list-style-type: none"> <li>Copy of NOC or NOC/c granted for the indication(s) under review</li> <li>Letter of Undertaking (only if NOC/c granted)</li> </ul> </li> </ul>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
	<p><b>Submission filed on a post-NOC basis:</b></p> <ul style="list-style-type: none"> <li>Copy of NOC or NOC/c granted for the indication(s) under review</li> <li>Letter of Undertaking (only if NOC/c granted)</li> </ul>	<input type="checkbox"/> <input type="checkbox"/>
<b>Clarimails and Clarifaxes</b>	<p><b>Submissions filed on a pre-NOC basis:</b></p> <ul style="list-style-type: none"> <li>At time of filing: Summary table of clinical Clarimails/Clarifaxes up to time of filing</li> <li>Ongoing basis until issuance of NOC or NOC/c: Revised Clarimail/Clarifax summary table(s)</li> </ul>	<input type="checkbox"/> <input type="checkbox"/>
	<p><b>Submission filed on a post-NOC basis:</b></p> <ul style="list-style-type: none"> <li>Summary table of any clinical Clarimails/Clarifaxes up to issuance of NOC or NOC/c</li> </ul>	<input type="checkbox"/>



Requirement	Specific items and criteria	Included
<b>Bioequivalence, efficacy, and safety evidence</b>		
<b>Common technical document</b>	• Section 2.5	<input type="checkbox"/>
	• Section 2.7.1	<input type="checkbox"/>
	• Section 2.7.3	<input type="checkbox"/>
	• Section 2.7.4	<input type="checkbox"/>
	• Section 5.2	<input type="checkbox"/>
	• Or a statement indicating which section(s) were not required by Health Canada	<input type="checkbox"/>
<b>Clinical studies and errata</b>	• Reference list	<input type="checkbox"/>
	• Additional source documentation for data reported in the tailored review template	<input type="checkbox"/>
<b>Clinical study reports</b>	• Complete clinical study reports for all pivotal studies as well as other studies that address key clinical issues	<input type="checkbox"/>
<b>Table of studies</b>	• Completed table of studies template (Microsoft Word or PDF document)	<input type="checkbox"/>
<b>Epidemiologic information</b>		
<b>Disease prevalence and incidence</b>	• Disease prevalence and incidence with specified breakdown (if available)	<input type="checkbox"/>
	• Document is referenced	<input type="checkbox"/>
<b>Number of patients accessing a new drug</b>	• Number of patients accessing the new drug up to within 20 business days of filing the submission (Note: this requirement is only for a new drug submission or a new combination product submission if one of the components is a new drug.)	<input type="checkbox"/>
	• Use the number of patients accessing new drug template	<input type="checkbox"/>
<b>Reimbursement status of comparators</b>		
<b>Reimbursement status of comparators</b>	• A completed template summarizing the reimbursement status of all appropriate comparators as a Microsoft Word document	<input type="checkbox"/>
<b>Pricing and distribution information</b>		
<b>Price and distribution Method</b>	• Submitted unit pricing to four decimal places	<input type="checkbox"/>
	• Method of distribution	<input type="checkbox"/>
<b>Additional letter for submissions filed on Pre-NOC basis</b>		
<b>Letter for sending NOC or NOC/c to CADTH</b>	<p><b>After NOC or NOC/c is issued:</b></p> <ul style="list-style-type: none"> <li>• A signed letter indicating whether any wording changes to the Health Canada–approved final product monograph result in revisions to the clinical or pharmacoeconomic information filed on a pre-NOC basis (use the provided letter template)</li> </ul>	<input type="checkbox"/>

## 1C. Clinical and Administrative Requirements: Resubmission

Section	Specific Items and Criteria	Included
<b>General information</b>		
<b>Application overview</b>	<ul style="list-style-type: none"> <li>Completed application overview template</li> </ul>	<input type="checkbox"/>
<b>Signed cover letter</b>	<ul style="list-style-type: none"> <li>Clear description of application being filed</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>The indication(s) to be reviewed</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Requested reimbursement conditions, if applicable</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Names and contact information for primary and backup contacts</li> </ul>	<input type="checkbox"/>
<b>Executive summary</b>	<ul style="list-style-type: none"> <li>Completed executive summary template for a resubmission</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Maximum 5 pages (excluding references)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Document referenced with all supporting references</li> </ul>	<input type="checkbox"/>
<b>Product monograph</b>	<ul style="list-style-type: none"> <li>A copy of the most current version of the Health Canada–approved product monograph</li> </ul>	<input type="checkbox"/>
<b>Declaration letter</b>	<ul style="list-style-type: none"> <li>Completed declaration letter template</li> </ul>	<input type="checkbox"/>
<b>Regulatory and HTA Status</b>	<ul style="list-style-type: none"> <li>At the time of filing: a completed template summarizing the status at selected regulatory and Health Technology Assessment agencies as a Microsoft Word document</li> <li>At the time of filing comments on the draft reports: updated copy of the template as a Microsoft Word document</li> </ul>	<input type="checkbox"/>
<b>Request for deviation</b>	<ul style="list-style-type: none"> <li>Request for deviation response letter or statement that a deviation was not requested (applications received on or after November 1, 2023)</li> </ul>	<input type="checkbox"/>
<b>Sponsor Clinical Evidence Template</b>		
<b>Submission template</b>	<ul style="list-style-type: none"> <li>Complete sponsor summary of clinical evidence template</li> </ul>	<input type="checkbox"/>
<b>RIS file with references</b>	<ul style="list-style-type: none"> <li>RIS file with the references that have been cited in the sponsor summary of clinical evidence template</li> </ul>	<input type="checkbox"/>
<b>Efficacy, effectiveness, and safety information</b>		
<b>Common technical document</b>	<ul style="list-style-type: none"> <li>Section 2.5</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Section 2.7.1</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Section 2.7.3</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Section 2.7.4</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Section 5.2</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Or a statement indicating any section(s) not required for the Health Canada submission</li> </ul>	<input type="checkbox"/>
<b>Clinical studies and errata that were included in the initial submission</b>	<ul style="list-style-type: none"> <li>Reference list of key clinical studies (published and unpublished) and any errata provided in the initial submission and any previous resubmissions</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Copies of studies addressing key clinical issues</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Copies of any errata (or a document stating that none found)</li> </ul>	<input type="checkbox"/>
<b>New clinical studies included in the resubmission</b>	<ul style="list-style-type: none"> <li>Reference lists of all new clinical studies and errata (or a document stating none is available) included in the resubmission that were not provided in the initial submission, or a previous resubmission</li> </ul>	<input type="checkbox"/>



