



Procedures for the CADTH pan-Canadian Oncology Drug Review

June 2020

Note: These procedures will be superseded by those described in the [*Procedures for CADTH Drug Reimbursement Reviews*](#) for all applications filed with CADTH on or after October 20, 2020. Should you have any questions, please contact requests@cadth.ca

Record of Updates

Update	Version	Reported on CADTH Website
Original	May 2011	May 17, 2011
1	February 2016	February 1, 2016
2	February 2016	February 25, 2016
3	March 2016	March 24, 2016
4	March 2017	March 16, 2017
5	June 2017	June 13, 2017
6	February 2018	February 13, 2018
7	August 2018	August 9, 2018
8	March 2019	March 28, 2019
9	June 2019	June 12, 2019
10	July 2019	July 31, 2019
11	August 2019	August 22, 2019
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13	February 2020	February 6, 2020
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16	June 2020	June 25, 2020

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Abbreviations

BIA	budget impact analysis
CAPCA	Canadian Association of Provincial Cancer Agencies
CONSORT	Consolidated Standards of Reporting Trials
DIN	Drug Identification Number
PAC	Pharmaceutical Advisory Committee
FWG	Formulary Working Group
ITC	indirect treatment comparison
NDS	new drug submission
NOC	Notice of Compliance
NOC/c	Notice of Compliance with conditions
PAC	Pharmaceutical Advisory Committee
PAG	Provincial Advisory Group
pCODR	CADTH pan-Canadian Oncology Drug Review
pCPA	pan-Canadian Pharmaceutical Alliance
pERC	pan-Canadian Oncology Drug Review Expert Review Committee
PMPRB	Patented Medicine Prices Review Board
P/T	Provincial or Territorial
QALY	quality-adjusted life-years
RCT	randomized controlled trial
VBA	Visual Basic for Applications

1. General Information

1.1 Purpose

The objective of this document is to outline the procedures and guidelines for the CADTH pan-Canadian Oncology Drug Review (pCODR) process. The procedures for the CADTH Common Drug Review (CDR) and CADTH Interim Plasma Protein Product Review (PPP) are currently documented separately and are available on the [CADTH website](#).

This document must be read in conjunction with any relevant issues of the [CADTH Pharmaceutical Reviews Update](#).

All references to number of days in this document are in business days unless otherwise specified. Key terms in this document are defined in Appendix 8.

1.2 Introduction

CADTH, through the pCODR process, evaluates clinical effectiveness, cost-effectiveness information and patient perspectives on cancer drugs or a class of cancer drugs conducted through a therapeutic review process, and uses this evaluation to provide cancer drug funding recommendations to Federal drug plans, Provincial/Territorial (P/T) Ministries of Health (excluding Quebec) and Provincial Cancer Agencies (referred to as “participating drug programs” hereafter). These recommendations are used by jurisdictions to guide their drug funding decisions.

CADTH’s pCODR process reduces duplication of effort by participating drug programs and ensures that reviews are done in a timely manner. The pCODR process brings consistency and clarity to the cancer drug review process, allowing for greater understanding by all stakeholders while ensuring funding decisions are informed by evidence that has been carefully evaluated by experts.

The pCODR process is guided by eight Guiding Principles as outlined on the CADTH website. As part of the eight Guiding Principles, the CADTH applies an ethical framework to its overall review process. Having transparent review processes and procedures, as outlined in these *Procedures for the CADTH pan-Canadian Oncology Drug Review*, is one component of that ethical framework.

Recommendations are made by a pan-Canadian independent body of pERC members. A pERC member is an appointed position of medical oncologists, hematologists, pharmacists, health economists and patient members. The pERC uses the evidence-based Clinical Guidance Report (hereinafter referred to as the “clinical report”) and pharmacoeconomic report as well as input provided by patient groups, registered clinicians and the Provincial Advisory Group (PAG) to evaluate the clinical evidence, cost effectiveness, clinician and patient perspectives of the drugs under consideration to make funding recommendations. The *pERC Deliberative Framework*, which considers clinical benefit, cost effectiveness, alignment with patient values and implementation feasibility, is used to guide the work of the pERC.

1.3 Changes to CADTH Procedures

CADTH may amend, from time to time, the *Procedures for the CADTH pan-Canadian Oncology Drug Review* and all matters related to its drug review processes in consultation with the participating drug programs. CADTH may also seek consultations with other stakeholders, from time to time, such as but not limited to pharmaceutical manufacturers or their representative organizations, tumour groups, and patient groups, for the purposes of revising this document. Amendments to and clarifications of the procedure and all related documents may be affected from time to time by means of communications issued by CADTH and posted on the CADTH website.

1.4 Disclosure of Information

CADTH is committed to providing an open and transparent drug review process and to being accountable for its recommendations to patients and the public. As such, CADTH considers it essential to be able to outline the evidence upon which pERC cancer drug reimbursement recommendations are made. In view of these principles, CADTH applies the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review* (Appendix 1) that outline a general approach to managing disclosable and non-disclosable information, as well as, the definitions of disclosable information and non-disclosable information for the purposes of pCODR reviews. These guidelines, which are available on the CADTH website, ensure that the disclosure of information obtained through the pCODR review process is handled and managed in a consistent manner and that procedures are in place to protect information that is non-disclosable according to definitions provided in the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*.

A sponsor will be deemed to have consented to the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review* when they file a submission or resubmission or supply other information to CADTH. By making a submission or resubmission to CADTH, the sponsor agrees that the sponsor will comply with all the requirements set out in the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*.

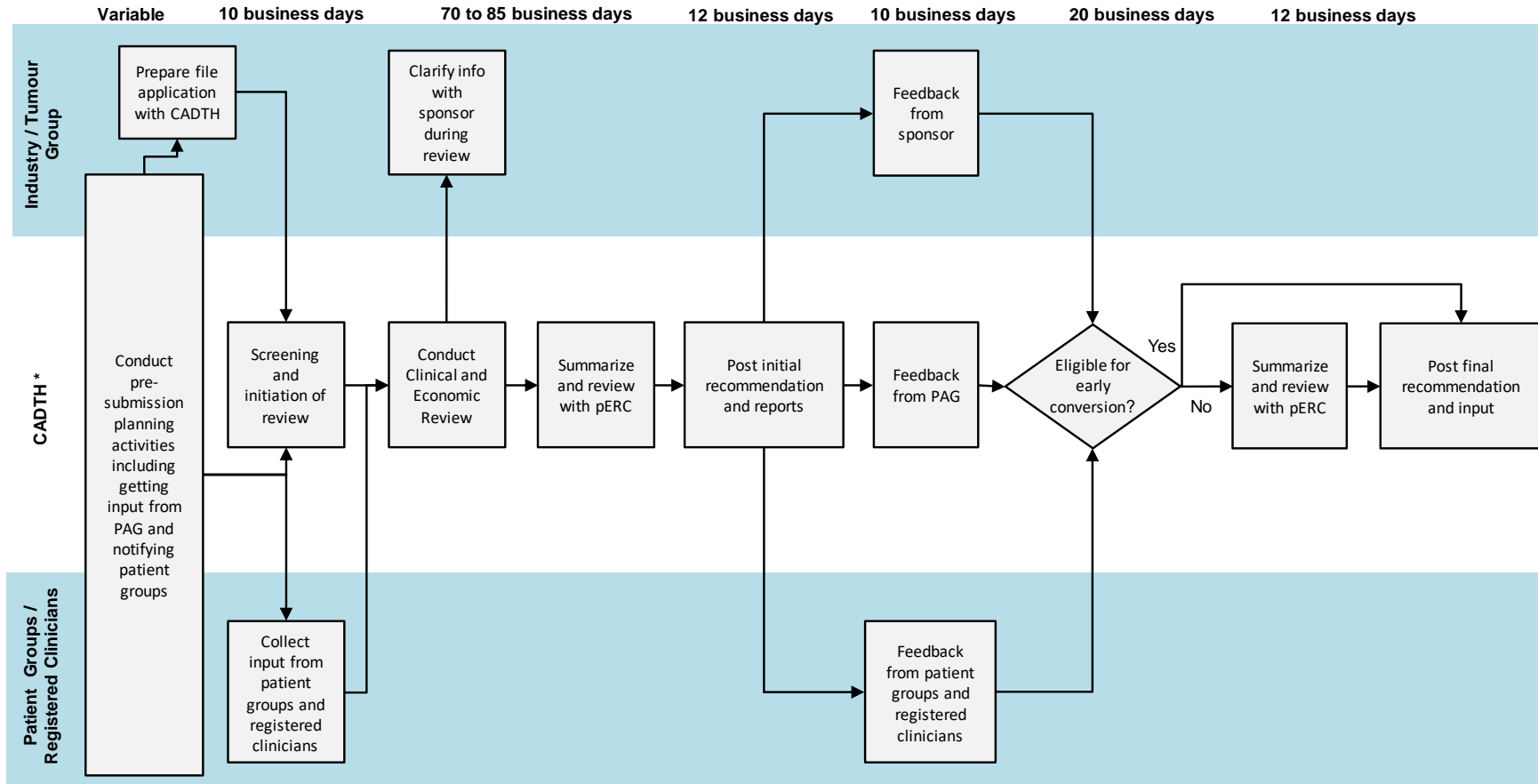
1.5 Code of Conduct, Communications and Conflict of Interest

CADTH's conduct, communications and conflicts of interest are governed by the [CADTH Code of Conduct](#) and [Conflict of Interest Guidelines](#).

1.6 Overview of CADTH's pCODR Review Process

An overview of the standard review process and estimated timelines is presented in Figure 1. Details of review process information that will be publicly available on the CADTH website are presented in section 4.3. Notwithstanding the foregoing, in the event of a submission being reviewed by CADTH that is a pre-NOC submission under review by Health Canada, CADTH will not post product strength, product format and NOC date, until such time as regulatory approval has been issued.

Figure 1: CADTH Standard Review Process for Oncology Drugs



* Includes CADTH, Clinical Guidance Panel, Economic Guidance Panel, pERC and PAG

2. Eligibility for the pCODR Process

2.1 Submission Eligibility

Eligible submissions for review through the CADTH pCODR process include new oncology drugs and oncology drugs with new indications that have or have not received a Notice of Compliance (NOC) or a Notice of Compliance with Conditions (NOC/c) from Health Canada. Submissions for drugs that have received an NOC or NOC/c are referred to as “post-NOC submissions”. Submissions for drugs with a pending NOC or NOC/c or are referred to as “pre-NOC submissions”.

2.2 Market Authorization Status at the Time of Filing

As described below, 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).

2.2.1 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.

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 finalized because the submission will not be placed on the pERC agenda until all required information, including a copy of the NOC or NOC/c, has been received by CADTH.

2.2.2 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 drug reimbursement review process.

2.2.3 Submissions for Unapproved Indications

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

- the drug is currently marketed in Canada;
- the DIN holder confirms that a submission to Health Canada is not pending for the indication of interest;
- 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 the above noted information when determining whether or not a submission may be filed for an indication that is not approved or undergoing review by Health.

CADTH will waive the category 1 requirements that are related to regulatory review and approval for these submissions: Common Technical Document; Health Canada NOC or NOC/c; and the table of Clarimails/Clarifaxes

2.3 Resubmission Eligibility

A resubmission is a review of any drug that has previously been reviewed by CADTH 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.

2.3.1 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 review committee in the final recommendation document. Table 1 summarizes the supporting information that must be filed for resubmissions.

Table 1: 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">• One or more new studies that address specific issues identified by the expert review committee in the final recommendation document• New pharmacoeconomic evaluation• New budget impact analysis
New cost information that significantly affects the cost-effectiveness of the drug	<ul style="list-style-type: none">• New pharmacoeconomic evaluation• New budget impact analysis

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.

2.3.2 Eligibility Assessment for Resubmissions

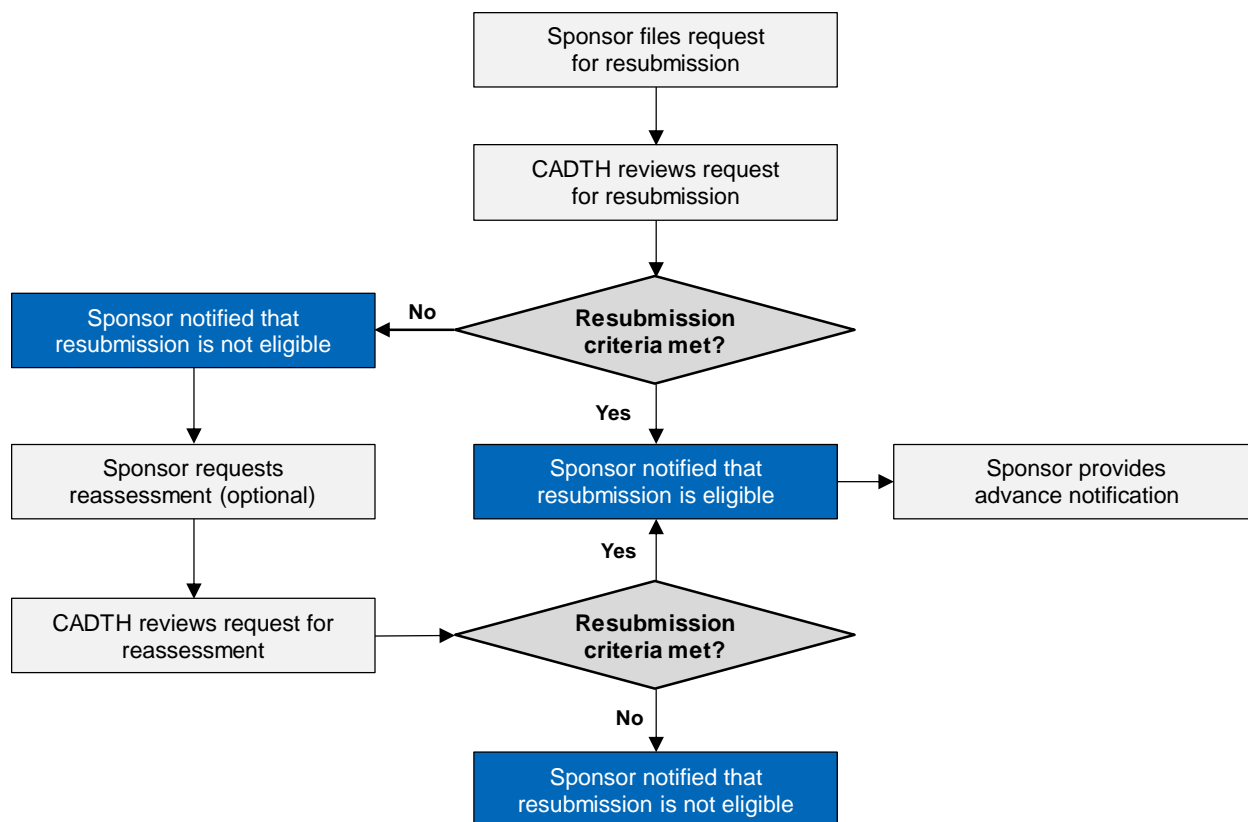
- Prior to filing a resubmission, sponsors are required to have its eligibility assessed by CADTH. Sponsors must provide the following information to requests@cadth.ca for evaluation by CADTH:
 - a completed [resubmission eligibility form](#)
 - copies of one or more new studies that address specific issues identified by the expert review committee in the final recommendation document.
- 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 review committee in the final recommendation document.
- CADTH may consult with members of the expert review committee and/or clinical experts to determine if the new information filed by the sponsor addresses the issues noted in the previous recommendation. However, the final decision regarding whether or not a resubmission 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.
- If CADTH determines that the sponsor's resubmission comprises new information and contains at least one study that addresses the specific issues identified by the expert review committee in the final recommendation document, the sponsor will be apprised in writing that the resubmission is eligible for review.
- If CADTH determines that the sponsor's resubmission does not comprise new information or does not address the specific issues identified by the expert review committee in the final recommendation document, the sponsor will be apprised in writing that the resubmission is not eligible.
- When a sponsor has been informed by CADTH that a resubmission is not eligible, the sponsor may file one written request for the decision to be reassessed by CADTH. The request for reassessment must clearly outline why the sponsor disagrees with CADTH's decision.
- Sponsors have 10 business days to file a request for reassessment after receiving notification from CADTH regarding the eligibility of a resubmission.
- Sponsors will only be entitled to have the eligibility decision reassessed once.
- CADTH will examine the reassessment request to determine whether the issue(s) raised change the conclusions regarding the eligibility of the resubmission. CADTH may consult with members of the expert review committee and/or clinical experts (as required). The final decision regarding whether or not a resubmission is eligible for review will be determined by CADTH.
- CADTH's consideration of each request for reassessment will typically be completed within 10 business days. 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 eligibility assessment on the CADTH website.
- CADTH will retain and dispose of documents associated with the resubmission in accordance with the *Disclosure of Information Guidelines for the CADTH pan-Canadian Oncology Drug Review*.

- All completed resubmission 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 is eligible for review by CADTH, sponsors are required to provide CADTH with advance notification for the pending resubmission. Advance notification for resubmissions must be provided in accordance with section 3.1.

2.3.3 Volume of Resubmissions

To ensure fair access to CADTH's review process for new drug submissions, CADTH may limit the number of resubmissions 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



2.4 Requests for Advice

A request for advice is used to address questions related to changes in contextual factors that may affect the ability of the participating jurisdictions to implement existing recommendations from CADTH's expert review committees. Contextual information can include items such as regulatory actions, changes in clinical practice, or other forms of information that have introduced implementation questions or challenges for the jurisdictions. The participating drug programs may file a request for advice regarding a previous final recommendation issued by 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.

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 DIN holder.

2.5.2 Tumour Groups and Drug Programs

The participating drug programs and provincially recognized clinician-based tumour groups may file a submission or resubmission through CADTH's drug reimbursement review processes. Prior to accepting a 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 2.7).

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 category 1 submission requirements or additional information for these submissions if they are unavailable or not relevant: Common Technical Document, Clinical Study Reports, Health Canada NOC or NOC/c, and/or Table of Clarimails/Clarifaxes.

Sponsors from tumour groups and the drug programs will be required to include an economic evaluation in their submission or resubmission. 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 category 1 requirements for the pending submission or resubmission.

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 Types of Reviews

Table 2 summarizes the type of review CADTH conducts for the different submission and resubmission categories for oncology drugs. The following types of reviews are currently conducted for oncology drugs:

- A standard review consists of CADTH conducting a systematic review of clinical evidence provided by the sponsor along with studies identified through its independent, systematic literature search, and an appraisal of the sponsor-provided pharmacoeconomic evaluation.
- A cell and gene therapy review is conducted in a manner similar to a standard review, but involves additional review and consideration of potential implementation issues and ethical challenges.

- A request for advice is used to address questions related to changes in contextual factors that may affect the ability of the participating jurisdictions to implement existing recommendations from CADTH's expert review committees.
- Resubmissions are conducted when new evidence is available for drugs that have previously been reviewed by CADTH for the indication of interest and for which a final recommendation has been issued.

Table 2: CADTH Review Types for Oncology Drugs

Review Type	Application	Eligible Sponsors
Standard review	<ul style="list-style-type: none"> • Submission for a new drug • Submission for a drug with a new indication • Submission for a new combination product 	<ul style="list-style-type: none"> • Industry • Tumour groups • Drug programs
Cell and gene therapy review	<ul style="list-style-type: none"> • Submissions for cell and gene therapies 	
Resubmission	<ul style="list-style-type: none"> • Drugs that have previously been reviewed by CADTH for the indication of interest and for which a final recommendation has been issued 	
Request for advice	<ul style="list-style-type: none"> • Changes in contextual information that may affect the ability to implement existing CADTH recommendations 	<ul style="list-style-type: none"> • Drug programs

2.7 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 Formulary Working Group (FWG) or pCODR Provincial Advisory Group (PAG) informing it that the drug is eligible for review and that the plans would like a submission to be filed with CADTH.
- The manufacturer will have 30 business days to respond to the FWG or PAG Chair 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 statement will be issued on the CADTH website indicating that “CADTH is unable to recommend reimbursement as a submission was not filed by the manufacturer”:
 - a manufacturer indicates that they are 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 review committees.
- These procedures 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 plan–initiated submissions provided the submission requirements can be addressed (e.g., provision of an economic model and pharmacoeconomic evaluation).

2.8 Eligible Drugs that have Become Genericized

Generic drugs are not typically reviewed through the CADTH's drug 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 plans 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 plans will provide guidance on a case-by-case basis as to whether a submission is required. Based on the input from the drug plans, CADTH may advise manufacturers of branded or generic products that are eligible for review (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 plans 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 participating drug plans 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 participating drug plans (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 participating 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 may contact CADTH at any time (requests@cadth.ca).

3. Pre-Submission Procedures

Pre-submission procedures include all those procedures related to the period before an anticipated submission or resubmission is filed with CADTH. Before a drug submission is made, CADTH works with the sponsor to prepare them for the filing process. This preparation includes receiving advance notification from a sponsor of an upcoming submission or resubmission, holding a pre-submission

meeting with the sponsor, setting up supports to assist both the sponsor and stakeholder groups through the review process, obtaining input from PAG, and notifying appropriate stakeholder groups of the pending review. It also involves determining the appropriate membership for clinical and economic guidance panels and identifying additional resources and expertise that will be part of the review.

Note: Subject to these procedures and the Disclosure of Information Guidelines for the for the CADTH pan-Canadian Oncology Drug Review, all pre-submission information provided by the sponsor to CADTH will remain confidential.

3.1 Advance Notification by the Sponsor

Sponsors must provide the pre-submission information requirements form before the anticipated date of filing the complete submission or resubmission. If a manufacturer, PAG, or a provincially recognized clinician-based tumour group wants to make a submission to CADTH, they must notify CADTH at least 120 calendar days in advance of an anticipated submission of their intent to submit. If a sponsor fails to meet the 120 calendar days advance notification requirement, a sponsor will be required to refile the pre-submission information with the corrected information and the time will be reset back to day zero for the sponsor until the requirement is fulfilled (i.e., the new starting date will be from the time of the receipt of the refiled date of the pre-submission requirement information form). If the anticipated received date falls on a weekend or statutory holiday, the following business day will be applied. The reset of the time will not apply to the updated information in the pre-submission requirement information form filed at the time of the submission or resubmission.

The information required by CADTH during the pre-submission phase is detailed in the pre-submission information requirements forms for [submissions](#) and [resubmissions](#). In order to ensure that the information remains secured, a sponsor must be registered with CADTH in order to access the form through the [Collaborative Workspaces](#).

Sponsors are required to advise CADTH of changes in the anticipated date of filing a submission or resubmission as soon as possible. Sponsors should confirm the targeted date of filing the complete submission or resubmission and the requested reimbursement criteria at least five business days prior to the posting date of a pending submission. Pending submissions and resubmissions are issued one month in advance of the anticipated filing date. If the sponsor does not confirm the targeted filing date and the requested reimbursement criteria in accordance with the above requirements, there may be a delay in the processing and review of the submission or resubmission as a result of the incomplete information filed by the sponsor.

3.2 Pre-submission Information

Pre-submission information is required by CADTH in order to optimize planning. A sponsor will be required to complete the pre-submission information requirements form using the online form. To meet the 120 calendar days advance notification requirements, all pre-submission information requirements must be completed using the online pre-submission information requirements form and submitted to CADTH. The pre-submission information requirements form will not be accepted if the mandatory fields are not completed. A sponsor will be required to refile the pre-submission information with the completed information and the time will be reset back to day zero for the sponsor until the requirement is fulfilled (i.e., the new starting date will be from the time of the receipt of the refiled date of the pre-submission information form). While some allowances may be made where information is not available to complete the economic section of the form, CADTH reserves the right to request further information be provided before scheduling a pre-submission meeting.

Tumour groups will need to work with one of their jurisdictional PAG members to bring forward their intention to make a submission or resubmission to CADTH through the completion of the pre-submission information requirements form. The PAG will assist in determining if the submission or resubmission would be of local or national scope before the tumour group would file a submission or resubmission.

Sponsors are requested to advise CADTH of changes in the anticipated date of filing a submission or resubmission as soon as possible. Sponsors should confirm the anticipated date of filing the complete submission or resubmission and the requested reimbursement criteria at least five business days prior to the posting date of a pending submission. Pending submissions are issued one month in advance of the anticipated filing date.

If the pre-submission information is not provided as outlined in this document or the anticipated submission or resubmission filing date is not confirmed in accordance with the above requirements, there may be a delay in the processing and review of the submission or resubmission by CADTH. The pre-submission information requirements form must be completed and updated at the time of filing a submission or resubmission to CADTH.

Sponsors should contact CADTH if they encounter difficulties obtaining the information necessary to complete the pre-submission information requirements form.

3.3 Pending Submission Requirements

Sponsors should confirm the targeted date of filing the complete submission or resubmission and the requested reimbursement criteria at least five business days prior to the posting date of a pending submission. Pending submissions are issued one month in advance of the anticipated filing date. Advance notice of this filing date will allow stakeholders to be notified and is intended to afford them sufficient time to prepare input on a pending submission.

Failure to provide the required Pre-submission Information or to confirm the anticipated filing date one month in advance may result in a delay in the processing and review of a drug Submission by CADTH.

3.4 Pre-submission Meetings

The purpose of a pre-submission meeting is to provide an opportunity for the sponsor to introduce a drug to CADTH. Information may be sought from CADTH on the submission or resubmission requirements for the drug, including the approach to the clinical and economic evaluation and a dialogue to gain insight into the potential need for CADTH to develop a provisional algorithm. Sponsors may also wish to discuss and clarify general requirements for a submission or resubmission and procedures for a specific drug or indication.

A pre-submission meeting will be scheduled by teleconference for each submission and resubmission, pending the completion of the pre-submission information requirements form. Sponsors may request an in-person pre-submission meeting with CADTH, but this will be limited to one meeting in a six-month period in order to ensure fair access to CADTH staff and relevant experts (if appropriate) involved in the review process. All pre-submission meetings will be scheduled for a maximum of up to one hour and sponsors are limited to one meeting per drug submission or resubmission.

Sponsors will be required to provide a completed pre-submission information requirements form in order to receive a pre-submission meeting date. Within five business days of receiving confirmation of the meeting date and time, the sponsor must provide CADTH with a draft meeting agenda and list of proposed attendees. CADTH will collaborate with the sponsor on the draft agenda and may include additional key topic areas to be discussed at the meeting. In these cases, CADTH will send the additional topics within five business days of receiving the draft agenda from the sponsor.

Five business days prior to the scheduled meeting, sponsors are required to provide a final agenda, the list of confirmed attendees and presentation slides to allow CADTH sufficient time to prepare for the discussion otherwise the meeting may be rescheduled without prejudice to the submission or resubmission.

3.5 Disclosure of Pre-submission Information

CADTH will treat all pre-submission information provided by the sponsor as non-disclosable. Details of the pre-submission information will be tracked internally by CADTH.

Updated pre-submission information must be provided to CADTH as part of the submission requirements, as described in section 6. Non-disclosable information in the updated pre-submission information requirements form that is provided at the time the submission or resubmission is filed, should be identified as outlined in the *Disclosure of Information Guidelines for the CADTH pan-Canadian Oncology Drug Review* (Appendix 1).

3.6 Public Notification by CADTH of a Pending Submission

Twenty business days prior to the anticipated date that the submission or resubmission will be filed, CADTH will post details of the pending submission or resubmission and issue an email communication to stakeholders. This will allow patient groups (or registered individual patient or caregiver in cases where there is no patient group) and registered clinicians time to prepare their input on the submission.

CADTH will post the drug name, the indication for review, and the funding conditions and/or criteria being requested by the sponsor of the pending submission, submission type (i.e., new drug or new indication), Notice of Compliance (NOC) status at the time of filing, the target submission date and a target deadline for receiving stakeholder input (i.e., patient group (or registered individual patients and caregivers when there is no patient group) and clinicians who are registered with CADTH. The posted information will be based on details provided in the pre-submission information requirements form, unless CADTH is otherwise notified by the sponsor. The deadline date for receiving patient group (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician input and other details are confirmed when the submission is received.

Once the submission or resubmission has been filed, CADTH posts the name of the drug under review, when it was received and a confirmed deadline date for receiving patient group (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician input and an email communication to stakeholders is issued.

If a submission or resubmission is not received based on the anticipated date, CADTH will modify the input deadline to ensure the review can benefit from the patient group (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician input and to not jeopardize the overall review timeline.

If there is a delay and the submission or resubmission is not received on the anticipated target date, the website will be updated to clarify that a delay has occurred. A new deadline for receiving patient group input (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician input will be confirmed on the website when the submission is received. Patient groups (or registered individual patient or caregiver in cases where there is no patient group) and registered clinicians should not submit their input until after the submission or resubmission has been received by CADTH and the deadline for input has been confirmed.

3.7 Pre-submission Planning

Prior to the submission or resubmission being received, CADTH will begin identifying resources for the review team such as notifying Clinical Guidance Panels and Economic Guidance Panel members and/or identifying additional expertise as needed on a review-specific basis.

3.8 Notifying the PAG and Collecting PAG Input

PAG input is used by CADTH as part of its review process and by pERC when formulating recommendations. PAG may submit information related to a drug under review by CADTH. A [template for submitting PAG input](#), related to enablers and barriers to implementation of recommendations is available on the CADTH website.

PAG will be notified by CADTH of an anticipated submission or resubmission when a sponsor has indicated their intent to file and has provided CADTH with the required pre-submission information form. CADTH will share pre-submission information with the PAG as they prepare their input for the drug under review.

4. Application and Screening Procedures

A submission to CADTH represents a submission to all participating drug programs. While these guidelines describe the information that CADTH requires to conduct the review of a drug, the individual participating drug programs may require more information to be submitted, for regulatory or decision-making purposes. The participating drug programs conduct an assessment of their own submission and will advise the sponsor on the completeness of their submission for their individual purposes. Sponsors will need to work with each of the participating drug programs to determine if their additional requirements. Please see for the [contact information for the participating drug programs](#) for complete details.

4.1 Content of the Submission

A submission or resubmission must adhere to the content, format, and organization guidelines stipulated described in section 6. If the submission or resubmission does not adhere to these guidelines, it will not be accepted for review by CADTH and will not enter in the review queue until the requirements are satisfied. The requirements for a submission or resubmission are generally the same for all sponsors. Select requirements may be waived at the discretion of CADTH, for example, if the sponsor is not the manufacturer of the drug under review and does not have access to all information required.

4.2 Filing a Submission

Sponsors are required to file submissions and resubmissions using the [Collaborative Workspaces](#). Sponsors who experience difficulties filing a submission or resubmission using Collaborative Workspaces should contact CADTH by email (requests@cadth.ca) for support or to arrange an alternate delivery method for the submission or resubmission requirements (e.g., by email or mailing a USB flash drive).

At the same time as filing a submission with CADTH, sponsors should contact individual participating drug programs, to determine if additional information is required. These individual drug programs will conduct their own assessment of the submission based on their specific requirements and applicable regulations.

4.3 Submission Tracking

The status of the review of all submissions, resubmissions, and requests for advice will be posted on the CADTH website including target dates in the review process such as the target pERC meeting date. See Table 3 for the type of information that is publicly tracked on the CADTH website as it becomes available.

In general, approximately one month prior to the anticipated submission date, after receiving confirmation from the sponsor to do so, CADTH will post details of a pending submission including the sponsor and the target submission date. Stakeholders will also be notified of the funding conditions and/or criteria being requested by the sponsor. This posting is essential to adequately notify stakeholders who may provide input into the review process. At a minimum, updates to project tracking information will occur weekly, but may be posted more frequently from time to time.

Table 3. Review Process Information Posted on the CADTH website

Brand Name
Generic Name
Tumour Type
Indication
Funding Request
Review Status
Pre-NOC Submission
NOC Date
Strength
Manufacturer
Sponsor
Submission Date
Submission Accepted for Review Date
Submission Type
*Stakeholder Input Deadline (target date)
Check-Point Meeting (target date)
pERC meeting (target date)
Initial Recommendation Issued (target date)
Feedback on Recommendation Deadline (target date)
Final Recommendation Issued (target date)
Notification to Implement Issued

* Patient groups (or registered individual patients and caregivers when there is no patient group) and clinicians who are registered with CADTH are eligible to provide input and feedback. Deadlines for input and feedback are by the end of the CADTH business day of the date noted.

4.4 Screening Submissions and Initiating the Review Process

4.4.1 Receipt of a Submission

Upon receipt of a submission or resubmission, CADTH will note the date and time the materials were received to identify the order in which it is screened. If the submission or resubmission is received by CADTH more than ten business days after the targeted filing date that was confirmed with CADTH one month prior to the submission or resubmission being filed, there may be a delay in the processing and review of the file, as previously secured review resources may need to be released to complete other reviews.

4.4.2 Screening a Submission or Resubmission

- Submissions and resubmissions are accepted on an ongoing basis and are screened in the order they are received.
- Collaborative Workspaces logs the date and time that applications for submissions and resubmissions 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 category 1 requirements.
- If the filed category 1 requirements for a submission or resubmission are deficient or require revision in order to meet the requirements, CADTH sends a notice to the sponsor advising what information needs to be included or revised in order to meet the requirements. Rescreening of category 1 requirements is completed by CADTH as soon as possible after receipt, but may take up to five days.
- Upon receipt of notification of a sponsor’s submission or resubmission, the drug plans may identify questions to be addressed in the review process and submit these to CADTH.
- On day 10 of the screening period, CADTH sends a letter to the sponsor advising whether or not the submission or resubmission requirements have been accepted for review.
- Following acceptance for review, the sponsor must also provide the category 1 requirements to all drug programs that require copies (please see for the [contact information for the participating drug programs](#) for complete details).

4.4.3 Accepting a Submission or Resubmission for Review

- If the submission or resubmission is accepted for review, CADTH will send an acknowledgement via email to the primary contact provided by the sponsor, and may include the target pERC meeting date and the target checkpoint meeting date. This information will also be posted on the CADTH website (see Table 3).
- When the submission or resubmission has been accepted for review, it is entered into the review queue, as described in section 4.4.4.
- When the review of a submission or resubmission has been initiated, CADTH will include the total fee payable by the sponsor. Fees will be charged at two process milestones for all submissions and resubmission. Please refer to the [Fee Schedule for CADTH Pharmaceutical Reviews](#) for additional information about the application fee schedules, milestones for payments and payment methods. CADTH’s Finance Department will issue an invoice for the proportion of the application fee owing. All CADTH application fees are due within 30 calendar days of receipt of an invoice.
- Sponsors should note that CADTH may request additional information even after a submission or resubmission has been accepted for review.

4.4.4 Order of Review

- Submissions and resubmissions are accepted on an ongoing basis. The date of receipt by CADTH is considered day zero for the purpose of calculating targeted time frames for the review.
- Target dates within the review process are then posted on the CADTH website. Only submissions and resubmissions that have been accepted for review are entered in the review queue.

- CADTH screens submissions and resubmissions in the order they are received, that is, on a “first-come, first-served” basis, and reviews are initiated based on the order in which they are accepted for review.
- In certain circumstances including, but not limited to, unavailability of review resources, CADTH may need to modify the order of placement on the pERC meeting agenda or to schedule the placement of a submission or resubmission on a pERC meeting agenda other than the posted targeted pERC meeting date.

CADTH can only accommodate a certain number of new submissions or resubmissions per pERC meeting. Even if a submission is targeted for deliberations at a certain pERC meeting, (as reported on the website), deliberations on a submission may be moved to the next possible pERC meeting.

Reasons for this include:

- times of peak activity
 - the number of submissions or resubmission on the meeting agenda
 - the complexity of submissions or resubmission on the meeting agenda
 - the number of reconsiderations of an initial recommendation
 - NOC or other category 2 requirements have not been received and assessed as complete
 - A delay in the review has occurred (see section 7.2).
- The assignment to the review queue and placement on the pERC meeting agenda are made jointly by CADTH and the pERC Chair. Consultation with the PAG is sought as required.
 - If a change is made to the target pERC meeting date for a submission, the sponsor will be notified and the CADTH website will be updated to reflect the new target pERC meeting date.

4.4.5 Initiation of a Review

- Upon initiation of the review, CADTH:
 - Provides the sponsor with a contact name within CADTH to whom all inquiries about that submission are to be directed.
 - Identifies issues, if any, related to the submission and communicates these to the sponsor.
 - Determines the appropriate approach for undertaking the review and develops a work plan for review of the submission.
 - Establishes a review team by identifying Clinical Guidance Panel members, Economic Guidance Panel members, methodological expertise and any additional expertise that may be required to conduct a pCODR review, based on the nature of the submission, and in consideration of the team members’ qualifications, expertise, and compliance with the [pCODR Conflict of Interest Guidelines](#).
 - Collates and forwards the PAG input on the submission to the review team, including recruited panel members.

4.5 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 [pCODR Conflict of Interest Guidelines](#).
- The review team is composed of individuals with methodological expertise (i.e., the methods team), members of the Clinical Guidance Panels and members of the Economic Guidance Panels.

- Additional expertise, including an ad hoc clinical panel with experience in the diagnosis and management of the condition for which the drug under review is indicated, may be required as determined by CADTH and/or the pERC Chair or PAG Chair.
- The names of members of a review team, including members of the ad hoc clinical panel or clinical leads who respond to the survey, will not be disclosed to the sponsor when communication with the sponsor is required, including at the checkpoint meeting.
- Names of individual panel members or individuals providing methodological expertise are not ascribed to individual clinical or pharmacoeconomic reports.

4.6 Disclosure of Information

CADTH is committed to providing an open and transparent drug review process and to the need to be accountable for its recommendations to patients and the public. As such, CADTH considers it essential to be able to outline the evidence upon which the pERC recommendations are made. In view of these principles, CADTH has outlined a general approach to managing the disclosure of information which is detailed in the *Disclosure of Information Guidelines for the pan-Canadian Oncology Drug Review* (see Appendix 1). During the submission screening, a high-level assessment will be conducted to determine if the information has been made disclosable (e.g., price of the drug and its relevant comparator[s], price of companion diagnostics, if applicable, submitted estimates of the incremental cost-utility or cost-effectiveness ratios, that is, the ICURs or ICERs) in order for the review to be accepted for review and proceed through the process. A more detailed assessment of disclosable and non-disclosable information is completed at the checkpoint meeting.

As a principle, it is expected that non-disclosable information within a submission or resubmission will be kept to a minimum. The definitions of disclosable information and non-disclosable information are outlined in the *Disclosure of Information Guidelines for the pan-Canadian Oncology Drug Review*. At the time of filing a submission or resubmission it is the responsibility of the sponsor to:

- Clearly highlight specific information in the submission or resubmission documents that is non-disclosable.
- Complete a [summary table](#) that identifies: the non-disclosable information, the location in the submission or resubmission, the exact wording of the non-disclosable information and the general justification for deeming it non-disclosable. The justification should identify which type of non-disclosable information is included, as defined in the *Disclosure of Information Guidelines for the pan-Canadian Oncology Drug Review*. This table is to be provided as a component of the submission or resubmission. If CADTH does not receive a completed table with a submission or resubmission or additional information filed by the sponsor, it will not be accepted for review.

Please refer to the *Disclosure of Information Guidelines for the pan-Canadian Oncology Drug Review* for definitions of disclosable information and non-disclosable information for the purposes of CADTH's review, requirements for sponsors, and detailed information on how non-disclosable information is managed by CADTH.

A sponsor is deemed to have consented to the Disclosure of Information Guidelines when it files a submission or resubmission or supplies other information related to the submission or resubmission to CADTH. The *Disclosure of Information Guidelines for the pan-Canadian Oncology Drug Review* constitute an agreement between CADTH and the sponsor.

5. Stakeholder Engagement

Patient group (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician input is used by CADTH as part of its process in reviewing drugs and by pERC in formulating funding recommendations. Registered patient groups (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician(s) are invited to submit information related to a drug submission under review by CADTH. The [pCODR Patient Engagement Guide](#) and a template for submitting patient group input and the [Patient Input Template](#) can be found on the CADTH website. For registered clinician(s), there will be a drug and indication specific template for clinician(s) to provide their input for each review. Patient groups (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician(s) are required to use the template on the CADTH website to submit their input.

Registered patient groups (or registered individual patient or caregiver in cases where there is no patient group) may submit patient-related information to CADTH. Please note that individual patient or caregiver input will not be accepted in cases where patient group(s) representing the particular tumour exist. In these cases, individual patients or caregivers who wish to provide input are encouraged to work with a patient group to have that group include the information in its submission. Individual patients or caregivers who wish to provide input on a drug or indication are encouraged to first contact CADTH for direction by emailing requests@cadth.ca.

Similarly, registered clinicians may submit information as set out in each designated *Registered Clinician Input on a Drug Review* template. Registered clinician(s) includes physicians who treat cancer patients (e.g., oncologist, urologist), oncology nurses and oncology pharmacists. Of note, the input from an oncology pharmacist and oncology nurse must be part of a joint submission with a registered physician treating the cancer indication. Registered clinician(s) who submit information on a specific drug and indication under review will not be eligible to participate as a Clinical Guidance Panel member for that same review. For each drug and indication under review, a clinician may only submit once (e.g., if a clinician submits an individual input, that clinician should not be included in a joint submission for that same drug and indication). Please note that comments may be attributed to a specific individual clinician and that registered clinicians who submit input will be identified as a contributor to the specific input. CADTH maintains the discretion to remove any information that may be out of scope of the review or not within the intent of the clinician input template.

- Patient groups (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician(s) must register with CADTH prior to submitting input on a drug review. Information on registration can be found on the CADTH website.
- Patient groups (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician(s) must submit input by the posted deadline date (within 10 business days of CADTH receiving a submission) in order that the information can be used by the review team to develop the review plan (i.e., protocol) – a critical step that takes place early in the review.
- Depending on how much time has passed since the original submission or previous resubmission had been filed with CADTH and the nature of the resubmission, patient groups (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician(s) may be notified of the receipt of the resubmission and invited to provide input.
- If patient groups (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician(s) are not notified and invited to provide input (e.g., in the event that only new cost information has been submitted), the most recent and relevant patient group (or registered

individual patient or caregiver in cases where there is no patient group) and registered clinician(s) input given on a previous submission related to the drug and indication under review will be provided to the review team to incorporate into the Clinical and pharmacoeconomic reports and to pERC for the purposes of their deliberations.