Section	Specific Items and Criteria	Included
	<ul style="list-style-type: none"> <li>Copies of all new clinical information and errata</li> </ul>	<input type="checkbox"/>
<b>Clinical study reports</b>	<ul style="list-style-type: none"> <li>Complete clinical study reports for all pivotal studies as well as other studies that address key clinical issues</li> </ul>	<input type="checkbox"/>
<b>Editorials</b>	<ul style="list-style-type: none"> <li>Reference list of editorial articles (or document stating none found)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Copies of editorial articles</li> </ul>	<input type="checkbox"/>
<b>Validity of outcome measures</b>	<ul style="list-style-type: none"> <li>Reference list for validity of outcome measures (or document stating none found)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Copies of validity of outcome measure references available</li> </ul>	<input type="checkbox"/>
<b>Table of studies</b>	<ul style="list-style-type: none"> <li>An updated tabulated list of all published and unpublished clinical studies using the provided table of studies template (Microsoft Word or PDF document)</li> </ul>	<input type="checkbox"/>
<b>Indirect comparison</b>	<ul style="list-style-type: none"> <li>Copies of any indirect comparisons used in the pharmacoeconomic evaluation</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Indirect comparison technical report</li> </ul>	<input type="checkbox"/>
<b>Epidemiologic information</b>		
<b>Disease prevalence and incidence</b>	<ul style="list-style-type: none"> <li>Disease prevalence and incidence data, with specified breakdown (if available)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Document is referenced</li> </ul>	<input type="checkbox"/>
<b>Reimbursement status of comparators</b>		
<b>Reimbursement status of comparators</b>	<ul style="list-style-type: none"> <li>A completed template summarizing the reimbursement status of all appropriate comparators as a Microsoft Word document</li> </ul>	<input type="checkbox"/>
<b>Pricing and distribution information</b>		
<b>Price and distribution method</b>	<ul style="list-style-type: none"> <li>Submitted unit pricing to 4four decimal places</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Method of distribution</li> </ul>	<input type="checkbox"/>
<b>Provisional algorithm for oncology drugs</b>		
<b>Provisional algorithm (only for oncology drugs)</b>	<ul style="list-style-type: none"> <li>Place in therapy template</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>A reference list (or statement that none are available)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Copies of studies that address sequencing of therapies</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Copy of the search strategy for sequencing of therapies</li> </ul>	<input type="checkbox"/>
<b>Companion diagnostic(s)</b>		
<b>Companion diagnostics</b>	<ul style="list-style-type: none"> <li>Reference list and copies of articles that highlight the clinical utility of the companion diagnostic(s)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Disclosable price for the companion diagnostic(s)</li> </ul>	<input type="checkbox"/>

## 1D. Clinical and Administrative Requirements: Reassessment

Section	Specific items and criteria	Included
<b>General information</b>		
<b>Application overview</b>	<ul style="list-style-type: none"> <li>Completed application overview template</li> </ul>	<input type="checkbox"/>
<b>Signed cover letter</b>	<ul style="list-style-type: none"> <li>Clear description of application being filed</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>The indication(s) to be reviewed</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Requested reimbursement conditions, if applicable</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Names and contact information for primary and backup contacts</li> </ul>	<input type="checkbox"/>
<b>Executive summary</b>	<ul style="list-style-type: none"> <li>Completed executive summary template for a resubmission</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Maximum 5 pages (excluding references)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Document referenced with all supporting references</li> </ul>	<input type="checkbox"/>
<b>Product monograph</b>	<ul style="list-style-type: none"> <li>A copy of the most current version of the Health Canada–approved product monograph</li> </ul>	<input type="checkbox"/>
<b>Declaration letter</b>	<ul style="list-style-type: none"> <li>Completed declaration letter template</li> </ul>	<input type="checkbox"/>
<b>Regulatory and HTA Status</b>	<ul style="list-style-type: none"> <li>At the time of filing: a completed template summarizing the status at selected regulatory and Health Technology Assessment agencies as a Microsoft Word document</li> <li>At the time of filing comments on the draft reports: updated copy of the template as a Microsoft Word document</li> </ul>	<input type="checkbox"/>
<b>Request for deviation</b>	<ul style="list-style-type: none"> <li>Request for deviation response letter or statement that a deviation was not requested (applications received on or after November 1, 2023)</li> </ul>	<input type="checkbox"/>
<b>Sponsor Clinical Summary Template</b>		
<b>Submission template</b>	<ul style="list-style-type: none"> <li>Complete sponsor summary of clinical evidence template</li> </ul>	<input type="checkbox"/>
<b>RIS file with references</b>	<ul style="list-style-type: none"> <li>RIS file with the references that have been cited in the sponsor summary of clinical evidence template</li> </ul>	<input type="checkbox"/>
<b>Efficacy, effectiveness, and safety Information</b>		
<b>New clinical studies</b>	<ul style="list-style-type: none"> <li>Reference lists of all new clinical studies and errata (or a document stating none is available) included in the reassessment</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Copies of all new clinical information and errata</li> </ul>	<input type="checkbox"/>
<b>Clinical study reports</b>	<ul style="list-style-type: none"> <li>Complete clinical study reports for all new studies included in the reassessment</li> </ul>	<input type="checkbox"/>
<b>Editorials</b>	<ul style="list-style-type: none"> <li>Reference list of editorial articles (or document stating none found)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Copies of editorial articles</li> </ul>	<input type="checkbox"/>
<b>Validity of outcome measures</b>	<ul style="list-style-type: none"> <li>Reference list for validity of outcome measures (or document stating none found)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Copies of validity of outcome measure references available</li> </ul>	<input type="checkbox"/>
<b>Table of studies</b>	<ul style="list-style-type: none"> <li>An updated tabulated list of all published and unpublished clinical studies using the provided table of studies template (Microsoft Word or PDF document)</li> </ul>	<input type="checkbox"/>
<b>Indirect comparison</b>	<ul style="list-style-type: none"> <li>Copies of any indirect comparisons used in the pharmacoeconomic evaluation</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>Indirect comparison technical report</li> </ul>	<input type="checkbox"/>