6. Requirements for Submissions and Resubmissions

- These requirements outline information that CADTH needs to undertake the clinical and economic reviews of oncology drugs. To expedite the screening of submissions or resubmissions for completeness and to facilitate the efficient use of documents, sponsors must provide the information in the order in accordance with the electronic file requirements (see Appendix 7).
- Submission requirements are subdivided into category 1, category 2, and additional information.
 - Category 1 information must all be included when the submission or resubmission is filed in order for the review to proceed.
 - Category 2 information is only applicable for submissions filed on a pre-NOC basis. Category 2 requirements must be provided to CADTH as soon as the NOC or NOC/c has been issued, and must be provided at least six business days prior to the targeted pERC meeting date. Please note any substantive changes (e.g., beyond minor edits and/or corrections) to the final Product Monograph compared to the draft Product Monograph will be deemed to be significant by CADTH and may result in the rescheduling of the posted targeted pERC meeting date. Depending on the nature, extent and complexity of the information, CADTH may need to adjust the timelines for the review. Category 2 requirements must be satisfied before the drug review is placed on the pERC agenda.
 - Additional Information includes information CADTH requires for completion of the review. CADTH may request additional information from Health Canada or the sponsor. The sponsor also has the responsibility of advising CADTH regarding any harm or safety issues, including both domestic and global alerts that may arise during the time that the Submission is under review. This may include any communiqués (e.g. “Dear Doctor” letters regarding harm and safety) and any confirmed labeling changes agreed to with international regulatory agencies (e.g., United States Food and Drug Administration [FDA], European Medicines Agency [EMA]) relevant to the submission while the submission is under review by CADTH.
- For all submission types, the clinical and pharmacoeconomic information provided should focus on the indication(s) to be reviewed by CADTH processes (unless otherwise specified).
- A brief description of the requirements for submissions and resubmissions is provided in Table 4 and Table 9, respectively. Detailed descriptions are provided in subsequent sections.
- Checklists describing the requirements for each type of submissions or resubmission can be found in Appendix 6. These checklists may assist sponsors in ensuring that all requirements have been included in the submission or resubmission.
- To expedite screening and for efficient use of documents throughout the review, sponsors must organize all submission information in the order prescribed in the category 1 requirements below and follow the electronic file folder format in Appendix 7.
- One copy of all category 1 requirements must be filed with CADTH as a single submission package and accepted for review by CADTH before it is initiated.

- Detailed descriptions of the information that comprise the category 1 requirements for submissions are described below. Specific requirements for a submission filed on a pre-NOC versus post-NOC basis are delineated in the descriptions that follow the table.
- The sponsor is responsible for ensuring that appropriate copyright permissions have been obtained for electronic copies of articles included in a submission or resubmission, to be shared among CADTH, the expert review committee, and the drug programs.

Table 4: Requirements for Submissions

Section	Specific Items and Criteria	Oncology Drug Review			
		Standard Review		Cell or Gene Review	
		Pre-NOC	Post-NOC	Pre-NOC	Post-NOC
General information	• Signed cover letter	Required	Required	Required	Required
	• Updated pre-submission information requirements form	Required	Required	Required	Required
	• Product monograph	Required	Required	Required	Required
	• Completed declaration letter template	Required	Required	Required	Required
	• Summary table listing non-disclosable information	Required	Required	Required	Required
Health Canada documentation	• NOC or NOC/c and Letter of Undertaking	Not required	Required	Not required	Required
	• Screening acceptance letter	Required	Not required	Required	Not required
	• Table of Clarimails or Clarifaxes	Required	Required	Required	Required
	• Copies of all Clarifaxes and responses	Required	Not required	Required	Not required
Efficacy, effectiveness, and safety information	• Common Technical Document sections 2.5, 2.7.1, 2.7.3, 2.7.4, and 2.7.6, or a statement indicating any section(s) are not available	Required	Required	Required	Required
	• Reference list and copies of key clinical studies	Required	Required	Required	Required
	• Study protocol for pivotal studies	Required	Required	Required	Required
	• Statistical analysis plan for pivotal studies	Required	Required	Required	Required
	• CONSORT diagrams	Required	Required	Required	Required
	• Clinical study reports for pivotal and key clinical studies	Required if filed on or after March 2, 2020			
	• Table of studies	Required	Required	Required	Required
	• Search strategies used to locate published studies	Required	Required	Required	Required
	• Reference list and copies of editorial articles and errata	Required	Required	Required	Required
	• Reference list and copies of new data	Required	Required	Required	Required
	• Reference list and articles for validity of outcomes	Required	Required	Required	Required
	• Indirect comparison with full technical report	May be required	May be required	May be required	May be required
Provisional algorithm	• Completed proposed place in therapy template	Required	Required	Required	Required
	• A reference list and copies of studies that address sequencing of therapies	Required	Required	Required	Required
	• Copy of the search strategy for sequencing of therapies	Required	Required	Required	Required

Section	Specific Items and Criteria	Oncology Drug Review			
		Standard Review		Cell or Gene Review	
		Pre-NOC	Post-NOC	Pre-NOC	Post-NOC
Economic information	• Pharmacoeconomic evaluation for the full population identified in the indication(s) to be reviewed by CADTH	Required	Required	Required	Required
	• Unlocked and fully executable economic model	Required	Required	Required	Required
	• Economic model supporting documentation	Required	Required	Required	Required
Budget impact analysis	• Aggregate pan-Canadian budget impact report	Required	Required	Required	Required
	• Aggregate pan-Canadian budget impact model	Required	Required	Required	Required
	• Supporting documentation used in budget impact analysis	Required	Required	Required	Required
Reimbursement status of comparators	• Completed template listing the reimbursement status of all relevant comparators	Required if filed on or after March 2, 2020			
Epidemiologic information	• Disease prevalence and incidence data	Required	Required	Required	Required
Pricing and distribution information	• Price per smallest dispensable unit to four decimal places	Required	Required	Required	Required
	• Method of distribution	Required	Required	Required	Required
Implementation plan	• Completed implementation plan template	Not required	Not required	Required	Required
Companion diagnostics	• Reference list and articles focused on clinical utility	May be required	May be required	May be required	May be required
	• Disclosable price	May be required	May be required	May be required	May be required
Category 2 requirements	• Signed cover letter	Required	Not required	Required	Not required
	• A copy of the NOC or NOC/c	Required	Not required	Required	Not required
	• Draft product monograph with tracked clinical and label review changes up to time of Health Canada approval	Required	Not required	Required	Not required
	• Clean and dated version of Health Canada–approved product monograph	Required	Not required	Required	Not required

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

6.1 Submission Requirements

6.1.1 General Information

a) Signed Cover Letter

A signed cover letter (an electronic signature is acceptable) from the sponsor, confirming that all the required information has been provided. It should also indicate:

- A clear description of the submission or resubmission being filed (i.e., category 1 requirements for post-NOC submission);
- The updated or new information that was not provided in the pre-submission information;
- The indication(s) to be reviewed by CADTH;
- A statement clarifying whether the submitted price is the current marketed price or the disclosable price that may become effective and disclosed following the release of the pERC Initial Recommendation;
- The names of the primary and backup contact(s) that CADTH can contact regarding the submission. [Note: the sponsor may designate the consultant(s) preparing the submission or resubmission as primary and/or backup contact(s)].

b) Updated Pre-submission Information Requirements Form

Pre-submission information requirements are outlined in section 3. Updates to pre-submission information should include but not be limited to:

- Revising any information that has changed since the pre-submission information was provided to CADTH, including all relevant comparators, which may include those that received an initial or final pERC recommendation, or are undergoing negotiations through the pan-Canadian Pharmaceutical Alliance, or is publicly funded including case-by-case funding.
- If a specific population has been defined in a submitted request for funding criteria, the rationale and supporting references for the specified population should be clearly identified.

c) Product Monograph

- Table 5 summarizes the product monograph requirements for submissions or resubmissions.
- 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 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 review 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 review committee, or the subsequent recommendation not reflecting the most currently available product monograph information relating to the drug under review.

Table 5: Requirements for Filing Product Monograph with CADTH

NOC Status	Submission Requirements
Pre-NOC	<ul style="list-style-type: none"> • At the time of filing the submission or resubmission: a copy of the most recent draft product monograph showing the company, drug brand, and non-proprietary names that correspond to the anticipated NOC. • As soon as available: <ul style="list-style-type: none"> ▪ 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 ▪ a copy of the clean and dated product monograph approved by Health Canada.
Post-NOC	<ul style="list-style-type: none"> • A copy of the most current version of the Health Canada–approved product monograph.

NOC = Notice of Compliance.

d) Declaration Letter

A completed [declaration letter template](#) 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 CADTH template, printed on company letterhead, and signed by an appropriate senior official.

e) Summary Table Listing Submitted Non-Disclosable Information

A completed [non-disclosable information template](#) submitted in Word format.

6.1.2 Health Canada Documentation

a) Health Canada NOC or NOC/c

Table 6 summarizes the NOC requirements for pre-NOC and post-NOC submissions.

Table 6: Requirements for Filing Notice of Compliance with CADTH

NOC Status	Submission Requirements
Pre-NOC	<ul style="list-style-type: none"> • 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 • 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)

NOC Status	Submission Requirements
	<ul style="list-style-type: none"> 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
Post-NOC	<ul style="list-style-type: none"> A copy of the NOC or NOC/c for the indication(s) for which the drug is to be reviewed by CADTH 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

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

b) Clarimails or Clarifaxes

Table 7 summarizes the requirements regarding Clarimails/Clarifaxes for pre-NOC and post-NOC submissions.

Table 7: Requirements for Filing Clarimails/Clarifaxes with CADTH

NOC Status	Submission Requirements
Pre-NOC	<ul style="list-style-type: none"> 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. 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. Copies of all Clarifaxes and responses to the point of the NOC or NOC/c being issued by Health Canada. As with all other documents provided to CADTH as part of the submission, specific information in the clarifaxes that may be potentially non-disclosable information must be clearly highlighted. 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.
Post-NOC	<ul style="list-style-type: none"> 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 point of the NOC or NOC/c being issued. 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.

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

c) Health Canada Screening Acceptance Letter

A copy of the Screening Acceptance Letter is required for all submissions filed on a pre-NOC basis indicating that an application has been accepted by Health Canada to review the drug of interest.

6.1.3 Efficacy, Effectiveness, and Safety Evidence

a) Common Technical Document

A copy of the Common Technical Document sections listed in Table 8 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 8: 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
2.7.6	Synopses of Individual Studies

b) Clinical Studies

- A reference list and copies of published and unpublished studies that address key clinical issues for the drug under review must be provided for all submissions. For all resubmission, the sponsor must provide a reference list and copies of all new clinical information that addresses specific issues identified by the expert review committee in the final recommendation document must be provided. Sponsors must include copies of any supplemental appendices that are associated with published studies.
- Head-to-head comparison clinical trials between the submitted drug product and principal comparators are of particular interest. If there are no head-to-head clinical trials, where possible, provide indirect data analyses comparing the drug under review to relevant comparators. While almost any study design may be considered, the pERC will, as part of the pERC Deliberative Framework, assess the level of uncertainty in trial results introduced by different study designs. *Note: Phase 1 studies and letters from clinicians should be not be provided.*
- The first file in the folder must be a reference list of the articles included in the folder.
- It is preferred that unpublished data are submitted in manuscript format; however, if unavailable in manuscript format, the following information should be included in clearly labelled sections:
 - Objective and rationale of study
 - Interventions
 - Study population (including eligibility criteria, baseline characteristics, and sample size)
 - Methods (including randomization method, blinding method, handling of withdrawals and drop-outs, allocation concealment, and outcome measurement)
 - Information about pre-planned extension of trial (if relevant)
 - Results (all beneficial and harmful patient effects, including an itemization of fatal and non-fatal serious adverse events; number of withdrawals and drop-outs with reasons; and measures of

dispersion, such as standard deviation or standard error, must be provided for continuous outcomes; numerators and denominators must be provided for dichotomous outcomes)

- Data analysis
- Conclusions

- Note: Unpublished information provided to CADTH will be managed according to the *Disclosure of Information Guidelines for the CADTH pan-Canadian Oncology Drug Review* (Appendix 1).

c) Study Protocol

A copy of the study protocol for the pivotal study(ies)

d) Statistical Analysis Plan

A copy of the statistical analysis plan for the pivotal study(ies)

e) CONSORT Diagrams

Diagrams following the CONSORT reporting standards or similar diagrams that document the flow of patients through the trials, identified as pivotal trials in Health Canada documentation. All information in the sections of the sample diagram is to be provided, including reasons for discontinuation and loss to follow-up at each stage of the study. If applicable, the following are to be incorporated into the CONSORT or similar diagram:

- Additional phases of the study (e.g., screening, washout, baseline, treatment, follow-up) and reasons for discontinuing between phases;
- Assessments at different time points and reasons for discontinuing between time points; and
- Analysis populations for each outcome if they differ (primary outcome, key secondary outcomes, harms) and reasons why patients were excluded from each outcome analysis.

f) Editorials and errata

A reference list and copies of editorials and errata 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.

g) 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. 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. If no new data are available, a placeholder document with a statement confirming this must be provided.

h) Validity of Outcome Measures

A reference list and copies of references supporting the validity of outcome measures (e.g., appropriate references could include disease dependent information that are informed by literature or key opinion leaders research, as well as numerous cancer-related research consortia that can be referred to for guidance) in studies (if available). If no references are provided, a statement is required to confirm that a search has been undertaken but no references have been located.

i) Table of Studies

A tabulated list of all published and unpublished clinical studies using the [table of studies template](#) must be provided. 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 [Collaborative Workspaces](#). 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 review committee. The sponsor will be apprised of any revisions to the anticipated timelines for the review.

j) Search Strategies

Search strategies used to locate published studies in medical literature databases. All search terms that were used (i.e., MESH headings and keywords) and the names of databases (e.g., MEDLINE, EMBASE, Cochrane, etc.) that were searched are required. Search results are not required.

k) 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.

6.1.4 Economic Information

a) Pharmacoeconomic Submission

The pharmacoeconomic submission for all submissions and resubmissions (with the exception of tailored reviews) consists of the following:

- a technical report of the pharmacoeconomic evaluation
- an economic model
- a technical report of the budget impact analysis
- a budget impact model
- any supporting material relevant to the pharmacoeconomic submission.

The technical reports of the pharmacoeconomic evaluation and budget impact analysis 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.

The economic submission (pharmacoeconomic evaluation and electronic model) should be undertaken in accordance with CADTH’s [Guidelines for the Economic Evaluation of Health Technologies: Canada \(4th edition\)](#).

b) Pharmacoeconomic Evaluation: Technical Report

The pharmacoeconomic evaluation must address the following requirements (which are summarized in the checklist provided in Appendix 4):

- The pharmacoeconomic analysis must be in the form of a cost-utility analysis. Only one type of economic evaluation should be submitted. While the submission must be in the form of a cost-utility analysis, life-years should be reported as part of the pharmacoeconomic evaluation.

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- 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.
 - The base case, and all scenario analyses must be conducted probabilistically.
 - The perspective of the publicly funded health care payer must be used in the base case.
 - A discount rate of 1.5% for both costs and quality-adjusted life-years (QALYs) must be used in the base case.
 - All relevant comparators, including treatments that are currently used off-label in Canadian practice must be included in the base case (and scenario analysis for the reimbursement request). If potentially relevant comparators are excluded from the pharmacoeconomic submission, CADTH may request that the sponsor include these comparators during the review process. CADTH may identify missing comparators during the screening phase and the submission will not be accepted for review. However, in some situations the absence of one or more relevant comparators may not be apparent until the submission has been accepted for review and initiated by CADTH. In these situations, CADTH will notify the sponsor regarding the deficiency and the timelines of the review may be affected (i.e., may result in the submission targeting a later meeting of the expert review committee).
 - If more than one comparator is included, results must be reported using a sequential analysis which indicates where the drug lies on the cost-effectiveness efficiency frontier. A suggested reporting format is presented in Appendix 3.
 - For submissions in which there are model inputs based on analysis of survival data, the sponsor must provide the Kaplan-Meier curve for each outcome, alongside the parametric distributions tested for model fit.
 - Results of the sponsor's base case and scenario analysis for the reimbursement-requested population (if different to 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) and by QALYs (e.g., benefits generated in each health or event state, benefits generated during the trial period versus the extrapolation period) must be reported based on the probabilistic results. A suggested reporting format is presented in Appendix 3.
 - Composite outcomes are generally not satisfactory to inform treatment effect estimates used in a pharmacoeconomic evaluation. Sponsors should base their pharmacoeconomic evaluation on the 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 submission targeting a later meeting of the expert review committee).
 - 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.

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- The specific price(s) submitted to CADTH for the lowest dispensable unit (to four decimal places) must be used in the sponsor's base-case analysis.

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

For additional information on the reporting of results and details of the pharmacoeconomic evaluation, sponsors should refer to the *Analysis and Reporting* sections of the [Guidelines for the Economic Evaluation of Health Technologies: Canada \(4th edition\)](#), as well as the [worked example](#).

c) Economic Model

The economic model must address the following requirements:

- An unlocked version of the electronic 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 model must be able to function in a standalone environment not requiring 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, 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.
- The 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 more than one 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 and report the analysis results sequentially.
- For submissions that use survival data, the sponsor's model must be flexible to easily assess all parametric distributions tested by the sponsor (at minimum, the distributions tested must include: Weibull, Gompertz, Exponential, Log-normal, Log-logistic, Generalized gamma, and Gamma). If any of these distributions are not possible, an acceptable rationale for exclusion must be provided. The sponsor should include one graph that is flexible to present the observed Kaplan-Meier curves and all fitted distribution curves assessed for each treatment and each survival outcome.
- 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 one business day (8 hours) it will be considered by CADTH to be excessive and will not be accepted by CADTH. Run time is determined by CADTH based on CADTH computing powers.

Deviations from these requirements must be discussed with, and accepted by CADTH, in advance of filing the submission. Please submit the following [template](#) to requests@cadth.ca with complete details of any proposed deviations from the requirements.

d) Budget Impact Analysis: Technical Report

The budget impact analysis must address the following requirements (which are summarized in the checklists provided in Appendix 4):

- The base case must reflect a pan-Canadian (national) drug program perspective (excluding Quebec), which should be derived from the following individual drug programs participating in CADTH's drug reimbursement review processes (i.e., British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador, and the Non-Insured Health Benefits Program).
- The base case must reflect the complete population identified in the Health Canada-approved indication for which the drug is being submitted to CADTH. If a sponsor is requesting reimbursement for a specific subgroup of the indicated population, or if there are any relevant subgroups, or potential for off-label use, 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 on which the budget impact analysis is based, the review may be suspended until a revised pharmacoeconomic submission reflecting the approved indication is provided.
- When forecasting the budget impact of a new treatment, four years of data must be presented: a one-year baseline period and a three-year forecast period in the base case. The base-case analysis must report costs by year. Discounting should not be applied within the budget impact analysis.
- Results should 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 budget impact analysis. In accordance with the economic evaluation, CADTH may determine that potentially relevant comparators were excluded from the pharmacoeconomic submission.
- The specific price(s) submitted to CADTH for the lowest dispensable unit (to four decimal places) must be used in the sponsor's base case.
- The technical report must incorporate a decision problem, methods, assumptions, and results that align with the submitted budget impact model.

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 budget impact analysis. 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 budget impact analysis (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.
- A scenario analysis must be presented that considers a broader Canadian health care-payer perspective for the following technologies:

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- 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 three 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, etc. if significant) should be considered.

e) Budget Impact Model

An unlocked version of the electronic budget impact model used in the technical report of the budget impact analysis is a requirement. Additional requirements include:

- The budget impact model must be programmed in Excel.
- The model must be able to function in a standalone environment not requiring 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.
- The BIA model must be flexible enough to be applied to the context of any of the individual participating drug programs, which may differ with respect to the funding of comparators or the design of the program responsible for drug reimbursement. 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.

Deviations from these requirements must be discussed with and accepted by CADTH in advance of filing the submission. Please submit the following [template](#) to requests@cadth.ca with complete details of the deviations from these requirements.

f) 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 (as a separate document) 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. In this document, please note the expected model run time.
- The full technical report of the indirect treatment comparison(s) (ITC), if one or more ITC 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 budget impact analysis. This includes but is not limited to

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 provide details of how input parameter values were derived, including a description of the study or data set, the analysis plan, and results of the analyses. Any modification or transformation of the results to use in the economic model must be described.
- 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.

6.1.5 Pricing and Distribution Information

a) Submitted Price

- The submitted price for the drug, reported to four 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 plans following completion of CADTH's review process.
- CADTH does not accept confidential submitted prices for drugs reviewed through the drug reimbursement review processes. The submitted price is disclosed in all applicable CADTH reports.
- Only one price (anticipated or current market price) to four decimal places per smallest dispensable unit is to be submitted per drug that is to be reviewed by CADTH (i.e., only one price for all indications undergoing review by CADTH concurrently).
- The submitted price must be used in the pharmacoeconomic evaluation and in the budget impact analysis (BIA) (budget impact reports and the models used to produce the results).
- The price(s) of other treatments included in the pharmacoeconomic evaluation and in the BIA (e.g., comparators, concomitant medications, etc.) are not considered to be confidential and may be disclosed by CADTH.

b) Method of Distribution

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

6.1.6 Provisional Algorithm

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 sequencing of therapies in relation to the drug under review, including the search strategy for those studies.

c) Search Strategy for Studies Addressing the Sequencing of Therapies

Search strategies for sequencing of therapies should include all search terms that were used (i.e., MESH headings and keywords) and the names of databases (e.g., MEDLINE, EMBASE, Cochrane, etc.) that were searched are required.

6.1.7 Reimbursement Status of Comparators

A completed [template](#) summarizing the reimbursement status of all appropriate comparators (for all submissions filed on or after March 2, 2020).

6.1.8 Implementation Plan for a Cell or Gene Therapy

A completed a [implementation plan template](#) that describes key aspects of their plans for implementing the product in Canada.

6.1.9 Companion Diagnostics

a) 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.

b) Price of Companion Diagnostic

The disclosable price for the companion diagnostic(s) must also be provided.