Section	Specific items and criteria	Included
<b>Epidemiologic information</b>		
<b>Disease prevalence and incidence</b>	• Disease prevalence and incidence data, with specified breakdown (if available)	<input type="checkbox"/>
	• Document is referenced	<input type="checkbox"/>
<b>Reimbursement status of comparators</b>		
<b>Reimbursement status of comparators</b>	• A completed template summarizing the reimbursement status of all appropriate comparators as a Microsoft Word document	<input type="checkbox"/>
<b>Pricing and distribution information</b>		
<b>Price and distribution method</b>	• Submitted unit pricing to 4four decimal places	<input type="checkbox"/>
	• Method of distribution	<input type="checkbox"/>
<b>Provisional algorithm for oncology drugs</b>		
<b>Provisional algorithm (only for oncology drugs)</b>	• Place in therapy template	<input type="checkbox"/>
	• A reference list (or statement that none are available)	<input type="checkbox"/>
	• Copies of studies that address sequencing of therapies	<input type="checkbox"/>
	• Copy of the search strategy for sequencing of therapies	<input type="checkbox"/>
<b>Companion diagnostic(s)</b>		
<b>Companion diagnostics</b>	• Reference list and copies of articles that highlight the clinical utility of the companion diagnostic(s)	<input type="checkbox"/>
	• Disclosable price for the companion diagnostic(s)	<input type="checkbox"/>

## 2. Pharmacoeconomic Requirements

Requirement	Specific items and criteria	Included
<b>Checklist of economic requirements</b>		
Checklist	Completed checklist of economic requirements	<input type="checkbox"/>
<b>Cost-Utility Analysis</b>		
Pharmacoeconomic evaluation: technical report	<b>Submission or Resubmission:</b>	
	• Pharmacoeconomic evaluation reflects the full population identified in the Health Canada indication(s) to be reviewed by CADTH	<input type="checkbox"/>
	• Scenario analysis of the population identified in the reimbursement request (if different from the population in the full indication)	<input type="checkbox"/>
	• Other relevant scenario analyses presented	<input type="checkbox"/>
	<b>Reassessments:</b>	
• Pharmacoeconomic evaluation reflects the scope of the reassessment:		<input type="checkbox"/>
▪ Population covered under the proposed revised reimbursement criteria		<input type="checkbox"/>
▪ Population covered under the current reimbursement criteria		<input type="checkbox"/>
▪ Relevant scenario analyses		<input type="checkbox"/>
• All relevant comparators have been included		<input type="checkbox"/>
• Rationale provided if potentially relevant comparators excluded		<input type="checkbox"/>

	<ul style="list-style-type: none"> <li>• Base case reflects the public health care payer perspective</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• 1.5% discount rate on costs and QALYs</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Treatment effect measures are based on composite end points</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Submitted price per smallest dispensable unit used</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• All submitted forms and strengths included</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Base case is presented probabilistically</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Base-case results are presented deterministically</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• All ICERs reported sequentially if more than one comparator is presented</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Results are presented in disaggregated format</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• QALYs, life-years and costs are reported</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• If relevant, companion diagnostic test information incorporated</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Alignment between the pharmacoeconomic evaluation technical report and the economic model</li> </ul>	<input type="checkbox"/>
Economic model	<ul style="list-style-type: none"> <li>• Model is programmed in Excel</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Model is fully unlocked and executable, and all code is provided</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Model functions in a stand-alone environment and does not require access to a web-based platform</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Probabilistic analyses run without error</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• CADTH can easily vary any individual input and view calculation</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Results of the probabilistic analysis are stable (congruence test provided)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• If used, seeding must be easily disabled or modifiable</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• The model runs treatments simultaneously and results of all comparators are presented</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• If relevant, flexible to assess all parametric distributions tested by the sponsor; present graphically the Kaplan-Meier and parametric curves to allow visual inspection of fit concurrently, within one graph</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Markov or event-time trace is provided via formulas within the Excel worksheets</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Model run time is no more than 1 business day (8 hours)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Does not require CADTH to agree to terms and conditions or have a legal disclaimer</li> </ul>	<input type="checkbox"/>
<b>Cost-Minimization Analysis</b>		
Pharmacoeconomic evaluation: technical report	<ul style="list-style-type: none"> <li>• Drug is a new treatment in an existing therapeutic class in which there are treatments already reimbursed</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Drug under review demonstrates similar clinical effects compared with the most appropriate comparator(s)</li> </ul>	<input type="checkbox"/>
	<b>Submission or Resubmission:</b>	<input type="checkbox"/>

	<ul style="list-style-type: none"> <li>• Pharmacoeconomic evaluation reflects the full population identified in the indication(s) to be reviewed by CADTH</li> <li>• Scenario analysis of the population identified in the reimbursement request (if different from the population in the full indication)</li> </ul>	<input type="checkbox"/>
	<p><b>Reassessments:</b></p> <ul style="list-style-type: none"> <li>• Pharmacoeconomic evaluation reflects the scope of the reassessment:               <ul style="list-style-type: none"> <li>▪ Population covered under the proposed revised reimbursement criteria</li> <li>▪ Population covered under the current reimbursement criteria</li> </ul> </li> </ul>	<input type="checkbox"/>
	• All relevant comparators have been included	<input type="checkbox"/>
	• Rationale provided if potentially relevant comparators excluded	<input type="checkbox"/>
	• Base case reflects the public health care payer perspective	<input type="checkbox"/>
	• 1.5% discount rate on costs if time horizon greater than 1 year	<input type="checkbox"/>
	• Submitted price per smallest dispensable unit used	<input type="checkbox"/>
	• All submitted forms and strengths included	<input type="checkbox"/>
	• All results are presented probabilistically unless rationale for absence of parameter uncertainty	<input type="checkbox"/>
	• Results are presented in disaggregated format	<input type="checkbox"/>
	• Alignment between the pharmacoeconomic evaluation technical report and the economic model	<input type="checkbox"/>
Cost calculations	• Excel workbook provided	<input type="checkbox"/>
	• Workbook is fully unlocked and all calculations provided	<input type="checkbox"/>
	• Model functions in a stand-alone environment, does not require access to a web-based platform, and all code is provided.	<input type="checkbox"/>
	• CADTH can easily vary any individual input and trace inputs through the workbook	<input type="checkbox"/>
	• If probabilistic, analyses run simultaneously for all comparators without error, and results are stable over multiple runs	<input type="checkbox"/>
	• Model run time is no more than 1 business day (8 hours)	<input type="checkbox"/>
	• Does not require CADTH to agree to terms and conditions or have a legal disclaimer	<input type="checkbox"/>
<b>Supporting documentation for the Pharmacoeconomic Evaluation</b>		
Supporting documentation	• Economic model user guide	<input type="checkbox"/>
	• Unpublished studies or analyses used to inform the pharmacoeconomic evaluation, including technical report(s) of the indirect comparison(s), utility studies, etc., provided within 1 folder. Reference numbering aligns with the pharmacoeconomic evaluation report.	<input type="checkbox"/>
	• All other supporting documentation (i.e., references) used and/or cited in the pharmacoeconomic evaluation provided within one folder. Reference numbering aligns with the pharmacoeconomic evaluation report.	<input type="checkbox"/>



	<ul style="list-style-type: none"><li>• Document summarizing key sources of information for the companion diagnostic test</li></ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"><li>• RIS file with economic references</li></ul>	<input type="checkbox"/>

## 3. Budget Impact Analysis Requirements

Requirement	Specific items and criteria	Included
<b>Budget impact analysis</b>		
Budget impact analysis: technical report	<ul style="list-style-type: none"> <li>• Base case reflects pan-Canadian (national) drug program perspective (excluding Quebec)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• For PPRP reviews, an analysis from the Canadian Blood Services perspective is provided.</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• For cell and gene therapies, products administered partially or solely in hospital, or infusion therapies, a scenario that considers the Canadian health system perspective has been provided</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Population(s) assessed in the base case and scenarios align with the economic evaluation</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Base-case analysis uses a 1-year baseline period and 3-year forecast period</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• All relevant comparators included (aligns with the economic evaluation)</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Submitted price per smallest dispensable unit used</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• All submitted forms and strengths are included</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Results presented deterministically</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Results presented for each specified jurisdiction before being aggregated to pan-Canadian results</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Report includes at minimum decision problem, methods, assumptions and results</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Alignment between the technical report and the model</li> </ul>	<input type="checkbox"/>
Budget impact model	<ul style="list-style-type: none"> <li>• Model is programmed in Excel</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Model is fully unlocked and executable, and all code is provided.</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Model functions in a stand-alone environment and does not require access to a web-based platform</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• CADTH must be able to vary individual parameters, view the calculations, and run the model to generate results</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Model is flexible and allows assessment of each specified individual drug program</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Input values specific to the individual drug program</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Breakdown of costs by perspective reported within the submitted model</li> </ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"> <li>• Does not require CADTH to agree to terms and conditions or have a legal disclaimer</li> </ul>	<input type="checkbox"/>
<b>Supporting documentation for the Budget Impact Analysis</b>		
Supporting documentation	<ul style="list-style-type: none"> <li>• Unpublished studies or analyses used to inform the BIA provided within one folder. Reference numbering aligns with the BIA report.</li> </ul>	<input type="checkbox"/>



## Procedures for CADTH Reimbursement Reviews

Requirement	Specific items and criteria	Included
	<ul style="list-style-type: none"><li>• All other supporting documentation (i.e., references) used and/or cited in the BIA provided within one folder. Reference numbering aligns with the BIA report.</li></ul>	<input type="checkbox"/>
	<ul style="list-style-type: none"><li>• RIS file with economic references</li></ul>	<input type="checkbox"/>





# Appendix 6: File Structure and Naming Format

## Instructions for Sponsors

Please carefully review the following file structure and naming conventions before assembling the application requirements. If you have any questions, please email [requests@cadth.ca](mailto:requests@cadth.ca) with the complete details of your question(s).

## Filing Requirements With CADTH

All materials must be submitted using the Pharmaceutical Submissions SharePoint site. Sponsors should review the [Pharmaceutical Submissions SharePoint Site – Setup Guide](#) for full instructions on how to setup a project folder for their submission and gain access to the site.

Sponsors must complete the steps outlined in the guide to request access to the site a minimum of **10 business days prior** to their submission of any document to CADTH (this is typically the Pre-Submission Meeting Request Form or the Advanced Notification Form [if not requesting a pre-submission meeting]). ***In the event the sponsor has not requested or received access prior to their target date for providing advance notification of the pending application, please contact CADTH immediately ([requests@cadth.ca](mailto:requests@cadth.ca)). CADTH will work with the sponsor to ensure that the application is not delayed due to the time frame for setting up the platform to securely receive the required documents.***

Files should be submitted as zipped (.zip) files. If there are several .zip files, the number of files should be noted in the file name (e.g., 1of4). The root folder(s) should be clearly named with the brand or generic drug name.

An email notification will be sent to the sponsor when the file has been submitted successfully.

The entire decoded file path, including the file name, cannot contain more than 400 characters. The limit applies to the combination of the folder path and file name after decoding.

Documents must be provided in PDF or Microsoft Word format, unless otherwise indicated in the requirement descriptions. These files must be unlocked, searchable, and printable. Document users must be able to extract information or combine documents.