6.1.10 Category 2 Requirements at Time of NOC or NOC/c

Category 2 information must be provided to CADTH as soon as the NOC or NOC/c has been issued to allow the review to be completed without delay, and must be provided at least six business days prior to the targeted pERC meeting date. Any substantive changes (e.g., beyond minor edits and/or corrections) to the final product monograph compared to the draft product monograph will be deemed to be significant by CADTH and may result in the rescheduling of the posted targeted pERC meeting date. Depending on the

nature, extent and complexity of the information, CADTH may need to adjust the timelines for the review. Category 2 requirements must be satisfied before the drug review is placed on the pERC agenda.

a) Signed Cover Letter

A signed cover letter (an electronic signature is acceptable) from the sponsor, confirming that all the required information has been provided. It should also indicate:

- A clear description of the documents being filed (i.e., category 2 requirements for a submission filed on a pre-NOC basis);
- the date the NOC or NOC/c was received;
- Intention to provide any remaining category 2 requirements as soon as the NOC or NOC/c has been issued to allow the review to be completed without delay, and must be provided at least six business days prior to the targeted pERC meeting date. Any substantive changes (e.g., beyond minor edits and/or corrections) to the final product monograph compared to the draft product monograph will be deemed to be significant by CADTH and may result in the rescheduling of the posted targeted pERC meeting date. Depending on the nature, extent and complexity of the information, CADTH may need to adjust the timelines for the review. Category 2 requirements must be satisfied before the drug review is placed on the pERC agenda.

b) Health Canada NOC or NOC/c

A copy of the NOC or NOC/c, dated and signed by Health Canada, as soon as it has been issued.

c) Product Monograph

The Health Canada-approved final product monograph (showing the date it was approved by Health Canada) and the company and product names that correspond to the NOC or NOC/c should be provided at the time of NOC or NOC/c, to allow the review to proceed as quickly as possible. The final product monograph should be accompanied by a version showing the revisions (with track changes visible). This is required so that review team members are able to focus on any changes that may have occurred from the initially provided version and the final labelling.

6.2 Additional Information

The following additional information may be requested by CADTH, and is assessed on a case-by-case basis. Additional Information is information CADTH requires for completion of the review and generally pertains to design, methodology and clinical data results. CADTH may request additional information from Health Canada or the sponsor. The Sponsor also has the responsibility of advising CADTH regarding any harm or safety issues, including both domestic and global alerts that may arise during the time that the submission is under review. This may include any communiqués (e.g. “Dear Doctor” letters regarding harm and safety) and any confirmed labeling changes agreed to with international regulatory agencies (e.g. FDA, EMA) relevant to the drug under review by CADTH.

Examples of additional information that may be requested are provided below.

6.2.1 Health Canada Documentation

a) Health Canada Reviewers' Report

CADTH may request the Health Canada reviewers' report for each submission or resubmission. To avoid delays in providing the report to CADTH, manufacturers are encouraged to request the report from Health Canada as soon as they are assured that a NOC or NOC/c will be issued and to forward it immediately to CADTH upon receipt.

b) Copies of Clarifaxes/Clarimails

CADTH may request copies of Clarifaxes/Clarimails concerning the drug under review (*Note: Clarifaxes on animal toxicology and chemistry, and/or manufacturing and control may not be relevant; it is up to the sponsor to determine whether or not these Clarifaxes/Clarimails have an impact on labelling for use in humans*).

6.2.2 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 should be provided in searchable electronic format (i.e., PDF or Microsoft Word).

6.2.3 Revised Economic Requirements

a) Revised economic model and report

CADTH may request the sponsor to provide an updated economic model and report based on clarification requests during the review. In these cases, the sponsor must provide both a clean and track changed version of the updated report, as well as a revised structured summary of economic information.

b) Revised budget impact analysis model and report

CADTH may request the sponsor to provide an updated budget impact analysis model and report based on clarification requests during the review. In these cases, the sponsor must provide both a clean and track changed version of the updated report, as well as revised structured summary of economic information.

All additional information provided will be managed in accordance with *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review* (Appendix 1).

Providing this information does not affect the review queue; however, if there is a delay in providing it or if the quantity and complexity of the requested information is significant, there may be a consequent delay in completion of the review.

Note: For additional information received during the review, please contact individual drug programs to see if they require this information as part of their submission.

6.3 Resubmission Requirements

Table 9 identifies the type of information that the sponsor must provide in filing a resubmission.

Table 9: Requirements for all Resubmissions

Section	Specific Items and Criteria
General information	<ul style="list-style-type: none">Signed cover letter

Section	Specific Items and Criteria
	<ul style="list-style-type: none"> • Product monograph • Completed declaration letter • Updated pre-submission information requirements form • Summary table listing non-disclosable information
New efficacy and/or safety information	<ul style="list-style-type: none"> • Reference list and copies of new clinical studies and errata • Updated table of studies • Search strategies used to locate published studies • Clinical study reports for new clinical studies (if filed on or after March 2, 2020) • Status of confirmatory studies for drug with NOC/c • Most recent interim analysis of confirmatory studies for drug with NOC/c • CONSORT diagrams
Provisional algorithm	<ul style="list-style-type: none"> • Completed proposed place in therapy template • A reference list and copies of studies that address sequencing of therapies • Copy of the search strategy for sequencing of therapies
Economic information	<ul style="list-style-type: none"> • New pharmacoeconomic evaluation for the full population identified in the indication(s) to be reviewed by CADTH • Unlocked and fully executable economic model
Budget impact analysis	<ul style="list-style-type: none"> • Aggregate pan-Canadian budget impact report • Aggregate pan-Canadian budget impact model • Supporting documentation used in budget impact analysis
Reimbursement status of comparators	<ul style="list-style-type: none"> • Completed template listing the reimbursement status of all relevant comparators • Reimbursement status of the drug under review
Pricing and distribution information	<ul style="list-style-type: none"> • Submitted price per smallest dispensable unit to four decimal places • Method of distribution
Companion diagnostics (if applicable)	<ul style="list-style-type: none"> • Reference list and articles focused on clinical utility • Disclosable price

6.3.1 General Information

a) Signed Cover Letter

A signed cover letter (an electronic signature is acceptable) from the sponsor, confirming that the information is new and stating the anticipated change or outcome. The letter should also provide:

- the rationale for the resubmission;
- The indication(s) to be reviewed by CADTH;
- A statement clarifying whether the submitted price is the current marketed price or the disclosable price that may become effective and disclosed following the release of the pERC Initial Recommendation;
- the names of the primary and backup contact(s) CADTH can contact regarding the resubmission.

b) Updated Pre-submission Information Requirements Form

Pre-submission information requirements are outlined in section 3. Updates to pre-submission information should include but not be limited to:

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- Revising any information that has changed since the pre-submission information was provided to CADTH, including all relevant comparators, which may include those that received an initial or final pERC recommendation, or are undergoing negotiations through the pan-Canadian Pharmaceutical Alliance, or is publicly funded including case-by-case funding.
 - If a specific population has been defined in a submitted request for funding criteria, the rationale and supporting references for the specified population should be clearly identified.

c) Product Monograph

- A copy of the most current version of the Health Canada–approved product monograph.
- 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 temporary suspension of the review.

d) Declaration Letter

A completed [declaration letter template](#) 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 CADTH template, printed on company letterhead, and signed by an appropriate senior official.

e) Summary Table Listing Submitted Non-Disclosable Information

A completed [non-disclosable information template](#) providing a summary of non-disclosable information that has been included in the submission to CADTH. Please ensure that this information is submitted in a Word format.

f) Product Monograph

A copy of the most recent product monograph, showing the date it was approved by Health Canada and the company and product names that correspond to the NOC or NOC/c.

6.3.2 New Clinical Information

a) List and Copies of New Clinical Information

- A list of all new information not included in the original submission, or previous resubmissions, which is being included in the current resubmission
- Copies of all new information and supporting documentation.
- Note: As per the pCODR Disclosure of Information Guidelines, information that the sponsor determines may be Non-Disclosable Information and that is provided in any of these documents must be specifically identified by highlighting and should be listed in the [Summary Table Listing Submitted Non-Disclosable Information](#).

b) Information if Drug has a Notice of Compliance with Conditions (NOC/c)

- Status of the confirmatory studies listed in the Letter of Undertaking if the resubmission is for a drug with an NOC/c.
- Most recent interim analysis results for confirmatory studies listed in the Letter of Undertaking.

c) CONSORT Diagrams

Diagrams following the CONSORT reporting standards or similar diagrams that document the flow of patients through the trials, identified as pivotal trials in Health Canada documentation. All information in the sections of the sample diagram is to be provided, including reasons for discontinuation and loss to follow-up at each stage of the study. If applicable, the following are to be incorporated into the CONSORT or similar diagram:

- Additional phases of the study (e.g., screening, washout, baseline, treatment, follow-up) and reasons for discontinuing between phases;
- Assessments at different time points and reasons for discontinuing between time points; and
- Analysis populations for each outcome if they differ (primary outcome, key secondary outcomes, harms) and reasons why patients were excluded from each outcome analysis.

d) Table of Studies

An updated tabulated list of all published and unpublished clinical studies using the [table of studies template](#) must be provided.

e) Search Strategies

Search strategies used to locate published studies in medical literature databases. All search terms that were used (i.e., MESH headings and keywords) and the names of databases (e.g., MEDLINE, EMBASE, Cochrane, etc.) that were searched are required. Search results are not required.

6.3.3 New Economic Information

The requirements for economic information in a resubmission are the same as those required for submissions. Please refer to the requirements outlined in section 6.1.4.

6.3.4 Pricing and Distribution Information

The requirements for pricing and distribution in a resubmission are the same as those required for submissions. Please refer to the requirements outlined in section 6.1.5.

6.3.5 Reimbursement Status

a) Reimbursement Status of Comparators

A completed [template](#) summarizing the reimbursement status of all appropriate comparators (for all submissions filed on or after March 2, 2020).

b) List of Funding Decisions by CADTH Participants

A summary of the funding status of the Drug by all participating Federal drug plans, P/T Ministries of Health and Provincial Cancer Agencies at the time of the resubmission, including all funding conditions and/or criteria if applicable.

6.3.6 Companion Diagnostics

The requirements for companion diagnostics in a resubmission are the same as those required for submissions. Please refer to the requirements outlined in section 6.1.9.

7. Review Procedures

Clinical and economic review procedures include all those procedures related to preparing the CADTH review reports.

7.1 Standard Review

7.1.1 Clinical Review

A review team prepares an evidence-based clinical report based on material provided by the sponsor, studies identified through independent systematic literature searches and input on the submission provided by the PAG, by registered patient groups (or registered individual patient or caregiver in cases where there is no patient group), registered clinician(s) and input from additional expertise, including the ad hoc clinical panel or clinical leads affiliated with provincial cancer agencies.

- The methods team and the Clinical Guidance Panel develop a review plan, also known as the protocol, for the review of the submission. Input on the protocol may be provided by PAG, pERC members, the Economic Guidance Panel and other experts, as required. The review team considers the patient-important outcomes and issues identified through patient group (or registered individual patient or caregiver in cases where there is no patient group) input when developing the protocol. Similarly, input from registered clinician(s) is also considered when developing the protocol.
- The methods team conducts an independent systematic literature search in line with the protocol to supplement the data provided in the submission. Guidance and clarifications are sought from the Clinical Guidance Panel on an on-going basis and as required.
- Relevant information provided through patient group (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician input is summarized and included in the clinical report. Input on key implementation issues.
 - Submitted patient group (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician input is summarized by CADTH and forwarded to the review team to use in the development of the review protocol.
 - The patient group (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician input are each incorporated into their own sections in the clinical report.
 - Any identifying personal information will be removed prior to sharing the patient group input (or registered individual patient or caregiver in cases where there is no patient group).
- Relevant information provided through PAG input is summarized and included in the clinical report.
 - Submitted PAG input is summarized by CADTH and then finalized by the PAG. This summary is forwarded to the review team to use in the development of the review protocol.
 - The PAG input is incorporated into its own section in the clinical report.
- The methods team summarizes and critically appraises the relevant information provided in the submission and identified through the independent literature search.
- The Clinical Guidance Panel members review the information summarized by the methods team and provide in the clinical report an interpretation of the systematic review results and clinical guidance for consideration by the pERC.

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- Regular and frequent interactions occur amongst the members of the review team throughout the process regarding the review of the submission.
 - For submissions that are filed on a pre-NOC basis, the clinical report may be revised to reflect the final product monograph or other information that is received when the NOC or NOC/c has been issued.

7.1.2 Economic Review

The Economic Guidance Panel reviews and appraises the pharmacoeconomic information provided in the submission, with input from the Clinical Guidance Panel and other members of the review team. The results, interpretation and guidance provided in the clinical report, as well as PAG input, patient group (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician input, where applicable and available, are used in the assessment of the pharmacoeconomic information provided in the submission. The pharmacoeconomic report is completed in accordance with a [standardized template](#).

- The Economic Guidance Panel determines whether the submitted pharmacoeconomic evaluation is supported by the clinical evidence. Results provided by the sponsor are confirmed, using the supplied economic model. When relevant, the model is rerun and revised cost-effectiveness estimates are determined.
- The Economic Guidance Panel identifies the assumptions and limitations in the submitted budget impact analysis.
- CADTH prepares cost comparison tables with support from the Economic Guidance Panel.
- The Economic Guidance Panel considers the relevant information provided through patient group (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician input, where applicable.
- Submitted patient group (or registered individual patient or caregiver in cases where there is no patient group) input is summarized and forwarded along to the Economic Guidance Panel to guide the evaluation of the submitted economic model and the assessment of the assumptions made in the submitted budget impact analysis.
- The patient group (or registered individual patient or caregiver in cases where there is no patient group) input relevant to the economic evaluation is incorporated as appropriate, and into the pharmacoeconomic report.
- The registered clinician input relevant to the economic evaluation is incorporated as appropriate, and into the pharmacoeconomic report.
- Relevant information provided through PAG input is summarized and included in the pharmacoeconomic report.
- Submitted PAG input is summarized by CADTH and then finalized by the PAG. This summary is forwarded to the Economic Guidance Panel to guide the evaluation of the submitted economic model and the assessment of the assumptions made in the submitted budget impact analysis.
- The PAG input relevant to the economic evaluation is incorporated as appropriate, and into the pharmacoeconomic report.
- The Economic Guidance Panel prepares the pharmacoeconomic report, reflecting its findings.

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- For submissions that are filed on a pre-NOC basis, the pharmacoeconomic report may be revised to reflect the final product monograph or other information that is received when the NOC or NOC/c has been issued.

7.2 Resubmissions

CADTH determines the nature of the resubmission, that is, if it is based on new cost information or new clinical information. If the resubmission is based on new cost information that significantly impacts the cost-effectiveness of the drug and does not form part of the original submission or previous resubmission, a pharmacoeconomic report will be prepared but a clinical report may not be prepared. If the resubmission is based on new clinical information that will affect the cost-effectiveness of the drug, the sponsor must also provide a new appropriate pharmacoeconomic evaluation and CADTH will prepare clinical and pharmacoeconomic reports.

CADTH reviews the resubmission and relevant documents that relate to the previous submission or resubmission reviewed for that drug, including the review reports, if any, and the pERC Final Recommendation, if issued.

7.2.1 Clinical Review

Procedures applied to conducting the standard clinical review for submissions (as described in section 7.1.1) typically apply to the review of resubmissions. In addition:

- The review team determines if a new systematic review is required and determines the appropriate approach to assess the new information.
- An independent literature search is conducted to identify any new relevant information and to supplement the data provided by the sponsor.

7.2.2 Economic Review

Procedures applied to conducting the economic review for submissions (as described in 7.1.2) typically apply to the review of resubmissions. In addition, if a clinical report is not prepared because the resubmission is based only on new cost information, the Economic Guidance Panel refers to the results and conclusions reported in the previous clinical report on that drug in the assessment of the submitted pharmacoeconomic information.

7.3 Cell or Gene Therapy Review

7.3.1 Clinical Review

The clinical review processes will be completed in accordance with CADTH's standard review procedures for oncology drugs as described in section 7.1.1.

7.3.2 Economic Review

The economic review process will be completed in accordance with CADTH's standard review procedures for oncology drugs as described in section 7.1.2; however, there will be additional consideration of a pan-Canadian budget impact analysis.

7.3.3 Implementation Plan Review

Sponsors will be required to complete a [template](#) with key details about their plans to implement the drug in the Canadian system. The drug plans 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 participating jurisdictions to reflect on potential implementation issues and corresponding mitigation strategies in an efficient manner.

7.3.4 Ethics Review

CADTH will identify and describe relevant ethical issues based on published and grey literature. 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. The ethics review will provide expert review committee with an overview of ethical considerations to inform their deliberations.

7.4 Checkpoint Meetings

- A checkpoint meeting with the sponsor will be held during the review. The purpose of the checkpoint meeting with the sponsor is:
 - (1) to directly clarify information in the submission or resubmission and any additional information being provided with members of the CADTH review team; and
 - (2) to discuss the management of non-disclosable information included in the submission or resubmission.

The checkpoint meeting is not for the purposes of confirming information that the CADTH review team will include in the report or to solicit the review team's interpretation of the submission. If procedures relating to the checkpoint meeting are not followed as outlined here in the *Procedures for the CADTH pan-Canadian Oncology Drug Review*, the review of the submission may be delayed or suspended.

- When a submission or resubmission is accepted for review, the sponsor will be notified of the target checkpoint meeting date. When notified of this date, the sponsor must contact CADTH to schedule the checkpoint meeting.
- If a checkpoint meeting is not held by the target date, CADTH cannot guarantee the review will be completed within the posted timelines and/or the review may be temporarily suspended.
- If the sponsor is not the manufacturer of the drug under review and the manufacturer has contributed substantive clinical or economic information to the review, the manufacturer may be invited to attend the checkpoint meeting with the sponsor.
- The checkpoint meeting will occur in two parts and the objective of each part of the meeting differs. Part one of the checkpoint meeting will be to clarify information in the submission or resubmission and any additional information being provided. Part two of the checkpoint meeting will be to discuss the management of non-disclosable information included in the submission or resubmission. Generally, part one and part two of the checkpoint meeting will be scheduled consecutively (with a short break in between), to minimize sponsor travel obligations.
- The checkpoint meeting will occur as a teleconference or in a webinar format with the review team to maintain their anonymity. CADTH will disclose a general list of individuals involved in reviews but will make best efforts to not divulge specific review teams as outlined in section 4.5. The anonymity of the review team is preserved by CADTH in order to protect CADTH participants from undue influence, to maintain the integrity of assessments without fear of reprisal and to limit the potential for harassment and intimidation of review team members in their professional capacity. The sponsor must not attempt to identify members of the review team during or any time after the interactive meeting. Both part one and

part two of the meeting will be recorded by CADTH and a record of the meeting will be retained on file at CADTH.

- Following the meeting, CADTH will provide the meeting attendees with a record of decisions from the meeting via email. Decisions will include both those related to additional information and clarification of the submission or resubmission as well as the review of non-disclosable information in the submission. The record of decisions may be shared with authorized recipients, as defined in the *Disclosure of Information Guidelines for the CADTH pan-Canadian Oncology Drug Review*.

7.4.1 Additional Information and Clarification of the submission

- While conducting the clinical and economic reviews, the review team considers whether it needs additional information from the sponsor or requires further clarification of information provided in the submission. If so, CADTH will compile a list of questions and provide them to the sponsor 10 business days in advance of the scheduled checkpoint meeting. If, when the need for additional information is identified by the review team and is determined to be time-sensitive information, CADTH will not wait until the checkpoint meeting but will contact the sponsor as soon as possible.
- At the checkpoint meeting, the sponsor will have an opportunity to provide responses to the clarifying questions and the request for additional information, which were provided 10 business days in advance by CADTH.
- An electronic version of the sponsor responses to the clarifying questions and requests for additional information must be provided to CADTH at least one business day in advance of the scheduled checkpoint meeting so that these can be provided to the review team prior to the interactive meeting to allow the review team sufficient time to review the responses.
- Any additional information provided to CADTH at this checkpoint meeting is subject to the *Disclosure of Information Guidelines for the CADTH pan-Canadian Oncology Drug Review*. Thus, the sponsor must also provide a supplement to the Summary of Non-Disclosable Information table that identifies any non-disclosable information included in the additional information. This supplementary table will be discussed during the review of non-disclosable information component of the checkpoint meeting.
- Attendees from CADTH can include CADTH staff, Clinical Guidance Panel members, Economic Guidance Panel members and individuals with methodological expertise who are assigned to the review team.
- Both parts of the checkpoint meeting will occur as a teleconference or in a webinar format. Sponsor attendees should include individuals with clinical and economic content expertise who will be able to provide adequate clarification to the review team. Sponsor attendees may differ for part one and part two of the meeting. No legal representation is permitted at the checkpoint meeting. The sponsor should select relevant attendees based on the nature and type of questions posed by CADTH; relevant attendees may be external to the sponsor's organization if necessary. A list of attendees must be provided to CADTH at least five business days in advance of the meeting, otherwise the meeting may be rescheduled to a later date and the overall review timelines will be adjusted.
- Members of the review team will be present at checkpoint meeting and anonymous communication between the review team and the sponsor will be facilitated by CADTH.
- The duration of part one of the checkpoint meeting will be a maximum of one hour. Sponsors will be provided with approximately 30 minutes to present responses to the submitted questions. The remainder

of the meeting will allow for further clarifications based on the submitted questions and presented responses.