Documents must be organized and labelled according to the file structure and naming format provided in this appendix.

If any extra supporting documents that do not have a designated folder are being submitted at the sponsor's discretion (e.g., clinical study reports), these should be appropriately named and filed in a logical location in the file structure.

## Providing Additional Information During the Review

If CADTH requests additional information during the review, sponsors must provide the requested information using the Pharmaceutical Submissions SharePoint site in the “4. Additional Information” folder.

Files should be submitted as zipped (.zip) files. The documents within the .zip file must be provided in PDF or Microsoft Word format. These files must be unlocked, searchable, and printable. Document users must be able to extract information or combine documents.

## Submission Requirements for a Standard Review



Represents 1 folder



Represents 1 file (unlocked, searchable, and printable)



### Brand Name



#### 1\_Brand Name\_General Information

- 1 - Application Overview
- 2 - Signed Cover Letter
- 3 - Executive Summary
- 4 - Product Monograph
- 5 - Declaration letter
- 6 - Regulatory-HTA Status
- 7 - Request for Deviation (applications received on or after November 1, 2023)



#### 2\_Brand Name\_Sponsor Clinical Evidence

- 1 - Brand Name Clinical Evidence
- 2 - Brand Name References (Note: this must a RIS file)



#### 3\_Brand Name\_Health Canada Documentation

- 1 - Health Canada NOC
- 2 - Letter of Undertaking (Note: only if applicable)
- 3 - Table of Clarimails



#### 4\_Brand Name\_Clinical Information




##### 4.1\_Common Technical Document

- 1 - Section 2.5
- 2 - Section 2.7.1
- 3 - Section 2.7.3
- 4 - Section 2.7.4
- 5 - Section 5.2




##### 4.2\_Clinical Studies and Errata


- \_List of Studies and Errata
- 1 - Trial Name\_Author\_Year
- 2 - Trial Name\_Author\_Year Erratum

 4.3\_Clinical Study Reports


- 1 - Trial Name
- 2 - Trial Name

 4.4\_Table of Studies


- Table of Studies

 4.5\_Editorials

- \_List of Editorials
- 1 - Author\_Year

 4.6\_New Data

- \_List of New Data
- 1 - Trial Name\_Author\_Year

 4.7\_Validity of Outcomes

- \_List of References
- 1 - Author\_Year

 4.8\_Indirect Comparison

- Indirect Comparison
- Technical report

 **5\_Brand Name\_Epidemiologic Information**

- Disease Prevalence and Incidence
- Number Patients Accessing New Drug (Note: only if applicable)

 **6\_Brand Name\_Comparator Status**

- Comparator Reimbursement Status


 **7\_Brand Name\_Economic**

- Pharmacoeconomic evaluation
- Economic model
- Checklist for economic requirements
- RIS file with economic references
- Supporting documentation

- Published
- Unpublished

 **8\_Brand Name\_BIA** 8.1\_BIA Report

- pan-Canadian BIA Report

 8.2\_BIA Model

- pan-Canadian BIA Model

 8.3\_BIA Supporting Documentation


- Published
- Unpublished

 **9\_Brand Name\_Pricing and Distribution**


- Pricing and Distribution

 **10\_Brand Name\_Provisional Algorithm**

- Brand Name\_Place In Therapy
- Brand Name\_List of References
- 1 - Author\_Year

 **11\_Brand Name\_Companion Diagnostic** 11.1\_Clinical Utility

- \_List of References
- 1 – Author\_Year

 11.2\_Price

- Companion Diagnostic Price

## Submission Requirements for a Complex Review



Represents 1 folder

- Represents 1 file (unlocked, searchable, and printable)



### Brand Name



#### 1\_Brand Name\_General Information

- 1 - Application Overview
- 2 - Signed Cover Letter
- 3 - Executive Summary
- 4 - Product Monograph
- 5 - Declaration letter
- 6 - Regulatory-HTA Status
- 7 - Request for Deviation (applications received on or after November 1, 2023)



#### 2\_Brand Name\_Sponsor Clinical Evidence

- 1 - Brand Name Clinical Evidence
- 2 - Brand Name References (Note: this must a RIS file)



#### 3\_Brand Name\_Health Canada Documentation

- 1 - Health Canada NOC
- 2 - Letter of Undertaking (Note: only if applicable)
- 3 - Table of Clarimails



#### 4\_Brand Name\_Clinical Information



##### 4.1\_Common Technical Document

- 1 - Section 2.5
- 2 - Section 2.7.1
- 3 - Section 2.7.3
- 4 - Section 2.7.4
- 5 - Section 5.2



##### 4.2\_Clinical Studies and Errata

- \_List of Studies and Errata
- 1 - Trial Name\_Author\_Year
- 2 - Trial Name\_Author\_Year Erratum



##### 4.3\_Clinical Study Reports

- 1 - Trial Name

- 2 - Trial Name

**4.4\_Table of Studies**

- Table of Studies

**4.5\_Editorials**

- \_List of Editorials
- 1 - Author\_Year

**4.6\_New Data**

- \_List of New Data
- 1 - Trial Name\_Author\_Year

**4.7\_Validity of Outcomes**

- \_List of References
- 1 - Author\_Year

**4.8\_Indirect Comparison**

- Indirect Comparison
- Technical report

**5\_Brand Name\_Epidemiologic Information**

- Disease Prevalence and Incidence
- Number Patients Accessing New Drug (Note: only if applicable)

**6\_Brand Name\_Comparator Status**

- Comparator Reimbursement Status

**7\_Brand Name\_Economic**

- Pharmacoeconomic evaluation
- Economic model
- Checklist for economic requirements
- RIS file with economic references
- Supporting documentation
  - Published
  - Unpublished

**8\_Brand Name\_BIA****8.1\_BIA Report**

- pan-Canadian BIA Report

 8.2\_BIA Model

- pan-Canadian BIA Model

 8.3\_BIA Supporting Documentation

- Published
- Unpublished

 **9\_Brand Name\_Pricing and Distribution**


- Pricing and Distribution

 **10\_Brand Name\_Implementation Plan** *(for cell and therapies only)*


- Implementation Plan

 **11\_Brand Name\_Provisional Algorithm** *(for oncology drugs only)*

- Brand Name\_Place In Therapy
- Brand Name\_List of References
- 1 - Author\_Year

 **12\_Companion Diagnostic** 12.1\_Clinical Utility

- \_List of References
- 1 - Author\_Year

 12.2\_Price

- Companion Diagnostic Price

## Submission Requirements for a Plasma Protein and Related Product Review



Represents 1 folder

- Represents 1 file (unlocked, searchable, and printable)



### Brand Name



#### 1\_Brand Name\_General Information

- 1 - Application Overview
- 2 - Signed Cover Letter
- 3 - Executive Summary
- 4 - Product Monograph
- 5 - Declaration letter
- 6 - Regulatory-HTA Status
- 7 - Request for Deviation (applications received on or after November 1, 2023)



#### 2\_Brand Name\_Sponsor Clinical Evidence

- 1 - Brand Name Clinical Evidence
- 2 - Brand Name References (Note: this must a RIS file)



#### 3\_Brand Name\_Health Canada Documentation

- 1 - Health Canada NOC
- 2 - Letter of Undertaking (Note: only if applicable)
- 3 - Table of Clarimails



#### 4\_Brand Name\_Clinical Information



##### 4.1\_Common Technical Document

- 1 - Section 2.5
- 2 - Section 2.7.1
- 3 - Section 2.7.3
- 4 - Section 2.7.4
- 5 - Section 5.2



##### 4.2\_Clinical Studies and Errata

- \_List of Studies and Errata
- 1 - Trial Name\_Author\_Year
- 2 - Trial Name\_Author\_Year Erratum



##### 4.3\_Clinical Study Reports

- 1 - Trial Name



- 2 - Trial Name



#### 4.4\_Table of Studies

- Table of Studies



#### 4.5\_Editorials

- \_List of Editorials
- 1 - Author\_Year



#### 4.6\_New Data

- \_List of New Data
- 1 - Trial Name\_Author\_Year



#### 4.7\_Validity of Outcomes

- \_List of References
- 1 - Author\_Year



#### 4.8\_Indirect Comparison

- Indirect Comparison
- Technical report



### 5\_Brand Name\_Epidemiologic Information

- Disease Prevalence and Incidence
- Number Patients Accessing New Drug (Note: only if applicable)



### 6\_Brand Name\_Comparator Status

- Comparator Reimbursement Status



### 7\_Brand Name\_Economic

- Pharmacoeconomic evaluation
- Economic model
- Checklist for economic requirements
- RIS file with economic references
- Supporting documentation
  - Published
  - Unpublished



### 8\_Brand Name\_BIA




#### 8.1\_BIA Report

- pan-Canadian BIA Report

 8.2\_BIA Model


- pan-Canadian BIA Model

 8.3\_BIA Supporting Documentation


- Published
- Unpublished

 **9\_Brand Name\_Pricing and Distribution**

- Pricing and Distribution

 **10\_Companion Diagnostic** 10.1\_Clinical Utility

- \_List of References
- 1 - Author\_Year

 10.2\_Price

- Companion Diagnostic Price

## Submission Requirements for a Tailored Review



Represents 1 folder

• Represents 1 file (unlocked, searchable, and printable)



### Brand Name



#### 1\_Brand Name\_General Information

- 1 - Application Overview
- 2 - Signed Cover Letter
- 3 - Executive Summary
- 4 - Product Monograph
- 5 - Declaration Letter
- 6 - Regulatory-HTA Status



#### 2\_Brand Name\_Health Canada Documentation

- 1 - Health Canada NOC
- 2 - Letter of Undertaking (Note: only if applicable; adjust following file numbers if necessary)
- 3 - Table of Clarimails



#### 3\_Brand Name\_Submission Template

- 1 – Tailored Review Submission Template



#### 4\_Brand Name\_Clinical Information



##### 4.1\_Common Technical Document

- 1 - Section 2.5
- 2 - Section 2.7.1
- 3 - Section 2.7.3
- 4 - Section 2.7.4
- 5 - Section 5.2



##### 4.2\_Source Documentation

- \_List of Documentation
- 1 - Name\_Year
- 2 - Name\_Year



##### 4.3\_Clinical Study Reports

- 1 - Trial Name
- 2 - Trial Name

**4.4\_Table of Studies**

- Table of Studies

**5\_Brand Name\_Epidemiologic Information**

- Disease Prevalence and Incidence

**6\_Brand Name\_Comparator Status**

- Comparator Reimbursement Status

**7\_Brand Name\_Pricing and Distribution**

- Pricing and Distribution

**8\_Brand Name\_BIA****8.1\_BIA Report**

- pan-Canadian BIA Report

**8.2\_BIA Model**

- pan-Canadian BIA Model

**8.3\_BIA Supporting Documentation**

- Published
- Unpublished

**9\_Companion Diagnostic****9.1\_Clinical Utility**

- \_List of References
- 1 - Author\_Year

**9.2\_Price**

- Companion Diagnostic Price

## Resubmission Requirements



Represents 1 folder

- Represents 1 file (unlocked, searchable, and printable)



### Brand Name



#### 1\_Brand Name\_General Information

- 1 - Application Overview
- 2 - Signed Cover Letter
- 3 - Executive Summary
- 4 - Product Monograph
- 5 - Declaration letter
- 6 - Regulatory-HTA Status
- 7 - Request for Deviation (applications received on or after November 1, 2023)



#### 2\_Brand Name\_Sponsor Clinical Evidence

- 1 - Brand Name Clinical Evidence
- 2 - Brand Name References (Note: this must a RIS file)



#### 3\_Brand Name\_Clinical Information



##### 3.1\_Common Technical Document

- 1 - Section 2.5
- 2 - Section 2.7.1
- 3 - Section 2.7.3
- 4 - Section 2.7.4
- 5 - Section 5.2