- Sponsors should limit questions to topics raised in the list of submitted questions. Questions outside the scope of the checkpoint meeting will not be addressed at the meeting.
- Any delays in providing additional information requested by the review team may result in a corresponding delay in the completion of the review.

7.4.2 Review of Non-Disclosable Information in the submission

- At part two of the checkpoint meeting, CADTH staff and the sponsor will discuss the management of non-disclosable information included in the submission. CADTH staff and the sponsor will go through the submitted [summary of non-disclosable information](#) tables and any submitted structured summaries, focusing on relevant information that may be included in the Clinical and pharmacoeconomic reports.
- If new non-disclosable information is provided in part one of the meeting, an addendum to the summary table of non-disclosable information an electronic version must be provided by the sponsor at least one business day in advance of the scheduled checkpoint meeting. No additional meeting materials are required.
- For this portion of the checkpoint meeting, attendees from CADTH will include only CADTH staff. Sponsor attendees should include at least one senior representative with the authority to make decisions regarding disclosure of information.
- The duration of part two of the checkpoint meeting will be a maximum of one hour.
- The summary of non-disclosable information tables provided in the submission or resubmission will be discussed with the sponsor to ensure that there is/are:
 - Agreement between CADTH and the sponsor on the information in the submission or resubmission that is non-disclosable information for the purposes of CADTH's review, as defined in the *Disclosure of Information Guidelines for the CADTH pan-Canadian Oncology Drug Review*.
 - Discussion of non-disclosable information that is within the scope of the review and could likely to be included in the clinical and/or pharmacoeconomic report that is provided to pERC.
 - Decisions on how non-disclosable information relevant to pERC deliberations will be used by CADTH during the review. These decisions will be guided by the *Disclosure of Information Guidelines for the CADTH pan-Canadian Oncology Drug Review*. Decisions may include but are not limited to:
 - If non-disclosable information will be excluded from the clinical and/or pharmacoeconomic report that is provided to pERC
 - If non-disclosable information is excluded, whether a description of the information that was excluded from the clinical and/or pharmacoeconomic report will be provided in the report.
 - If non-disclosable information will be included in the clinical and/or pharmacoeconomic report that is provided to pERC but will be redacted from the publicly posted clinical report and/or pharmacoeconomic report and associated pERC recommendations.
 - If non-disclosable information is included but redacted, if the redaction is indefinite or for a time-limited period and the agreed upon expiry date of the time-limited redaction.
 - If non-disclosable information is included but redacted, what the publicly posted reason for the redaction will be and the public description of the redacted information.

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- a) A checkpoint meeting *Record of Decisions* will be provided to the sponsor two business days from the date of the meeting.
 - b) If agreement on how to manage the disclosure of information in the submission cannot be reached at the meeting, the sponsor will have five business days following receipt of the checkpoint meeting *Record of Decisions* to propose a resolution such as, but not limited to, acceptable wording for public disclosure or use of alternative information that is publicly available and conveys the same intent.

7.5 Delay in the Review Process

- During the review, CADTH considers whether additional information is required from the sponsor. If additional information is required, CADTH will contact the sponsor. Any delays in the sponsor providing such information may result in a corresponding delay in the completion of the review.
- In exceptional circumstances, all information for a review may not be finalized at the time of filing and may be provided during the course of the review. Depending on the nature, extent and complexity of the information, CADTH may need to adjust the timelines for the review. All information in a submission is considered final six business days prior to the targeted pERC meeting.
- The review team may request an extension of deadlines from CADTH, depending on the volume or complexity of material to be reviewed. CADTH shall have the discretion to grant an appropriate extension. The sponsor will be notified of any extensions and reasons for the extensions granted by CADTH. Resulting changes in the target review dates on the CADTH website and a general explanation of the changes will be publicly posted on the website.

7.6 Completing the Clinical Guidance and Pharmacoeconomic Reports

Once the review team has completed the clinical and pharmacoeconomic reports, the reports are checked for completeness and compliance with the [Clinical Guidance Report template](#) and the [Pharmacoeconomic Report template](#) and the sponsor/CADTH agreed handling of non-disclosable information. The reports are then finalized for inclusion in the pERC brief.

8. Recommendation Procedures

8.1 pERC Meeting and Deliberation Procedures

pERC meeting and deliberation procedures include all those procedures related to the preparation for and conduct of the pERC meeting.

Pre-NOC submissions will not be placed on the pERC meeting agenda until the drug has Canadian market authorization and CADTH has received all submission including a copy of the NOC or NOC/c and a final Health Canada approved product monograph. Please note that any substantive changes (e.g., beyond minor edits and/or corrections) to the final Product Monograph compared to the draft Product Monograph will be deemed to be significant by CADTH and may result in the rescheduling of the posted targeted pERC meeting date. Depending on the nature, extent and complexity of the information, CADTH may need to adjust the timelines for the review.

8.1.1 CADTH pCODR Expert Review Committee

- pERC is established in accordance with the [pERC Terms of Reference](#).

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- All pERC members must comply with the [pCODR Conflict of Interest Guidelines](#) and the [CADTH Code of Conduct](#).

8.1.2 Committee Briefing Materials

CADTH compiles the materials for the pERC meeting into the committee brief for delivery to pERC and to the PAG and which can be used by the pERC in its deliberations on a submission. The pERC brief includes the following information upon which pERC will deliberate:

- Clinical and pharmacoeconomic reports which include a summary of the patient group input, registered clinician input and PAG input
- The original patient group and clinician submissions
- Summary report about key implementation issues
- May or may not include key published studies summarized in the clinical and pharmacoeconomic reports
- CADTH therapeutic review reports are included in the pERC brief materials when available and relevant for a cancer drug class review conducted through the therapeutic review process

8.1.3 Preparation for the Expert Committee meeting

- The agenda for the expert review committee meeting is set by CADTH and the committee Chair.
- Before a submission is placed on the pERC agenda, all submission requirements must be met. All information in a submission is considered final six business days prior to the targeted pERC meeting.
- The committee brief will be delivered to pERC members (with copies to participating drug programs and to the Canadian Association of Provincial Cancer Agencies [CAPCA] and through CAPCA to its Board of Directors) before the expert committee meeting.
- Although the full submission, as applicable will be available at the pERC meeting, it will not routinely be sent to pERC members in advance, but will be available upon request.

8.1.4 The Expert Committee Meeting

- The pERC meets on a monthly basis on a pre-specified day of each month.
- pERC members declare all conflicts of interest prior to deliberations on each submission, in accordance with the [pCODR Conflict of Interest Guidelines](#).
- Attendees at the expert committee meeting will be in accordance with the [pERC Terms of Reference](#).
- At the expert committee meeting, pERC members consider and discuss the committee briefing materials for each submission on the meeting's agenda so as to make a reimbursement recommendation. pERC members who represent their various areas of expertise (e.g., oncologists, economists, and patient members) will, respectively, summarize the clinical information (including registered clinician input, where available), the economic information and the patient input for each submission.
- The PAG Chair and/or PAG members may attend the pERC meeting and will be provided an opportunity on the agenda to summarize the PAG input on the submission (Note: No new information will be allowed at this time).
- The pERC Chair may invite members of the review team, including Clinical Guidance Panel members or Economic Guidance Panel members and/or external experts to provide input in person at a pERC meeting and other observers, as applicable. (Note: No new information will be allowed at this time).

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- If pERC needs additional information, either from the review team or from the sponsor, or from external experts, the pERC Chair will determine if the additional information may be impactful and if the deliberations should be deferred. If the deliberation is deferred, the matter will be sent back to CADTH to collect the additional information and the deliberation upon the submission will be deferred to a subsequent pERC meeting, pending the collection of such information. (Note: No new information will be allowed at this time).
 - If the committee briefing materials are complete, pERC will consider the pERC brief and make a recommendation.

8.1.5 pERC Deliberative Framework

In making its recommendation, the expert review committee will follow the pERC Deliberative Framework, which includes assessing:

- overall clinical benefit of the drug in appropriate populations, taking into consideration information on effectiveness, safety, burden of illness and need
- alignment with patient values based on patient group input
- cost-effectiveness relative to current accepted therapy
- drug program perspectives on enablers and barriers to implementation of a recommendation as obtained through PAG input.

The framework is described in Table 10 and Table 11 and provides an outline of all the elements that should be considered by pERC during its review, and reinforces that no single element over-rides another, but rather that pERC uses the sum of all elements to formulate a funding recommendation. The framework can be applied to all oncology drugs and situations including situations such as rare cancers or end of life care. In addition, the framework reinforces that there is no threshold that must be met for any single element in the review; rather, it is the individual drug, disease and context that determine pERC's information needs for each element of the framework.

Table 10: Criteria Definitions and Sources of the pERC Deliberative Framework

Criteria	Definition	Sub-Criteria	Source
Overall Clinical Benefit	A measure of the <u>net health benefit</u> of using the drug to diagnose or manage a cancer related condition (e.g., lung cancer) or cancer care related issue (e.g., skeletal related events in metastatic disease)	<ul style="list-style-type: none"> • Effectiveness • Safety • Burden of Illness • Need 	Clinical Guidance Report provided by Clinical Guidance Panel, which incorporates the pCODR systematic review and registered clinician input
Alignment with Patient Values	An assessment made after considering information on patient values	<ul style="list-style-type: none"> • Patient values 	Patient advocacy group input sought at beginning of the review
Cost Effectiveness	A measure of the <u>net efficiency</u> of the drug and companion technology compared to other drug and non-drug alternatives (no cut-off threshold)	<ul style="list-style-type: none"> • Economic evaluation • Costs, cost per QALY, cost per life year gained, cost per clinical event avoided • Uncertainty of net economic benefits 	Economic Report, which incorporates the Economic Guidance Panel review of the pharmacoeconomic model.
Feasibility of Adoption into the Health System	An assessment of the ease with which the drug can be adopted into the overall health care and cancer care systems	<ul style="list-style-type: none"> • Economic Feasibility – Budget Impact Assessment • Organizational Feasibility 	<p>Provincial Advisory Group input</p> <p>Economic Report, which incorporates evaluation of budget impact assessment assumptions</p>

Note: pERC Deliberative Framework adapted from Johnson, Sikich, Evans et al. Health technology assessment: A comprehensive framework for evidence-based recommendations in Ontario. International Journal of Technology Assessment in Health Care, 25, pp 141-150. 2009

Table 11: Detailed Description of Each Element of the pERC Deliberative Framework.

Criteria	Sub-Criteria	Sub-Criteria Definitions
Overall Clinical Benefit	Effectiveness (systematic review in the Clinical Guidance Report)	The <u>potential health impact</u> of the drug compared to the other drug and non-drug alternatives, measured in terms of <u>relevant patient outcomes</u> such as mortality, morbidity, quality of life. <u>Magnitude, direction and uncertainty</u> of effect should be considered.
	Safety (systematic review in the Clinical Guidance Report)	<u>Frequency and severity</u> of adverse effects associate with the new drug compared to other drug and non-drug alternatives.
	Burden of Illness (Clinical Guidance Report, patient advocacy group input)	Incidence, prevalence or other measure of <u>disease burden</u> on the population.
	Need (Clinical Guidance Report, patient advocacy group input)	<u>Availability of an effective alternative</u> to the drug technology.
Alignment with Patient Values	Patient Values (patient advocacy group input)	<u>Patient based values</u> which bear on the appropriate use and impact of the drug.
Cost effectiveness	Economic Evaluations (CADTH pharmacoeconomic report and pharmacoeconomic model review)	A measure of the <u>net cost</u> or efficiency of the drug and companion technology <u>compared to other drug and non-drug alternatives</u> . The <u>uncertainty</u> of results should be considered.
Feasibility of Adoption into Health Systems	Economic Feasibility (evaluation of budget impact assessment in the CADTH pharmacoeconomic report)	The <u>net budget</u> impact of the new drug on other drug and health system spending, including companion testing technology.
	Organizational Feasibility (Provincial Advisory Group input)	The <u>ease</u> with which the new drug can be adopted, with an assessment of health system <u>enablers</u> and <u>barriers</u> to implementation, inclusive of all elements: operational, capital, human resources, legislative and regulatory requirements

Note: pERC Deliberative Framework adapted from Johnson, Sikich, Evans et al. Health technology assessment: A comprehensive framework for evidence-based recommendations in Ontario. *International Journal of Technology Assessment in Health Care*, 25, pp 141-150. 2009

8.1.6 pERC Recommendations

- A recommendation by pERC shall be made for each submission and resubmission.
- A record of decisions will be taken of the committee's deliberations so that there is a record of the meeting, of attendance at the meeting, of recommendations made and of any pERC-related decisions. A recording of the meeting will also be kept by CADTH.
- pERC recommendations will, in every case, be accompanied by reasons for the recommendation and key messages. CADTH may be tasked with the responsibility of preparing a draft of the reasons for the recommendation and key messages, for detailed review and approval by the committee.
- The recommendation, reasons for the recommendation and key messages shall contain a sufficient explanation as to address the main issues and be sufficiently detailed to demonstrate that the committee has considered all the material before it and applied the *pERC Deliberative Framework*.

8.2 Posting Initial Recommendations and Guidance Reports

Procedures for the preparation of public posting of Initial Recommendations and reports are described in this section. For more details related to procedures associated with the public posting of Initial Recommendations and guidance reports see the *Disclosure of Information Guidelines for the CADTH pan-Canadian Oncology Drug Review* (Appendix 1).

8.2.1 Redaction of Non-Disclosable Information

- If the clinical or pharmacoeconomic reports include non-disclosable information, this will be handled as decided at the checkpoint meeting with the sponsor and in accordance with the *Disclosure of Information Guidelines for the CADTH pan-Canadian Oncology Drug Review* (Appendix 1). If any non-disclosable information was included in the clinical report or the summary of the pharmacoeconomic report to be publicly disclosed, and has been redacted, it will be noted that the sponsor requested that this information not be disclosed and the reason why it was redacted, pursuant to the *pCODR Disclosure of Information* guidelines. The timeframe for which this redaction will remain in place will also be stated.
- If the pERC Initial Recommendation includes non-disclosable information, this will be handled as decided at the checkpoint meeting with the sponsor and in accordance with the *Disclosure of Information Guidelines for the CADTH pan-Canadian Oncology Drug Review* (Appendix 1). If non-disclosable information is redacted from the pERC Recommendation, CADTH will indicate that non-disclosable information was used to make the funding recommendation and that the sponsor requested that this information not be disclosed and the reason why it was redacted, pursuant to the *Disclosure of Information Guidelines for the CADTH pan-Canadian Oncology Drug Review*. The timeframe for which this redaction will remain in place will also be stated.
- CADTH recognizes that the information owner retains the right to make a final decision in relation to the release of information into the public domain. CADTH reserves the right to determine how non-disclosable information is used in the pCODR review process, including pERC deliberations, if at all. Under certain circumstances, information that the owner has decided not be allowed into the public domain will be accepted for inclusion in the pCODR review process and pERC deliberations under agreement not to disclose such information, once it has been agreed mutually by CADTH and the sponsor to be non-disclosable (see Appendix 1). In other circumstances, information that the owner has decided not be allowed into the public domain will be accepted for inclusion in the pCODR review process and pERC deliberations under agreement not to disclose such information for a defined time-limited. CADTH will always strive for the shortest time period of non-disclosure possible.

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- If agreement on the handling of non-disclosable information cannot be reached, CADTH will not use the information in the clinical report, pharmacoeconomic report, or pERC deliberations. Only in rare circumstances, where CADTH is of the view that the inclusion of such information in the clinical and/or pharmacoeconomic reports is necessary for the integrity of pERC recommendations (e.g., important safety/harms information), CADTH reserves the right to use such information and CADTH will note that while the sponsor refused to propose a means of disclosure of the information that was acceptable by CADTH, the information was nonetheless used to preserve the integrity of the pERC recommendations.
 - Four business days before the posting of the initial recommendation document and CADTH reports, the sponsor and/or the manufacturer of the drug under review (if not the sponsor) will be provided with the clinical report, the pharmacoeconomic report, and the summary of the pharmacoeconomic report to be publicly posted. Reports will also be provided to the manufacturer of the drug under review (if not the sponsor) if the manufacturer contributed substantive clinical or economic information to the submission and if they attended the checkpoint meeting. The reports will be made available to the sponsor via secure electronic transmission. An email notification will be sent to the submission contact with a unique, time-limited and user-specific link to the clinical report, pharmacoeconomic report, and the summary of the pharmacoeconomic report.
 - Reports are provided to the sponsor and/or manufacturer of the drug under review for the following purposes only:
 - to verify that non-disclosable information has been handled in the manner agreed upon at the checkpoint meeting with the sponsor, and as documented in the *Record of Decisions* and the *Addendum to the Record of Decisions*;
 - to understand the disposition of any additional information provided by the sponsor after the checkpoint meeting that is non-disclosable;
 - to identify any gross factual errors prior to the public posting of the reports.

Interpretative comments provided by the sponsor and/or manufacturer would not be considered.

- If during the review of the report, the sponsor and/or manufacturer of the drug under review identify any discrepancies or errors, they should be submitted in writing to CADTH within the three-business day period, in accordance with the format outlined in the *Disclosure of Information Guidelines for the CADTH pan-Canadian Oncology Drug Review*. CADTH will consider the proposed discrepancies and errors and make revisions or additional redactions to the clinical report, the pharmacoeconomic report, and the pERC Initial Recommendation as deemed necessary by CADTH and prior to public posting of these documents.

8.2.2 Public Posting of the Initial Recommendation and Guidance Reports

- The pERC Initial Recommendation, CADTH Clinical Guidance Report, and a summary of the CADTH pharmacoeconomic report will be publicly posted on the CADTH website 10 business days following the pERC meeting at which the pERC Initial Recommendation was made. Notification will be sent via e-mail to stakeholders indicating the posting and calling for stakeholder feedback on the pERC Initial Recommendation.
- If a submission is withdrawn (either because of withdrawal of market authorization by Health Canada or voluntary withdrawal by the sponsor) but a pERC Initial Recommendation has been made, CADTH will proceed to publicly post the pERC Initial Recommendation.

8.3 Feedback on Initial Recommendations

- The sponsor, the manufacturer of the drug under review (if not the sponsor), PAG, registered patient groups (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician(s) who submitted input on the submission or resubmission at the beginning of the review process, may provide feedback on the pERC Initial Recommendation (Table 12).
- Feedback must be provided within 10 business days of the pERC Initial Recommendation being posted on the CADTH website.
- Feedback must be provided in conformity with the templates provided on the CADTH website and should relate only to the pERC Initial Recommendation. Any commentary on the content of the CADTH clinical and pharmacoeconomic reports must be related to the pERC Initial Recommendation.
- New information should not be provided in the feedback by any of the stakeholders and will not be considered by the pERC in their reconsideration of the initial recommendation. New information may be appropriate for a resubmission (see section 2.2).
- Any information provided in the feedback will be managed according to the *Disclosure of Information Guidelines for the CADTH pan-Canadian Oncology Drug Review* (Appendix 1). To ensure that the pCODR review process is transparent and accountable, CADTH considers it essential that information that is within scope provided in the feedback is fully disclosable.
- For resubmissions, if registered patient groups (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician(s) are not notified during the review process to provide input on the resubmission and input given by registered patient groups (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician(s) on a previous submission related to the drug and indication under review is provided to the review team to incorporate into the clinical and pharmacoeconomic reports, the registered patient groups (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician(s) that provided that original input will be contacted and informed that they are eligible to provide feedback on the initial recommendation for the resubmission.

Table 12: Stakeholders Eligible to Provide Feedback on Initial Recommendations

Source	Scope of Feedback
Sponsor and/or Manufacturer	The sponsor and the manufacturer of a drug under review and that is the subject of a pERC Initial Recommendation (if not the sponsor) can provide feedback on a pERC Initial Recommendation.
PAG	PAG can provide feedback on a pERC Initial Recommendation. Feedback may include the perspectives of individual PAG members and/or the perspective of the group.
CAPCA Board of Directors	The CAPCA Board of Directors can provide feedback specifically on implementation considerations submitted by PAG
Patient Group(s)	Each registered patient group (or registered individual patient or caregiver in cases where there is no patient group) that provided patient input on a submission or resubmission to CADTH at the outset of a review on the drug that is the subject of a pERC Initial Recommendation can provide feedback on the pERC Initial Recommendation.
Registered Clinician(s)	Registered clinician(s) that provided input on a submission or resubmission to CADTH at the outset of a review on the drug that is the subject of a pERC Initial Recommendation can provide feedback on the pERC Initial Recommendation.

8.3.1 Review of Feedback on the Initial Recommendation and Eligibility for Early Conversion

Upon receipt of the feedback on the pERC Initial Recommendation, CADTH, in consultation with the pERC Chair and pERC members, will review the feedback provided on the pERC Initial Recommendation.

a) Scope of Feedback

- Feedback will be screened by CADTH, in consultation with the pERC Chair to ensure that it is within the scope of the feedback that was solicited, as outlined in the guidelines and templates for providing feedback on the Initial Recommendation.
- If feedback is out of scope, it will not be considered in the decision of whether or not early conversion criteria are met and will be redacted from the posted feedback. A notation will be made in the posted feedback that the redaction was due to a determination that the feedback was out of scope.
- If feedback, from any of the stakeholders includes new information, the information will not be considered and will be redacted from the posted feedback. A notation will be made in the posted feedback that the redaction was due to new information being submitted which may be eligible for a resubmission. It is up to the stakeholder who provided the new information to determine if a resubmission will be pursued.

b) Early Conversion of an Initial to a Final Recommendation

- An assessment will be made by the pERC Chair and pERC members to determine if criteria for early conversion of a pERC Initial Recommendation to a pERC Final Recommendation are met.
- Criteria for early conversion are as follows:
 - No feedback on the Initial Recommendation was provided that was within the scope of the feedback requested; or
 - There is unanimous consensus from stakeholders on the recommended clinical population outlined in the Initial Recommendation; or
 - The Initial Recommendation is an unequivocal positive recommendation, and there are no substantive comments from eligible stakeholders.
- If any of these conversion criteria are met, editorial changes to the recommendation may be made, and the Final Recommendation will be posted on the CADTH website two business days after the end of the recommendation feedback deadline date.
- There shall be no right to provide further feedback on a pERC Final Recommendation.
- If none of these conversion criteria are met, the Initial Recommendation will be returned to pERC for further deliberation and reconsideration at the next possible pERC meeting. The next possible pERC meeting may be the next chronological meeting date or the pERC meeting subsequent to that one, depending on the volume and/or complexity of the reconsideration.

c) Changes to CADTH Reports Following Feedback on Initial Recommendation

If it is decided that the Initial Recommendation will be returned to pERC for further deliberation and reconsideration, prior to a pERC meeting, CADTH, in consultation with the pERC Chair, may decide the revisions to the clinical or pharmacoeconomic report are required. Revisions may address factual errors or clarifications but will not contain any new information.

8.4 Summarizing and Reviewing Feedback with pERC and PAG

- These procedures include those procedures related to summarizing and reviewing feedback on the Initial Recommendation with pERC and PAG.
- If criteria for early conversion of a pERC Initial Recommendation to a pERC Final Recommendation are not met, the reconsideration is placed on the agenda of the next possible pERC meeting.

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- The date of the target pERC meeting at which the feedback will be considered will be posted on the CADTH website two business days after the end of the recommendation feedback deadline date.

8.4.1 Information Provided to pERC on Reconsiderations of Initial Recommendations

- CADTH prepares the pERC reconsideration brief, which includes the following information upon which the pERC will deliberate:
 - The pERC Initial Recommendation
 - Feedback received on the Initial Recommendation that is within the scope of the feedback requested.
 - If required, a revised clinical and/or pharmacoeconomic report.
 - If applicable, stakeholder feedback from for a cancer drug class review conducted through the therapeutic review process
 - The pERC brief from the initial deliberations (see section 8.1.2).
- The pERC reconsideration brief is delivered to pERC members and the PAG before the scheduled pERC meeting at which the Initial Recommendation is reconsidered.

8.4.2 pERC Consideration of Feedback on the Initial Recommendation

See section 8.1 for procedures for preparation for the pERC meeting, the pERC meeting and pERC recommendations. In addition:

- pERC shall review and consider the pERC reconsideration brief. It may view the submission a resubmission afresh and consider and decide whether, based on the evidence and with regard to the pERC Deliberative Framework (section 8.1.5), the pERC Initial Recommendation should be maintained or changed.
- There shall be no right to provide further feedback on a pERC Final Recommendation.

8.5 Preparing and Posting Final Recommendations, Reports, and Feedback

These procedures include all those procedures related to the preparation and public posting of final recommendations, clinical and pharmacoeconomic reports and feedback. For more details related to publicly posting final recommendations, reports, and feedback see the following:

- [Disclosure of Information Guidelines](#) (Appendix 1)
- [pCODR Procedural Review Guidelines](#) (Appendix 3)
- [pCODR Patient Engagement Guide](#)
- [pCODR Patient Group Template](#)
- [pCODR Registered Clinician Template](#)
- [pCODR Conflict of Interest Guidelines](#)

8.5.1 Finalizing Recommendations

- A final determination of a submission or resubmission shall be deemed to have taken place when:
 - A pERC Initial Recommendation has been made, early conversion criteria are met (see section 8.3.1) and the pERC Final Recommendation is publicly posted on the CADTH website.
 - A pERC Initial Recommendation has been made, pERC has considered the stakeholder feedback (see section 8.4.2) and made a pERC Final Recommendation that is publicly posted on the CADTH website.

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- There shall be no right to provide further feedback on a pERC Final Recommendation and a submission or resubmission may not be withdrawn following public posting of the pERC Final Recommendation.
 - A procedural review of a publicly posted pERC Final Recommendation may be requested as outlined in section 9.1.2 and in the *pCODR Procedural Review Guidelines* (Appendix 3).
 - A Notification to Implement a pERC Final Recommendation will be issued via email by CADTH, as outlined in section 9.1.1, and participating drug programs may then proceed to implement the pERC Final Recommendation.

8.5.2 Public Posting of CADTH Documents

a) Final Recommendation

- If a final recommendation is a result of meeting early conversion criteria, it will be publicly posted on the CADTH website two business days after the end of the recommendation feedback deadline date.
- If a final recommendation is a result of a reconsideration by pERC based on feedback provided on an Initial Recommendation, the final recommendation will be publicly posted on the CADTH website 10 business days after the pERC meeting at which the final recommendation was made.
- When a pERC Final Recommendation is posted on the CADTH website, a notification will be sent via email to stakeholders indicating the posting has occurred.
- If a submission or resubmission is withdrawn (either because of withdrawal of market authorization by Health Canada or voluntary withdrawal by the sponsor) but a pERC Final Recommendation has been made, CADTH will proceed to publicly post the pERC Final Recommendation.

b) Final Clinical Guidance Report and Pharmacoeconomic Report

- If the clinical or pharmacoeconomic reports were revised as a result of feedback that was provided on the Initial Recommendation, the reports posted at the time of the Initial Recommendation will be replaced with final reports. The final reports are publicly posted 10 business days after the pERC meeting at which the Final Recommendation was made or, for those meeting the criteria for early conversion, two business days after the end of the recommendation feedback deadline date.
- When the final clinical and pharmacoeconomic reports are publicly posted on the CADTH website, a notification will be sent via email to stakeholders indicating the posting has occurred.

c) Stakeholder Feedback

- Feedback that was received on the Initial Recommendation by eligible stakeholders and which was in scope of the feedback that was solicited, will be posted on the CADTH website. If feedback is provided that is not in scope of the feedback that has been solicited, it will be redacted prior to posting and the reason for the redaction (i.e. that it was out of scope, will be stated). To ensure that the pCODR review process is transparent and accountable, CADTH considers it essential that information that is within scope provided in the feedback is fully disclosable.
- When the stakeholder feedback on the pERC Initial Recommendation is publicly posted on the CADTH website, a notification will be sent via email to stakeholders indicating the posting has occurred.

d) Conflict of Interest Declarations

- Patient group (or registered individual patient or caregiver in cases where there is no patient group) and registered clinician conflict of interest declarations providing input on a submission or resubmission or providing feedback on a pERC Initial Recommendation will be posted on the CADTH website.
- Conflict of interest declarations of pERC Members and of PAG members are posted on the CADTH website and updated on an annual basis or as needed, in accordance with the [pCODR Conflict of Interest Guidelines](#).

8.5.3 Time-Limited Redactions in Final Recommendations and Final Guidance Reports

- Final recommendations and reports posted on the CADTH website will be reviewed by CADTH from time to time and non-disclosable information that is redacted in reports and recommendations may be publicly disclosed at the expiration of the sponsor/CADTH agreed upon period for time-limited redactions.
- If non-disclosable information was redacted and included in the publicly posted clinical report, pharmacoeconomic report, or pERC Final Recommendation with the agreement between CADTH and the sponsor that the redaction was time-limited; in exceptional circumstances such as the sponsor and/or manufacturer providing evidence of imminent publication, CADTH may grant a brief extension of no greater than one month to the expiry of the time-limited redaction.

9. End of the pCODR Process

These procedures relate to relevant activities following the end of the pCODR process. More details related to these procedures can be found in the *pERC Deliberative Framework* (section 8.1.5), the *pCODR Disclosure of Information Guidelines* (Appendix 1), and *pCODR Procedural Review Guidelines* (Appendix 3).

9.1.1 Recommendation Implementation and Funding Decisions

- Until CADTH has issued a Notification to Implement, the pERC Final Recommendation will not be implemented by the participating drug programs.
- Ten business days following posting of the pERC Final Recommendation, if a request for a procedural review has not been submitted, CADTH will issue a Notification to Implement a pERC Final Recommendation and indicate on the CADTH website that this has been issued. Each of the participating drug programs may then proceed to implement the pERC Final Recommendation.
- Fifteen business days following the submitted date of an application for a procedural review, if a request for a procedural review has been submitted to CADTH, and the request has not been accepted, CADTH will issue a Notification to Implement a pERC Final Recommendation and indicate on the CADTH website that this has been issued. Each of the participating drug programs may then proceed to implement the pERC Final Recommendation.
- If a procedural review request is submitted and is accepted by CADTH, a pERC Final Recommendation will only be implemented when the procedural review is complete and a Notification to Implement a pERC Final Recommendation has been issued by CADTH.

9.1.2 Procedural Review

a) Grounds for a Procedural Review

- A procedural review is a determination of whether CADTH and/or pERC have complied with review processes and procedures. A procedural review may be requested on the basis that:
 - i. CADTH failed to act in accordance with its procedures in conducting the review, as described in the *Procedures for the CADTH pan-Canadian Oncology Drug Review*, or
 - ii. pERC failed to apply its deliberative framework in formulating its recommendation, as outlined in the *pERC Deliberative Framework* (section 8.1.5).
- These grounds relate only to whether or not the pCODR drug review process was followed and not to the content of the pERC Final Recommendation. Differences in the interpretation and use of data during the review do not constitute grounds for a procedural review, e.g. the selection of comparators, the use of data sets, the place in therapy. In addition, disagreement with CADTH's approach to managing non-disclosable information that was provided in the submission or resubmission, 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 *Disclosure of Information Guidelines for the CADTH pan-Canadian Oncology Drug Review* (Appendix 1).

b) Requesting a Procedural Review

- A procedural review can be requested within 10 business days of a pERC Final Recommendation being publicly posted on the CADTH website, by any one of the parties who participated in the pCODR review of that drug, which could include: the sponsor, the manufacturer of the drug under review (if not the sponsor), the PAG, a registered patient group (or registered individual patient or caregiver in cases where there is no patient group) or registered clinician(s) who provided input on the review or feedback on the pERC Initial Recommendation.
- If a review participant wishes to request a procedural review, the [pCODR Procedural Review Request Form](#) must be completed and submitted, along with all supporting documentation, within ten business days of a pERC Final Recommendation being posted. Intent to submit supporting documentation after the ten-day period will not be considered sufficient.
- Multiple review participants may submit a request for a procedural review of a pERC Final Recommendation but each participant may only submit one request.
- A request for a procedural review of a pERC Final Recommendation can only be submitted once. If the submission or resubmission is re-deliberated upon, as a result of a procedural review, once the pERC Final Recommendation is posted no further requests for an additional procedural review of the associated recommendation can be made. A Notification to Implement a pERC Final Recommendation will be issued.

c) Screening a Request for a Procedural Review

- Senior CADTH staff consulting with the Pharmaceutical Advisory Committee (PAC), will review the [pCODR Procedural Review Request Form](#) and supporting documentation and determine if grounds for a procedural review exist. The decision of whether to accept or not accept the request for a procedural review will be made within 15 days of the submitted date of an application for a procedural review. This decision will be communicated to the requestor and posted on the CADTH website.
- While screening the request for a procedural review, CADTH, on the advice of the PAC Chair and Vice-Chair, may determine that additional clarification is required from the party who made the request. Clarification must be provided by the procedural review requestor, as outlined by CADTH, within 15 days

of a Final Recommendation being posted on the CADTH website, otherwise the request for a procedural review may be rejected.

- If the request for a procedural review is not accepted, the party who made the request will be notified by CADTH and a Notification to Implement a pERC Final Recommendation will be issued so that the participating drug programs can proceed to implement the pERC Final Recommendation
- If the request for a procedural review is accepted, the party who made the request will be notified by CADTH and a procedural review will be conducted as outlined below in the Conducting a Procedural Review section.

d) Conducting a Procedural Review

- The CADTH President and Chief Executive Officer will appoint three to five members from the PAC, as needed. The PAC panelists will consider the evidence and make a recommendation to the CADTH President and Chief Executive Officer. In certain circumstances, the panel conducting the procedural review may determine that additional expertise is required and may request advice from external experts while conducting the procedural review.
- The Procedural Review Panel will review the [pCODR Procedural Review Request Form](#) and supporting documentation provided by the requestor. As may be required throughout the procedural review, the Panel may request additional information from the requestor, the pERC, or CADTH or other participants in the review process.
- At the beginning of the procedural review, pERC or CADTH has the option to provide a provisional response to the Procedural Review Panel.
- For the duration of the procedural review, it will be indicated on the CADTH website that a procedural review is being conducted.
- The CADTH President and Chief Executive Officer will make the decision based on PAC's recommendation, and will determine the outcome(s) of the procedural review. This determination will be communicated to the requestor, the Pharmaceutical Advisory Committee, and CADTH.

e) Outcomes of a Procedural Review

- The Procedural Review Panel may determine that:
 - i. No changes are required and CADTH issues a Notification to Implement a pERC Final Recommendation.
 - ii. Steps in the pCODR review process must be revisited and/or the pERC recommendation must be re-deliberated by pERC at the next possible pERC meeting. A re-deliberation may result in the pERC Final Recommendation being maintained or being changed.
- If steps in the pCODR review process must be revisited and/or the submission or resubmission re-deliberated, the submission or resubmission would receive priority placement on the pERC meeting agenda at which it will be re-deliberated and work on the submission or resubmission would be prioritized as per section 4.4.4 of this document.
- If the submission or resubmission is re-deliberated by the pERC, details and outcomes of the procedural review will be communicated in the pERC Final Recommendation.

9.1.3 Disposition of Submission Documents

The issuance of the *Notification to Implement* a pERC Final Recommendation by CADTH signals the completion of the pCODR review process. CADTH then undertakes the steps detailed in this section regarding the disposition of documents associated with the review. CADTH follows the same steps in the disposal of documents associated with a withdrawn submission.

a) Retrieval

CADTH retrieves all paper and electronic copies of the submission documents from the review team.

b) Archiving

Archiving of submission documents is carried out as follows:

- CADTH retains one complete CD/DVD set of the submission, where available, and one complete set of all documents (paper and/or electronic) associated with the review of a drug, on file in secure storage for as long as there may be a need to consult the documents.
- CADTH undertakes regular reviews of archived material. Any material that CADTH determines to be no longer required is disposed of as described in section c)
- All other extra copies of paper and electronic documents associated with the review of a drug are disposed of as described below in section c).

c) Disposal

CADTH disposes of any paper documents associated with the submission by confidential shredding. Any additional CD/DVD sets provided in the submission are destroyed. CADTH advises the sponsor, in writing, that it has disposed of the extra copies of documents.

10. Temporary Suspension

10.1 Suspension Due to Incomplete Information

In the event that CADTH is unable to conduct a thorough review and/or an appraisal of a submission or resubmission 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 the information required in order to re-initiate the review process.
- 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 suspended submission or resubmission is tracked on CADTH's website.

10.2 Suspension following Notice of Deficiency or Notice of Non-Compliance

- For submissions filed on a pre-NOC basis that receive a notice of deficiency (NOD) or notice of non-compliance (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.

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- 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 for suspension rather than mandatory withdrawal will be made solely at the discretion of CADTH on a case-by-case basis. If CADTH determines that temporary suspension is not appropriate, the submission will have to be withdrawn in accordance with section 11.
 - 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.
 - Any new clinical data filed with Health Canada to address the issue.
 - Advance notification of a minimum of six 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 submission or resubmission 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. CADTH also has the discretion to extend the temporary suspension as deemed necessary.
- CADTH’s decision to temporarily suspend the review of a submission 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 suspended submission or resubmission is tracked on the CADTH website.

11. Withdrawal from the Process

11.1 Withdrawal Procedure

- A submission or resubmission will be withdrawn if:
 - the sponsor voluntarily requests withdrawal of the submission or resubmission
 - Health Canada has withdrawn market authorization

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- Health Canada will not be issuing market authorization
 - CADTH has determined that temporary suspension following the issuance of an NOD or NON is not appropriate
 - A sponsor may request that a submission be withdrawn from the review process up to the time that a pERC Final Recommendation is posted on the CADTH website.
 - In all cases where marketing authorization has been withdrawn or will not be issued by Health Canada, the sponsor must advise CADTH, in writing, as soon as possible.
 - All requests for withdrawal must be provided in writing and contain the following information:
 - name and signature of the sponsor;
 - reason for the withdrawal;
 - if market authorization was withdrawn, the date on which market authorization was withdrawn.
 - Upon receipt of a request for withdrawal from a sponsor, CADTH will withdraw the submission or resubmission as follows:
 - CADTH will stop its review of the submission or resubmission and will inform the sponsor of this in writing and post this information on the website.
 - If PAG is not the sponsor, CADTH will notify PAG when it receives a request for withdrawal.
 - If the manufacturer of the drug under review is not the sponsor, CADTH will notify the manufacturer that it has received a request for withdrawal.
 - CADTH will post the general reason for the withdrawal on the website.
 - If PAG is not the sponsor, PAG may request, within 20 business days of notification of the request for withdrawal, or at the next scheduled PAG meeting (whichever occurs first) that CADTH continues the review of the drug that is the subject of the withdrawn submission.
 - CADTH will advise the sponsor of PAG's request regarding whether or not the review of the drug will continue.
 - When PAG requests that CADTH continue the review of a drug, the review will be based on information available in the public domain and will proceed as a submission by PAG.
 - CADTH will retain one complete copy of the submission or resubmission on file.
 - Notwithstanding the foregoing, if at the time of the voluntary withdrawal, a pERC Initial Recommendation or pERC Final Recommendation has been made by pERC but has not yet been publicly posted, CADTH will proceed with public posting of the recommendation.
 - If a sponsor wishes to re-initiate a review of a voluntarily withdrawn submission, the sponsor is required to file a complete submission in accordance with section 4 in order for the review to proceed. The submission is to include a list of changes since the previous submission was withdrawn. All updated documents (not limited to new information, e.g., updated Product Monograph) must be provided.
 - Sponsors who withdraw from the pCODR 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 copies of the withdrawn submission or resubmission (as described in section 9.1.3).

11.2 Refiling with CADTH After Withdrawal

- The sponsor is required to file a complete submission or resubmission in accordance with section 4.
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- The refiled submission or resubmission must include a list of the changes made as compared with the initial submission or resubmission 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 an NOC or NOC/c, the sponsor is required to file the submission on a post-NOC basis.
 - Submissions and resubmissions being refiled after withdrawal will be screened according to the procedure described in section 4.4.
 - CADTH considers the nature of the submission or resubmission being re-filed and determines the appropriate approach for conducting the review.

12. Implementation Advice

After a final recommendation has been issued, CADTH provides implementation support for the drug programs, pCPA, and CAPCA to assist in developing and refining reimbursement conditions for certain drug products and/or developing a provisional algorithm for treatment sequencing (Figure 3). This support is distinct from CADTH's drug reimbursement review processes and is offered for the purposes of assisting jurisdictions in implementing recommendations from CADTH and/or making reimbursement policy decisions.

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

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

Implementation advice reports will typically be prepared after the expert review committee has issued a recommendation in favour of reimbursement and will not generally be initiated in situations where the expert review committee has recommended that the drug under review not be reimbursed by the drug programs.

12.1 Implementation Advice Regarding a Drug Reimbursement Recommendation

12.1.1 Eligibility and Function

After a final recommendation has been issued, CADTH provides implementation support for the participating jurisdictions and pCPA as required. This support is distinct from CADTH's drug reimbursement review processes and is offered for the purposes of assisting jurisdictions in operationalizing recommendations from CADTH and/or making reimbursement policy decisions.

At the request of the participating jurisdictions, CADTH may convene panels of clinical experts to assist the jurisdictions in developing and refining reimbursement conditions for certain drug products undergoing

negotiation through the pCPA process. These will typically occur after the expert committees have issued a recommendation in favour of reimbursement and provides guidance to CADTH and the jurisdictions that a panel of clinical specialists could be convened to further develop and/or refine the reimbursement conditions proposed in the recommendation. These situations may arise when the committee concludes that the comparative clinical benefit of the drug has been demonstrated, but a panel of clinical specialists would be required 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). These panels will only be established at the request of the drug programs that participate in CADTH's drug reimbursement review processes.

12.1.2 Stakeholder Engagement

a) Drug Manufacturers

The sponsor 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 (e.g., given the opportunity to review and comment on the draft advice report).

b) Patient Group and Clinician Input

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

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 report.

12.1.3 Panel Composition

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, CAPCA, and/or the participating drug programs. The number of clinical specialists included on the panels may vary based on input from the participating jurisdictions and the complexity of the issues 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 pCPA, CAPCA, and/or the participating drug plans. 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.

12.1.4 Implementation Advice Report

CADTH consults with clinical experts and drafts an implementation advice report that addresses the issues raised by the public drug programs. The draft implementation advice report is provided to the manufacturer, drug programs, CAPCA, and/or pCPA for review and comment.

The draft implementation advice report from the panel will be provided to the manufacturer and drug plans for review and comment. The manufacturer will have five 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 manufacturer and drug plans with the expert panel and the guidance report will be revised as required. CADTH will prepare responses to the comments which will be provided to the manufacturer at the same time as they are issued the final 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. Manufacturers will not have the opportunity to request any redactions.