##### 3.2\_Clinical Studies and Errata

- \_List of Studies and Errata
- 1 - Trial Name\_Author\_Year
- 2 - Trial Name\_Author\_Year Erratum



##### 3.3\_New Clinical Studies

- \_List of New Clinical Studies
- 1 - Trial Name\_Author\_Year
- 2 - Trial Name\_Author\_Year



##### 3.4\_Clinical Study Reports


- 1 - Trial Name
- 2 - Trial Name



##### 3.5\_ New Editorials and Errata

- \_List of Editorials and Errata
- \_No Editorials or No Errata (Note: *placeholder document, only if applicable*)

- 1 - Author\_Year\_Editorial
- 2 - Trial Name\_Author\_Year\_Erratum

 3.6\_Verification of Outcomes

- List of References
- 1 - Author\_Year

 3.7\_Updated Table of Studies

- Table of Studies

 3.8\_Indirect Comparison

- Indirect Comparison
- Technical report

 **4\_Brand Name\_Epidemiologic Information**


- Disease Prevalence and Incidence

 **5\_Brand Name\_Comparator Status**

- Comparator Reimbursement Status

 **6\_Brand Name\_Economic**

- Pharmacoeconomic evaluation
- Economic model
- Checklist for economic requirements
- RIS file with economic references

 Supporting documentation

- Published
- Unpublished

 **7\_Brand Name\_BIA** 7.1\_BIA Report

- pan-Canadian BIA Report

 7.2\_BIA Model

- pan-Canadian BIA Model

 7.3\_BIA Supporting Documentation

- Published
- Unpublished

 **8\_Brand Name\_Pricing and Distribution**

- Pricing and Distribution


 **9\_Brand Name\_Provisional Algorithm**


- Brand Name\_Place In Therapy



- Brand Name\_List of References
- 1 - Author\_Year

### 10\_Companion Diagnostic

-  10.1\_Clinical Utility
  - \_List of References
  - 1 - Author\_Year

-  10.2\_Price
  - Companion Diagnostic Price

## Standard Reassessment Requirements



Represents 1 folder

- Represents 1 file (unlocked, searchable, and printable)



### Brand Name



#### 1\_Brand Name\_General Information

- 1 - Application Overview
- 2 - Signed Cover Letter
- 3 - Executive Summary
- 4 - Product Monograph
- 5 - Declaration letter
- 6 - Regulatory-HTA Status
- 7 - Request for Deviation (applications received on or after November 1, 2023)



#### 2\_Brand Name\_Sponsor Clinical Evidence

- 1 - Brand Name Clinical Evidence
- 2 - Brand Name References (Note: this must a RIS file)



#### 3\_Brand Name\_Clinical Information



##### 3.1\_Clinical Studies and Errata

- \_List of Clinical Studies and Errata
- 1 - Trial Name\_Author\_Year
- 2 - Trial Name\_Author\_Year



##### 3.2\_Clinical Study Reports

- 1 - Trial Name
- 2 - Trial Name



##### 3.3\_Editorials

- \_List of Editorials
- \_No Editorials (*Note: placeholder document, only if applicable*)
- 1 - Author\_Year



##### 3.4\_Validity of Outcomes

- List of References
- 1 - Author\_Year



##### 3.5\_Updated Table of Studies

- Table of Studies



##### 3.6\_Indirect Comparison

- Indirect Comparison
- Technical report



## 4\_Brand Name\_Epidemiologic Information

- Disease Prevalence and Incidence

## 5\_Brand Name\_Comparator Status

- Comparator Reimbursement Status

## 6\_Brand Name\_Economic

- Pharmacoeconomic evaluation
- Economic model
- Checklist for economic requirements
- RIS file with economic references
- Supporting documentation
  - Published
  - Unpublished

## 7\_Brand Name\_BIA

### 7.1\_BIA Report

- pan-Canadian BIA Report

### 7.2\_BIA Model

- pan-Canadian BIA Model

### 7.3\_BIA Supporting Documentation

- Published
- Unpublished

## 8\_Brand Name\_Pricing and Distribution

- Pricing and Distribution

## 9\_Brand Name\_Provisional Algorithm

- Brand Name\_Place In Therapy
- Brand Name\_List of References
- 1 - Author\_Year

## 10\_Companion Diagnostic

### 10.1\_Clinical Utility

- \_List of References
- 1 - Author\_Year

### 10.2\_Price

- Companion Diagnostic Price

## Appendix 7: Key Definitions

The following are high-level definitions for key terms used in this document. Readers should consult the appropriate sections of the document for more detailed context as it relates to some terms.

**Active substance:** A therapeutic substance that has pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease (refer to new active substance).

**Additional information:** Additional information includes any information that is additional to the documents that are required for an application to be accepted for review by CADTH. This information is requested from the sponsor by CADTH in order to complete the review or to clarify information.

**Application:** Written documentation filed by a sponsor to have a drug reviewed through CADTH's reimbursement review process.

**Appropriate comparator:** Typically, a drug listed by one or more drug programs for the indication under review. However, the choice of appropriate comparator(s) in reviews by CADTH is made on a case-by-case basis.

**Biosimilar:** A biosimilar is a biologic drug (i.e., a drug derived from living sources versus a chemically synthesized drug) that demonstrates a high degree of similarity to an already authorized biologic drug (i.e., a "reference product" that has been authorized in Canada, or in some circumstances can be an authorized non-Canadian biologic from a jurisdiction that has an established relationship with Health Canada).

**Business day:** Any day (other than a Saturday, Sunday, statutory holiday, or company holiday) on which the CADTH office in Ottawa (Ontario, Canada) is open for business during regular business hours. Please refer to the [CADTH Holiday Schedule](#).

**Business hours:** Any weekday (excluding statutory and company holidays) from 8:00 a.m. to 4:00 p.m. Eastern time.

**CADTH review team:** A team assembled by CADTH to undertake a reimbursement review. The review team may include CADTH staff, contracted reviewers, and external experts with appropriate qualifications and expertise.