12.2 Development of Provisional Algorithms

12.2.1 Eligibility and Initiation

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

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

12.2.2 Stakeholder Engagement

a) Industry Engagement

CADTH introduced a revised provisional algorithm process in June 2020 to broaden engagement with drug manufacturers, to ensure the following:

- all drug manufacturers whose products may be directly impacted by the provisional algorithm are notified that the review is being undertaken by CADTH and that the position of one or more of their products may be impacted as a result; and,
- allow all drug manufacturers whose products may be directly impacted to provide input into the process.

For drug manufacturers other than the sponsor for the drug recently 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 that manufacturer's product(s). CADTH will notify all impacted manufacturers (i.e., DIN holders) with the following information:

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

Upon notification that the algorithm is being developed by CADTH, all manufacturers with products that fall 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 provided using a template provided by CADTH and must not contain any confidential information (all information included will be considered disclosable by CADTH).

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

b) Patient and Clinician Group Engagement

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

c) Drug Program Engagement

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

12.2.3 Panel Composition and Deliberative Process

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

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

The deliberations regarding the provisional algorithm will be focused on addressing specific policy questions raised by the jurisdictions. This will typically be focused on understanding the implications of one or more new 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 condition:

- unmet therapeutic need for patients (particularly those in understudied populations)
- evidence supporting particular sequences of therapies (if available)
- clinical experience and opinion that support particular sequences 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.

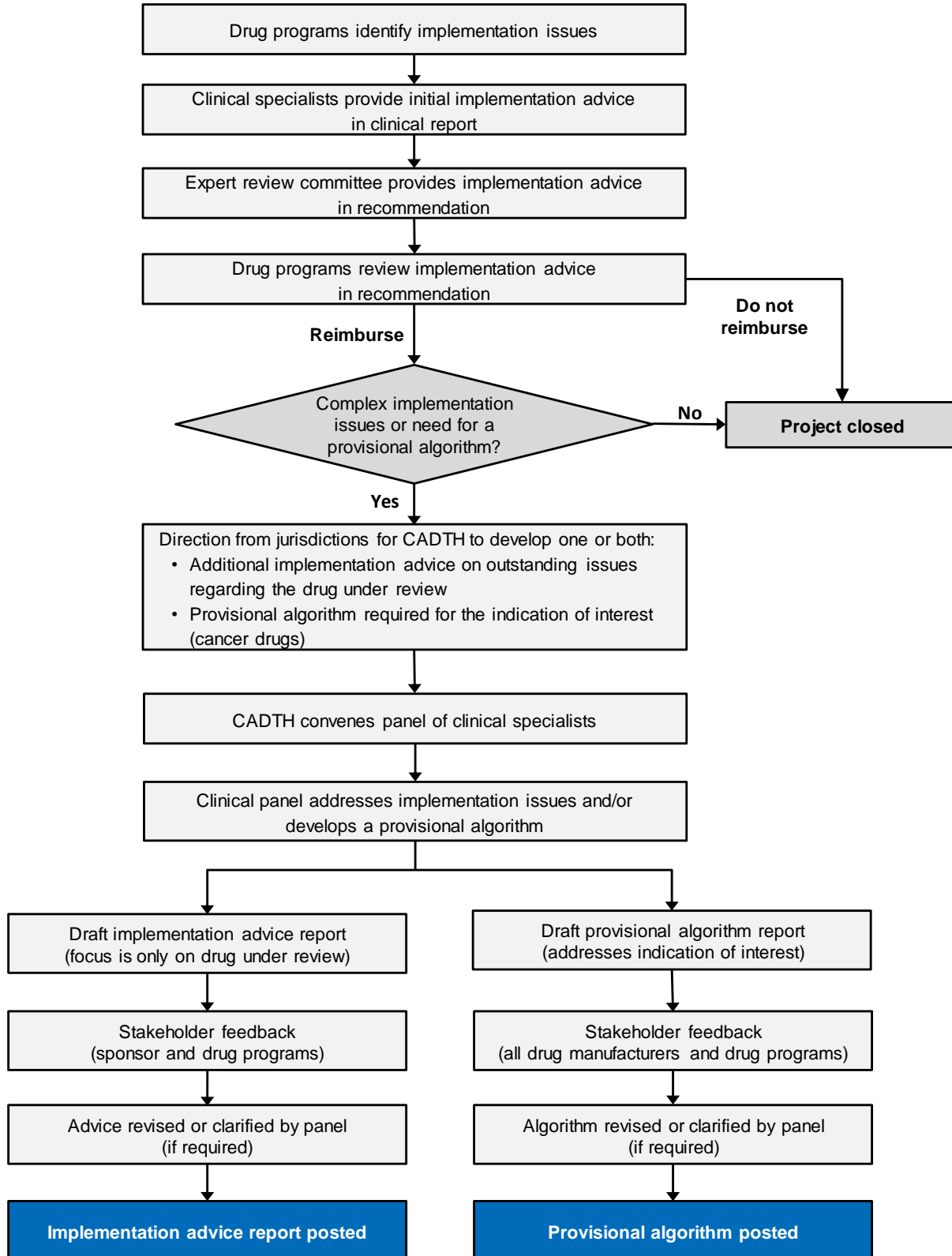
Clinical and economic evidence to inform the optimal treatment sequence is typically limited; therefore, the clinical experience and knowledge of Canadian specialists with expertise in the diagnosis and manage of patients with the condition of interest will often form the basis of the advice offered by panel. The rationale for the panel's proposed provisional algorithm will be documented.

12.2.4 Provisional Algorithm Reports

CADTH drafts the provisional algorithm report based on the advice from the implementation panel. The draft implementation advice report is provided to the drug manufacturers, drug programs, CAPCA, and/or pCPA for review and comment. The drug manufacturers will have five 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 manufacturers and drug programs with the implementation panel and the algorithm report may be revised as required.

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

Figure 3: CADTH Implementation Advice and Provisional Algorithm Processes



13. Reassessment of Drugs through the CADTH Therapeutic Review Process

A therapeutic review is an evidence-based review of publicly available sources regarding a therapeutic category of drugs or a class of drugs in order to support drug reimbursement decisions, drug policy decisions, and to encourage the optimization of drug therapy. Therapeutic reviews may be useful in any scenario where there is uncertainty regarding the comparative clinical effectiveness and cost-effectiveness of drugs in a particular therapeutic category or drug class. Please refer to the [CADTH Therapeutic Review Framework and Process](#) document for the detailed steps.

Initiation and Topic Identification

Topic identification includes both reactive projects (i.e., for which a specific request was received from a CADTH customer) and proactive projects (i.e., a project identified by CADTH in anticipation that targeted technologies may have a significant impact on the Canadian publicly funded health system). Factors related to policy issues used to identify potential therapeutic review topics are set out in the [CADTH Therapeutic Review Framework and Process](#).

Stakeholder Engagement

Throughout the therapeutic review project, CADTH provides multiple opportunities for stakeholder engagement, allowing 10 business days for stakeholder feedback. Stakeholder engagement opportunities during a therapeutic review and the requirements are described in detail in the [CADTH Therapeutic Review Framework and Process](#). To ensure that the review process is transparent and accountable, CADTH considers it essential that any information provided to inform the therapeutic review is fully disclosable.

Timelines

The typical timeline for the issuance of the expert committee recommendation for a therapeutic review may range between six to nine months after the project protocol and the list of included studies are finalized. Exact timelines are determined by CADTH in consultation with the Pharmaceutical Advisory Committee or with the Provincial Advisory Group for oncology drugs. CADTH publishes on the website the targeted pERC meeting date upon which a therapeutic review may be deliberated.

Reports and Recommendation

The primary outputs from a therapeutic review will typically include the Therapeutic Review Science (HTA) Report, Therapeutic Review Recommendations Report, and knowledge mobilization tools. It is important to note that the output from a CADTH therapeutic review may revised pERC recommendations for drugs that have previously been reviewed through the pCODR process.

Existing pERC recommendations that could be revised as a result of the therapeutic review will be identified and communicated to stakeholders during the scoping phase of the therapeutic review process. This could include drugs where existing pERC recommendations have not been issued at the time a CADTH therapeutic review is initiated, but will be reviewed through the pCODR process before the therapeutic review has been completed.

As part of the deliberative process for a therapeutic review, pERC will consider whether or not the results of a therapeutic review suggest that any existing recommendations that were issued through the pCODR process should be revised. Proposed revisions to existing pERC recommendations will be posted for stakeholder

feedback at the time the draft therapeutic review recommendations are posted. The following information will be included: the recommendation that may be revised as a result of the therapeutic review

- the revised reimbursement conditions that are being proposed
- the rationale for the revision

Stakeholders will have opportunity to provide feedback. pERC will consider the stakeholder feedback, the evidence from the therapeutic review, and the final therapeutic review recommendations and determines if any existing pERC recommendations should be revised. Depending on stakeholder feedback and the final therapeutic review recommendations, this could result in revisions that were not initially identified at the time of stakeholder feedback.

CADTH will issue the revised pERC Final Recommendation. Posting of the revised pERC Final recommendation may occur before posting of the final therapeutic review reports. The revised recommendation will be an abbreviated document noting the following key information:

- the drug and indication of interest
- the recommendation, including any conditions (if applicable)
- a statement indicating that the revised recommendation has been issued as a result of a CADTH therapeutic review
- a disclaimer indicated that the revised recommendation supersedes the previous pERC recommendation for the drug and indication of interest.

Once the therapeutic review recommendation has been finalized by pERC, the committee determines if the new recommendation will supersede any existing pERC recommendations that were issued through the pCODR process. If a determination is made that the new recommendation would supersede a previous pERC Final Recommendation, a disclaimer will be added to the previous pERC Final Recommendation stating that it has been superseded by the revised pERC Final Recommendation.

14. Request for Advice

A request for advice is a written request made by the Pharmaceutical Advisory Committee (PAC) or by the Provincial Advisory Group (PAG), to the pERC for advice on specific therapeutic, clinical, pharmacoeconomic or implementation issues, regarding a pERC Recommendation, which may result in a new recommendation. PAC or PAG will set out the issue(s) or question(s) that is needed to be addressed by pERC. This information will be published on CADTH website.

In the case of a request for advice filed by PAC or PAG, the following provisions will apply:

- The request for advice will be regarding a previous pERC Final Recommendation.
- A request for advice will not be assigned to the review queue.
- The date on which CADTH receives a request for advice is considered day zero for the purpose of calculating the time frame for determining the approach for the request.
- CADTH determines the appropriate approach for responding to the request for advice and develops a workplan for its review within 10 business days of receipt.
- CADTH may seek direction from the pERC chair and members on how to proceed with the request for advice.

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- CADTH establishes a review team, based on the nature of the request for advice and in consideration of the proposed team members' qualifications, expertise, and compliance with the *pCODR Conflict of Interest Guidelines*. The names of the review team members will not be disclosed to the manufacturer.
 - The steps in the review of a request for advice are as follows:
 - stakeholders, including the sponsor/manufacturer(s) of the drug(s) in question, patient groups and registered clinician(s) will be apprised that a request is being undertaken and the reasons for the review, and those stakeholders who provided input on the original submission in question are invited to comment or provide information using *pCODR's feedback on a Request for Advice* template to help inform the question(s) or issue(s) raised by PAC or PAG within ten (10) business days of the posting of the request for advice.
 - the request for advice is assigned to a review team.
 - a protocol to address the question or issue is established.
 - the review team conducts a literature search. The studies and material identified through the literature search and any information or data provided by the stakeholder(s) are supplied to the review team to consider as part of the review. To ensure that the pCODR review process is transparent and accountable, CADTH considers it essential that any information provided to inform the request for advice is fully disclosable.
 - CADTH publishes on the website the targeted pERC meeting date upon which a request for advice may be deliberated.
 - When considering a request for advice, pERC may address the request by providing one of the following:
 - a revised pERC recommendation that would supersede a previous pERC Final Recommendation
 - a pERC record of advice document containing additional context and/or clarifications regarding a pERC final recommendation.

In either case, the pERC record of advice or revised pERC recommendation and supporting report will be posted 10 business days following the pERC Meeting on the CADTH website.

Important Notes:

1. PAC or PAG may withdraw a request for advice by submitting to CADTH in writing and providing the reason for the withdrawal.
2. For greater clarity, a request for advice by PAC or PAG will not be subject to a procedural review as outlined in the *pCODR Procedural Review Guidelines*.

Appendix 1: Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review

1. Purpose

CADTH's pan-Canadian Oncology Drug Review (pCODR) program has developed the following disclosure of information guidelines to ensure appropriate steps and procedures are in place so that the disclosure of information obtained through the pCODR review process is handled and managed in a consistent manner. These Guidelines, together with the *Procedures for the CADTH pan-Canadian Oncology Drug Review*, provide clarity to CADTH and Sponsors/Contributors on how to both appropriately protect and disclose information, allowing for a drug review process that is transparent and accountable.

2. Use

CADTH complies with these guidelines when handling information, as part of the pCODR review process. By filing a submission or resubmission or by supplying other information to CADTH once a submission or resubmission has been filed, each sponsor/contributor hereby consents to the application of the disclosure of information guidelines. The disclosure of information guidelines constitute an agreement between CADTH and the sponsor/contributor.

The *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review* are applicable to information received as part of a pCODR submission or resubmission; they are not applicable to pre-submission information that is received by CADTH. CADTH will treat all pre-submission information provided by the sponsor as non-disclosable, subject to the information that may be posted for a pending submission as set out in the pCODR Procedures.

3. Definitions

For the purposes of these guidelines:

- 3.1. A **Contributor** is anyone who has an opportunity to provide input into the pCODR review process for a specific drug review and includes the Sponsor, the manufacturer of the drug product if they are not the Sponsor, the Provincial Advisory Group and, registered clinician(s) and patient groups.
- 3.2. A **Sponsor** is the person, corporation or entity submitting a drug to CADTH for review and may include the manufacturer of the drug product, a provincially-recognized clinician-based Tumour Group, or the Provincial Advisory Group.
- 3.3. **Disclosable Information** is any information that falls into either of the following two categories:
 - a) All information included in a submission or resubmission, or anything received by CADTH related to the product after a submission or resubmission has been filed with CADTH unless such information has been clearly identified by a contributor or sponsor as non-disclosable information (see definition of non-disclosable information); or
 - b) Any information that has been identified by a sponsor or contributor as non-disclosable where such information falls into any one of the following categories:
 - i) the information has been put into the public domain, in written or electronic form, anywhere in the world;
 - ii) the information is comprised of a structured summary of evidence from clinical trials provided by the sponsor/contributor where such information has not been put into the public domain, in written or

electronic form, anywhere in the world. This summary should follow a recognized format for a full trial report, such as that provided by the CONSORT statement. See: www.consort-statement.org;

- iii) the information is comprised of an unpublished structured summary or clinical report which the sponsor/contributor has agreed to put in the public domain where such summary or report has not been put into the public domain prior to the expiry of the time frame for disclosure agreed upon by the sponsor with CADTH, which shall be no greater than six to 12 months from the date of posting of a pERC Initial Recommendation; notwithstanding, if the sponsor/contributor requests for a time frame of greater than six months, the sponsor/contributor must provide a confirmation letter (e.g., acceptance letter from a publication) that the information has been submitted and will be put into the public domain;
- iv) the information is comprised of a description of the design, methods and results of the economic model and the design, methods and overview of results of the budget impact analysis used in the submission or resubmission;
- v) the information is comprised of the list price of a drug after the drug has been made available for sale and marketing in Canada (i.e., after launch); for greater clarity, a sponsor must provide a disclosable price or market price at the time that the submission is made to CADTH for each submission or resubmission;
- vi) the information is comprised of the list price of the relevant comparator(s) included in a submission or resubmission;
- vii) the information is comprised of the disclosable price or market price for companion diagnostic(s) at the time that the submission is made to CADTH for each submission or resubmission (if applicable);
- viii) the information was already in the possession of pCODR review participants (pCODR staff and partners, CADTH Pharmaceutical Advisory Committee, pERC members, clinical and economic guidance panel members, tumour groups, registered clinician(s), patient groups, Provincial Advisory Group [PAG], cancer agencies, Federal, P/T governments, P/T health authorities, Health Canada, Patented Medicine Prices Review Board (PMPRB), Canadian Association of Provincial Cancer Agencies [CAPCA] or pan-Canadian Pharmaceutical Alliance [pCPA]) without restriction as to its use or disclosure; or
- ix) the information is rightfully disclosed to pCODR review participants by a third party who is not under any obligation as to confidentiality or non-disclosure.

3.4. Subject to the exceptions noted in subsection 3.3b) above, Non-Disclosable Information is information that is any one of the following:

- a) Scientific, clinical, or technical information supplied by a sponsor/contributor in a document that is clearly marked “non-disclosable”, “not disclosable”, or “confidential”;
- b) Marked “non-disclosable”, “not disclosable”, or “confidential” due to the commercially sensitive nature of the information, including the executable form of the health economic and budget impact analysis models, market research data, manufacturer drug market share forecasts, assumptions on competitor market share projections, and budget impact analysis results; or
- c) Scientific, technical or commercial information not previously put into the public domain, in written or electronic form anywhere in the world, received as a result of the exchange of information described in the section on Access to Information and Freedom of Information Legislation and that relates to a manufacturer’s business or a manufacturer’s drug product.

4. Principles

- To ensure that the pCODR review process is transparent and accountable, CADTH considers it essential that the evidence upon which pERC's recommendations are based be publicly available.
- When circumstances warrant public posting of information by CADTH regarded by the owner as non-disclosable or in accordance with these guidelines, both parties will negotiate in good faith to seek to find a mutually acceptable solution, recognizing the need for CADTH to support its recommendations with evidence available in the public domain and the information owner's right to determine a global publication strategy.
- CADTH recognizes that the information owner retains the right to make a final decision in relation to the release of information into the public domain. CADTH reserves the right to determine how non-disclosable information is used in the pCODR review process, including pERC deliberations, if at all. Under certain circumstances, information that the owner has decided not be allowed into the public domain will be accepted for inclusion in the pCODR review process and pERC deliberations under agreement not to disclose such information, once it has been agreed mutually by CADTH and the sponsor to be non-disclosable (see subsection 3.4). In other circumstances, information that the owner has decided not be allowed into the public domain will be accepted for inclusion in the pCODR review process and pERC deliberations under agreement not to disclose such information for a defined time-limited period [see subsection 3.3b)iii)]. CADTH will always strive for the shortest time period of non-disclosure possible.
- All disclosable information may be publicly disclosed in the absolute discretion of CADTH.

5. Procedure for Determining if Information is Non-Disclosable Information

- Information identified by the sponsor as non-disclosable information is not non-disclosable information until such information is confirmed as such through the procedure outlined below.
- During the submission process, the sponsor and CADTH will have a checkpoint meeting (as indicated in the section 7.4 and Appendix 2), at which point the information identified as non-disclosable information by the sponsor will be discussed. If agreement on how to manage the disclosure of information in the Submission cannot be reached at the meeting, the sponsor will have five business days to propose a resolution such as, but not limited to, acceptable wording for public disclosure, use of alternative information that is in the public domain and conveys the same intent or time-limited non-disclosure.
- CADTH will have five business days to review the proposed resolution and determine whether or not it is acceptable, whether there may be delay in the review to allow for further discussion with the sponsor on mutually acceptable approaches to disclosure and whether or not to refrain from using the information in the Clinical Guidance Report and/or Pharmacoeconomic Report.
- If agreement cannot be reached, CADTH will not use the information in the Clinical Guidance Report and/or Pharmacoeconomic Report or pERC deliberations. Only in rare circumstances, where CADTH is of the view that the inclusion of such information in the clinical and/or pharmacoeconomic reports is necessary for the integrity of pERC recommendations (e.g., important safety/harms information), CADTH reserves the right to use such information and pCODR will note that while the sponsor refused to propose a means of disclosure of the information that was acceptable by CADTH, the information was nonetheless used to preserve the integrity of the pERC recommendations.

6. pCODR Structure and Access to Information and Freedom of Information Legislation

6.1. pCODR Structure

pCODR is a program of CADTH that is designed to assess the clinical evidence and cost effectiveness of new cancer drugs and patient and clinician perspectives, and uses this information to make recommendations to the federal, provincial and territorial governments to help guide their cancer drug funding decisions.

6.2. Application of Freedom of Information and Protection of Privacy Legislation to CADTH

Given its nature, pCODR, a program of CADTH, is not subject to federal or provincial freedom of information and protection of privacy legislation. CADTH is a private, not-for-profit organization and is therefore not subject to either federal access to information or provincial/territorial freedom of information statutes. However, many of the P/T health authorities and other partner organizations of CADTH are subject to such legislation. Each P/T health authority and other partner is responsible for interpreting and complying with the applicable legislation, including with regard to third party notification. Any Freedom of Information or Access to information request should be made through the appropriate P/T health authorities or partner organization and not to CADTH.

Sponsors are asked to consent to the information in their submission or resubmission being shared with federal, P/T governments, P/T health authorities, drug plans, Health Canada, PMPRB and the PCPA by signing a [letter template](#). Each of these bodies has their own disclosure of information procedures and are subject to provincial and federal access to information and freedom of information legislation. CADTH has no jurisdiction or control over these procedures and statutory requirements. sponsors/contributors should be aware of these procedures and requirements when including non-disclosable information in a submission or resubmission.

6.3. Information Received by CADTH through Access to Information or Freedom of Information Legislation

When information is received by CADTH through access to information or freedom of information legislation, it is treated in the same way as a submission or resubmission, according to these guidelines. Any non-disclosable information received by CADTH through access to information or freedom of information legislation is treated as non-disclosable information pursuant to these guidelines.