**CADTH Canadian Drug Expert Committee:** An appointed, national, independent advisory committee to CADTH that makes drug-related recommendations and provides drug-related advice through the CADTH Common Drug Review and therapeutic review processes.

**Cancelled review:** The cessation of the review before all steps of the review process are completed.

**Committee brief:** A compilation of the materials regarding a drug under review by CADTH, prepared by CADTH staff for the members of the expert committee.

**Companion diagnostic test:** A medical device that provides information that is essential for the safe and effective use of corresponding drugs or biological products. They can identify patients who are likely to benefit or experience harms from particular therapeutic products, or monitor clinical response to optimally

guide treatment adjustments. Companion diagnostics detect specific biomarkers that predict more favourable responses to particular therapeutic products.

**Date of acceptance for review:** The date on which CADTH has confirmed with the sponsor that the key requirements for initiating the review process have been met.

**Date of filing:** The date on which an application is received by CADTH.

**Date of initiation:** The date on which the assigned CADTH review team begins work on a review.

**Drug:** An active substance considered to be a drug under the Canadian Food and Drugs Act and Food and Drug Regulations that has been granted by Health Canada (or will be granted in the case of a submission filed on a pre-Notice of Compliance basis) a Notice of Compliance or Notice of Compliance with conditions, and is approved for human use.

**Drug programs:** The federal, provincial, and territorial drug programs participating in the CADTH Reimbursement Review processes.

**Final recommendation:** A document that provides guidance to the drug programs participating in CADTH's reimbursement review processes to make a reimbursement decision for the drug under review. Final recommendations are non-binding to the drug programs.

**Formulary Working Group:** A working group of the CADTH Pharmaceutical Advisory Committee. Formulary Working Group provides advice to CADTH on pharmaceutical issues and helps with the effective jurisdictional sharing of pharmaceutical information.

**Generic drugs:** Copies of Canadian reference products (i.e., Health Canada–approved brand name drugs) that demonstrate bioequivalence on the basis of pharmaceutical equivalence (i.e., they contain identical amounts of the identical active medicinal ingredients as the reference product, in comparable dosage forms, but do not necessarily contain the same non-medicinal ingredients as the Canadian reference product, and the conditions of use fall with those of the Canadian reference product) and bioavailability characteristics, where applicable, with the Canadian reference product. Generic drugs are not typically reviewed through CADTH's reimbursement review processes.

**New active substance:** A therapeutic substance that has never before been approved for marketing in Canada in any form. It may be:

- a chemical or biological substance not previously approved for sale in Canada as a drug
- an isomer, derivative, or salt of a chemical substance previously approved for sale as a drug in Canada but differing in properties regarding safety and efficacy.

**New combination product:** Consists of 2 or more drugs that have not been previously marketed in Canada in that combination. It may consist of either 2 or more new drugs, 2 or more previously marketed drugs, or a combination of new drug(s) and previously marketed drug(s).



**New drug:** A therapeutic substance that has never before been approved for marketing in any form, regardless of when the Notice of Compliance or Notice of Compliance with conditions was issued. It may be:  
a chemical or biological substance not previously approved for sale in Canada as a drug  
an isomer, derivative, or salt of a chemical substance previously approved for sale as a drug in Canada but differing in properties regarding safety and efficacy.

**New indication:** A disease condition for which the use of a particular drug has not previously been approved by Health Canada.

**New information:** New clinical information and/or new cost information that was not part of an originally filed application.

**Notice of Compliance:** Authorization issued by Health Canada to market a drug in Canada when regulatory requirements for the safety, efficacy, and quality are met.

**Notice of Compliance with conditions:** Authorization issued by Health Canada to market a drug under the Notice of Compliance with conditions policy. This indicates that the sponsor has agreed to undertake additional studies to confirm the clinical benefit of the product.

**Patient group:** An organized group of patients or caregivers in Canada.

**pCODR Expert Review Committee:** An appointed, national, independent advisory committee to CADTH that makes drug-related recommendations and provides drug-related advice through the CADTH pan-Canadian Oncology Drug Review and therapeutic review processes.

**Post-Notice of Compliance:** The timing of filing a submission after Health Canada has granted a Notice of Compliance or Notice of Compliance with conditions for the indication(s) to be reviewed by CADTH.

**Pre-Notice of Compliance:** The timing of filing a submission before Health Canada has granted a Notice of Compliance or Notice of Compliance with conditions for the indication(s) to be reviewed by CADTH, and for which the anticipated date of Notice of Compliance or Notice of Compliance with conditions is within 180 calendar days of the submission being filed.

**Provincial Advisory Group:** A working group of the CADTH Pharmaceutical Advisory Committee. The Provincial Advisory Group provides advice to CADTH on pharmaceutical issues and helps with the effective jurisdictional sharing of pharmaceutical information.

**Queuing:** A delay in the initiation of a review by CADTH.

**Reasons for recommendation:** These represent the key considerations and rationale used by the expert committee in formulating the recommendation.

**Request for reconsideration:** A written request from a sponsor or the drug programs for a draft recommendation to be reconsidered by the expert committee.



**Sponsor:** A person, corporation, or entity eligible to file an application for a reimbursement review by CADTH. The sponsor could be a manufacturer, a supplier, a corporation, or entity recruited by the manufacturer or the supplier.

**Submitted price:** 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 following completion of the CADTH's review. The submitted price will be disclosed in all applicable CADTH reports.

**Suspended review:** The temporary cessation of a reimbursement review by CADTH. This occurs if questions or issues arise outside of the regular review process or if the CADTH review team is unable to perform a thorough assessment of the application due to incomplete or non-transparent information. Once the issue is resolved, the review proceeds from the point at which it was suspended.

**Therapeutic review:** An evidence-based review of publicly available sources regarding a therapeutic category of drugs (e.g., antihypertensive drugs) or a class of drugs (e.g., angiotensin-converting enzyme inhibitors) in order to support drug reimbursement and policy decisions and encourage the optimization of drug therapy. The scope and depth of the review are determined by jurisdictional needs.