7. Handling Non-Disclosable Information

7.1. Responsibilities of CADTH

- CADTH is responsible for ensuring that the review process is transparent and accountable. As such, CADTH considers it essential that the evidence upon which pERC's recommendations are based be publicly available.
- CADTH will request the sponsor to reconsider any restrictions on disclosure of information if there appears to be no obvious reason for the restrictions, or when such restrictions would make it difficult or impossible for CADTH to show the evidence on which a recommendation is based.
- CADTH will provide an opportunity to the sponsor, prior to pERC deliberations, to create a common understanding between CADTH and the sponsor of the non-disclosable information in the submission or resubmission, as defined by these guidelines, and to understand the management of information not previously put into the public domain.

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- CADTH will not put any review documents into the public domain before the product has received Canadian regulatory approval even though a submission or resubmission may start before Canadian regulatory approval has been granted.
 - CADTH will use reasonable care to prevent the unauthorized use, disclosure, publication or dissemination of non-disclosable information in a submission or resubmission. CADTH is responsible for redacting and/or removing information that has been agreed to be non-disclosable information by both the sponsor and CADTH.
 - CADTH will provide an opportunity to the sponsor to review the Clinical Guidance Report and the Pharmacoeconomic Report, after these reports have been reviewed by the pERC but before they are put into the public domain. The purpose of this opportunity is for the sponsor to:
 - verify that CADTH has adhered to the management of information not previously put into the public domain, as agreed to by CADTH and the sponsor and to understand the disposition of information further provided by the sponsor after the checkpoint meeting.
 - Identify and request the redaction of non-disclosable information that has been included in the executive summary of CADTH's Pharmacoeconomic Report (i.e., the portion of the report that will be posted on the CADTH website).
 - CADTH will not disclose non-disclosable information in a submission or resubmission to any third party except as permitted by these guidelines, or as required by law or by order of a legally qualified court or tribunal.
 - CADTH will use the non-disclosable information in a submission or resubmission solely for the purpose of carrying out its responsibilities with respect to the pCODR process.
 - CADTH has in place secure filing and storage, a password protected web portal and processes for tracking submissions and resubmissions which may contain non-disclosable information
 - CADTH has in place internal processes for dealing with non-disclosable information in a submission or resubmission as described in this guideline.

7.2. Responsibilities of the Sponsor/Contributor

- Material identified as non-disclosable information within a submission or resubmission is expected to be kept to a minimum. It is not acceptable to mark an entire submission or resubmission as non-disclosable. When the sponsor/contributor believes that part of a submission or resubmission or statement should be treated as non-disclosable, they must clearly state the reason for this.
- If a submission or resubmission, or anything received by CADTH related to the product after a submission or resubmission has been filed contains non-disclosable information, it is the responsibility of the sponsor/contributor to clearly identify through highlighting that information which they consider to be non-disclosable information. Highlighted information shall also be listed in the [non-disclosable information template](#) that is filed by the sponsor.
- A summary table listing submitted [non-disclosable information](#) must also be completed with a general justification for considering any highlighted information as potentially non-disclosable. The justification shall identify which subsection of the definition of non-disclosable information in section 3.4 of these guidelines is being applied and how the information meets the definition. This table shall also provide a proposed timeframe for when the potentially non-disclosable information may be put into the public domain by the sponsor or a third party. This table shall be included as part of a submission or resubmission that is filed with

CADTH. If CADTH does not receive a completed table with a submission or resubmission or submitted document, it will not be accepted for review by CADTH. It is only this table and its contents which shall form the basis of confirming non-disclosable information as outlined in the procedures of section 5.

- The sponsor will commit to putting into the public domain, any clinical or economic information that was determined to be relevant to pERC deliberations, and which was agreed to be redacted from Clinical Guidance Reports, Pharmacoeconomic Reports, or pERC recommendations due to the non-disclosable nature ascribed to the information at that point. This redaction shall be time-limited, for the duration that was agreed to by CADTH and the sponsor or for up to six to 12 months from the time of the posting of the pERC Initial Recommendation, whichever is the lesser. As outlined in subsection 3.3(b)(iii) of this guideline, if the sponsor/contributor requests a time frame of greater than six months, the sponsor/contributor must provide a confirmation letter (e.g., acceptance letter from a publication) that the information has been submitted and will be put into the public domain.
- Care should be taken when submitting information relating to individuals. Personal identifiers and sensitive information will be removed.
- Sponsors submitting a drug for review must sign a [statement](#) declaring that all unpublished studies known to the sponsor have been disclosed to CADTH.

7.3. Sharing of Information

- CADTH may release any sponsor-supplied information received through the pCODR process, 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)
 - pan-Canadian Pharmaceutical Alliance office representative(s)
 - Canadian Association of Provincial Cancer Agencies (CAPCA) representative(s)
 - Canadian Blood Services representative(s)
 - members and observers of CADTH's advisory committees and their associated working groups.
- All persons described above (with the exception of staff of Cancer agencies, Federal, P/T governments, P/T health authorities, Health Canada, PMPRB, CAPCA, pCPA) are required to sign a confidentiality agreement requiring them to comply with these guidelines.
- The submission or resubmission, which may include non-disclosable information, may be discussed amongst any or all of these groups and any of the bodies name in the letter signed by the sponsor/contributor acknowledging unrestricted communication about the drug under review. This letter must be provided using a [CADTH template](#).
- As described in the [Notice to Industry: Aligned Reviews Between Health Canada and Health Technology Assessment Organizations](#), an optional information sharing process has been established to permit Health Canada and CADTH to exchange information regarding the drug under review, for submissions filed with CADTH on a pre-NOC basis. 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), potentially avoiding delays in the issuance of CADTH's recommendation.

- CADTH Staff, the Methods Team, Clinical and Economic Guidance Panel members, PAG and CADTH Pharmaceutical Advisory Committee members must abide by the confidentiality clauses contained in their Code of Conduct and/or Conflict of Interest Guidelines.
- Submission or resubmission documents may be shared by organizations, in whole or in part, to third parties when it is necessary to enable the organization to contribute to pERC’s deliberations and recommendation and the third party has seen and agreed to be bound by the terms of a confidentiality agreement.

7.4. Documents and Information that May Be Shared

- The following documents and the information contained in them, including non-disclosable information may be shared with the authorized recipients and may be posted on a secure, password protected web portal, accessible only by persons authorized according to these guidelines:
 - Drug submission or resubmission
 - CADTH Clinical and Pharmacoeconomic reports
 - pERC Initial and Final Recommendations
 - Expert committee briefing materials
 - other review related documents that are generated through the pCODR review process
- The documents listed in the table below will be posted on the CADTH website. After CADTH has posted these documents on its website they are considered in the public domain and disclosable information.

Table 13: CADTH Documents

Document	Earliest Estimated Timeline for Posting ^a
CADTH Clinical Guidance Report	80 business days
CADTH Pharmacoeconomic Report executive summary	80 business days
pERC Initial Recommendation	80 business days
Sponsor feedback on pERC Initial Recommendation	90 business days
PAG feedback on pERC Initial Recommendation	90 business days
pERC Final Recommendation	90 business days

^a For the purposes of calculating these timelines, Day 0 is the day the submission or resubmission is accepted for review by CADTH and assuming market authorization has been issued.

- In addition, tracking information indicating the status of a submission or resubmission in the review queue will be publicly posted on the CADTH website, as outlined in the pCODR Procedures document. Notwithstanding the foregoing, in the event of a submission being reviewed prior to regulatory approval for the drug product, CADTH will not post product strength, product format and NOC date, until such time as regulatory approval has been issued.
- It is the responsibility of authorized recipients and any other party that has signed a confidentiality agreement for the review to treat all review documents listed in Table 13 that are not in the public domain as non-disclosable information until CADTH puts those documents into the public domain. Authorized recipients which are organizations that have signed a non-disclosure or confidentiality agreement are required to bind the individuals of their organization to the requirements of the agreement.

7.5. Referring to Non-Disclosable Information in CADTH Documents That are Publicly Available

- In its Clinical Guidance Reports, Pharmacoeconomic Reports, and pERC recommendation briefs, CADTH reserves the right to use any material submitted during the review process that is not marked as “non-disclosable”, “not disclosable,” or “confidential”, or unpublished information which the sponsor/contributor has agreed with CADTH may be put into the public domain.
- If the sponsor/contributor identifies non-disclosable information in the submission, resubmission, or other information provided to CADTH after the submission or resubmission has been filed, and CADTH has agreed to allow for its use in the review process and consideration by pERC, pursuant to the procedures outlined in these guidelines, CADTH will redact the non-disclosable information prior to posting on the public website. In the case of redactions, CADTH will ‘black out’ the non-disclosable information. The documents may make reference to and indicate the type of information that was redacted (e.g., harms, efficacy, economic evidence) and that the sponsor requested this non-disclosable information be redacted, pursuant to the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*. CADTH may also make reference to the name of the study or such relevant information. CADTH may make reference to any time-limit to redaction that has been agreed to by the sponsor and CADTH.
- CADTH expects that non-disclosable information referred to or redacted from the Clinical Guidance Reports, Pharmacoeconomic Reports, and/or pERC recommendations will be published upon notification by the sponsor that it can be publicly disclosed or in accordance with the date that the information may be disclosed agreed to by the sponsor and CADTH, whichever is earlier.

7.6. Archiving of Non-Disclosable Documents

In addition to the details outlined in the *Procedures for the CADTH pan-Canadian Oncology Drug Review* document regarding the disposition of submission or resubmission documents, CADTH undertakes the following steps regarding the retrieval, archiving and disposal of non-disclosable information:

- all paper and electronic copies of the submission or resubmission documents are retrieved from the review team at the completion of the review.
- one (1) complete CD/DVD set of the submission and one complete set of all documents (paper and/or electronic) associated with the review of a drug are retained on file in secure storage for as long as there may be a need to consult the documents.
- all other extra copies of paper and electronic documents associated with a review are disposed of as described below.
- regular reviews of archived material are undertaken by CADTH. Any material that is no longer required is disposed of as described below.

7.7. Disposal of Non-Disclosable Documents

CADTH will dispose of any paper documents associated with the submission or resubmission by confidential shredding. Any additional CD/DVD sets provided in the submission are destroyed. CADTH will advise the sponsor, in writing, that it has disposed of the extra copies of documents at the completion of the review of the submission or resubmission.

Appendix 2: Checkpoint Meetings

1. Purpose of Checkpoint Meeting

The purpose of the checkpoint meeting with the sponsor is:

1. to directly clarify information in the submission or resubmission and any additional information being provided with members of the CADTH review team; and
2. to discuss the management of non-disclosable information included in the submission or resubmission.

The checkpoint meeting is not for the purposes of confirming information that CADTH will include in the report or to solicit the CADTH review team's interpretation of the data within the submission or resubmission.

The checkpoint meeting with the sponsor will be conducted as outlined in the section 7.3. Information and details provided in this section give additional guidance around the conduct of the checkpoint meeting with the sponsor and any required follow-up actions resulting from the checkpoint meeting.

If procedures relating to the checkpoint meeting are not followed as outlined below or as outlined in section 7.3, the review of the submission or resubmission may be delayed or suspended by CADTH.

2. General Format of the Checkpoint Meeting

The checkpoint meeting will occur in two parts and the conduct of each part of the meeting differs.

- Part one of the checkpoint meeting will be to clarify information in the submission or resubmission and any additional information being provided.
- Part two of the checkpoint meeting will be to discuss the management of non-disclosable information included in the submission or resubmission.

Part one and part two of the checkpoint meeting will be scheduled consecutively with a short break in between.

If the sponsor is not the manufacturer of the drug under review and the manufacturer has contributed substantive clinical or economic information to the review, the manufacturer may be invited to attend the checkpoint meeting with the sponsor.

The checkpoint meeting for both part one and part two will occur as a teleconference or in a webinar format. The checkpoint meeting will occur as a teleconference or in a webinar format to maintain the anonymity of the CADTH review team members. CADTH may disclose a general list of individuals involved in pCODR reviews but does not divulge submission specific review teams as outlined in section 4.5. The anonymity of the review team is preserved by CADTH in order to protect participants from undue influence, to maintain the integrity of assessments without fear of reprisal and to limit the potential for harassment and intimidation of review team members in their professional capacity. The sponsor must not attempt to identify members of the review team during the interactive meeting.

Both part one and part two of the meeting will be recorded by CADTH and a record of the meeting will be retained on file at CADTH.

Sponsor attendees may differ for part one and part two of the meeting. No legal representation is permitted at the checkpoint meeting. A list of all attendees must be provided to CADTH at least five business days in advance of the meeting, otherwise the meeting may be cancelled. If a checkpoint meeting is not held by the target date, CADTH cannot guarantee the review will be completed within the posted timelines and/or the review may be temporarily suspended.

3. Clarification of Information – Part One of the Checkpoint Meeting

The procedures outlined below relate to part one of the checkpoint meeting.

- At part one of the checkpoint meeting, the sponsor will have an opportunity to provide, directly to the CADTH review team, responses to the clarifying questions and the request for additional information, which were sent to the sponsor ten business days in advance.
- An electronic version of the sponsor responses to the clarifying questions and requests for additional information must be provided to CADTH at least one business day in advance of the scheduled checkpoint meeting so that these can be provided to the CADTH review team prior to the interactive meeting.
- The duration of part one of the checkpoint meeting will be a maximum of one hour. Sponsors will be provided with approximately 30 minutes to present responses to the submitted questions. The remainder of the meeting will allow for further clarifications based on the submitted questions and presented responses.
- Sponsors should limit questions for the review team to topics raised in the list of submitted questions. Questions outside the scope of the checkpoint meeting will not be addressed at the meeting.
- Sponsor attendees should include individuals with clinical and economic content expertise who will be able to provide adequate clarification on the content of the submission or resubmission to the CADTH review team.
- Attendees from CADTH can include CADTH staff, Clinical Guidance Panel members, Economic Guidance Panel members and individuals with methodological expertise who are assigned to the review team.
- Anonymous communication during the meeting between the CADTH review team and the sponsor will be facilitated by CADTH.

4. Review of Non-Disclosable Information - Part Two of the Checkpoint Meeting

The procedures outlined below relate to part two of the checkpoint meeting.

- At part two of the checkpoint meeting, CADTH and the sponsor will discuss the management of non-disclosable information included in the submission or resubmission.
- The duration of part two of the checkpoint meeting will be a maximum of one hour. At the meeting, CADTH and the sponsor will go through the submitted summary of non-disclosable information tables, focusing on relevant information that may be included in CADTH's clinical and pharmacoeconomic reports.
- If new non-disclosable information is provided in part one of the meeting, an addendum to the summary table of non-disclosable information an electronic version must be provided by the sponsor at least **one business day** in advance of the scheduled checkpoint meeting. No additional meeting materials are required.
- Sponsor attendees should include at least one senior representative with the authority to make decisions regarding disclosure of information.
- Attendees from CADTH will typically include review team members.

5. Checkpoint Meeting Decisions

CADTH will write a *Record of Decisions* for the checkpoint meeting. Decisions will include both those related to additional information and clarification of the submission as well as the review of non-disclosable

information in the submission or resubmission. Both pending decisions and decisions agreed upon at the checkpoint meeting will be documented.

The *Record of Decisions* will be provided to the sponsor and/or manufacturer within two business days of the checkpoint meeting via secure electronic transmission. An email notification will be sent to the sponsor's contact(s) with a unique, time-limited and user-specific link to the Record of Decisions.

Decisions made at the meeting will not be open for further negotiation and discussion following the checkpoint meeting.

Upon receipt of the Record of Decisions, the sponsor will have five business days to submit proposed resolutions to items noted as pending decisions. The sponsor should provide the resolution to CADTH through the secure [Collaborative Workspaces](#).

CADTH will have five business days to review the proposed resolutions. If agreement cannot be reached, CADTH will not use the information in the Clinical Guidance Report or the Pharmacoeconomic Report provided to pERC.

An *Addendum to the Record of Decisions* will be written by CADTH and provided to the sponsor via secure electronic transmission, within five business days of receiving the proposed resolutions from the sponsor. The *Addendum* will outline CADTH's final decisions on the management of non-disclosable information in the review. An email notification will be sent to the sponsor's contact(s) with a unique, time-limited and user-specific link to the *Addendum to the Record of Decisions*.

CADTH may share the *Record of Decisions* and *Addendum to the Record of Decisions* with authorized recipients, as defined in the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*.

6. Verification of Handling Non-Disclosable Information Following the Checkpoint Meeting

Four business days prior to the posting of the pERC initial recommendation and the CADTH reports, the sponsor will be provided with the opportunity to verify that non-disclosable information was handled in the manner agreed upon at the checkpoint meeting, and as documented in the *Record of Decisions* and the *Addendum to the Record of Decisions*.

The CADTH clinical report, pharmacoeconomic report, and the executive summary of the economic report to be publicly posted will be made available to the sponsor via secure electronic transmission. An email notification will be sent to the sponsor's contact(s) with a unique, time-limited and user-specific link to the CADTH reports.

If during the review of the report, the sponsor and/or manufacturer of the drug under review identify any discrepancies or errors, they should be submitted in writing to CADTH within the three business day period through [Collaborative Workspaces](#). CADTH will consider the proposed discrepancies and errors and make revisions or additional redactions to the CADTH clinical and pharmacoeconomic reports and the pERC Initial Recommendation as deemed necessary by CADTH and prior to public posting of these documents. Discrepancies and errors should be documented in the [template for verification of handling non-disclosable information](#).

Appendix 3: Procedural Review Guidelines for the CADTH pan-Canadian Oncology Drug Review

1. What is a procedural review?

The procedural review is a determination of whether CADTH and/or pERC have complied with review processes and procedures. After a pERC Final Recommendation for a drug reviewed by CADTH has been publicly posted on the CADTH website, a request for a procedural review may be submitted on the grounds that CADTH failed to act in accordance with its procedures in conducting the review or that pERC failed to apply its deliberative framework in formulating the pERC Final Recommendation. CADTH is committed to following its posted review processes, including ensuring that the pERC deliberative framework is applied in formulating recommendations. A party who has participated in CADTH's review of a drug through the pCODR process and who believes that the process has not been followed as set out in the *Procedures for the CADTH pan-Canadian Oncology Drug Review* or that the *pERC Deliberative Framework* was not applied, may submit a procedural review request on these grounds. These grounds relate only to whether or not process was followed and not to the content of the pERC Final Recommendation. The request for a procedural review is screened by the CADTH in accordance with the process outline below.

2. Who can submit a procedural review request?

Any one of the parties who participated in CADTH's review of a drug through the pCODR process may submit a request for a procedural review:

- the sponsor of the drug submission,
- the manufacturer of the drug under review, if they contributed information to the submission or if they provided feedback on the pERC Initial Recommendation,
- the Provincial Advisory Group (PAG),
- Registered patient groups (or individual patient or caregiver in cases where there is no patient group) who provided input on the drug under review or feedback on the Initial Recommendation, or
- Registered clinicians who provided input on the drug under review or feedback on the Initial Recommendation

Multiple parties may submit a request for a procedural review of a pERC Final Recommendation but each of these parties may submit only one request per pERC Final Recommendation.

3. On what basis can a procedural review request be submitted?

A procedural review request may be submitted on the basis that:

- CADTH failed to act in accordance with its procedures in conducting the review
- pERC failed to apply its deliberative framework in formulating its recommendation

These grounds relate only to whether or not process was followed and not to the content of the pERC Final Recommendation. Differences in the interpretation and use of data during the review do not constitute grounds for a procedural review, e.g. the selection of comparators, the use of data sets, the place in therapy. In addition, disagreement with CADTH's approach to managing non-disclosable information that was provided in the submission or resubmission, 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 *Procedures for the CADTH pan-Canadian Oncology Drug Review* and the *Disclosure of Information Guidelines for the CADTH pan-Canadian Oncology Drug Review*.

4. When can a procedural review request be submitted?

A procedural review request must be submitted within 10 business days of a pERC Final Recommendation being publicly posted on the CADTH website. Following the conduct of a procedural review, further procedural review requests related to the associated pERC Final Recommendation cannot be made. When the pERC Final Recommendation is posted following a re-deliberation, a Notification to Implement a pERC Final Recommendation will be issued by CADTH, indicating that the participating drug programs can proceed to implement the recommendation and that no further procedural review requests are permitted.

5. How is the procedural review process initiated?

A party who has participated in CADTH's review of a drug through the pCODR process completes a [pCODR Procedural Review Request Form](#). The form is submitted, along with supporting documentation to CADTH either via email or through the Collaborative Workspaces within 10 business days of a pERC Final Recommendation being issued. No extensions will be granted to the 10-business day period and all supporting documentation must be submitted within this period. Intent to submit supporting documentation after the 10-business day period will not be considered sufficient for initiation of the procedural review process.

6. Who conducts the procedural review?

Procedural review requests are reviewed by senior CADTH staff consulting with the Pharmaceutical Advisory Committee. CADTH may ask for clarification or additional information from the party making the request to assist in determining if grounds for a procedural review exist. This clarification must be provided by the procedural review requestor, as outlined by CADTH, within 15 days of a Final Recommendation being posted on the CADTH website, otherwise the request for a procedural review may not be accepted.

- If the request for a procedural review is not accepted, the party who made the request will be notified in writing by CADTH. A Notification to Implement a pERC Final Recommendation will be issued by CADTH, allowing the participating drug programs to proceed with implementation of the pERC Final Recommendation.
- If the request for a procedural review is accepted, the party who made the request will be notified in writing by CADTH. CADTH will adjudicate the procedural review request and will determine which steps in the pCODR review process must be revisited in order to ensure that CADTH procedures have been followed appropriately. This may include re-deliberation by pERC at the next possible meeting.

7. How is a procedural review conducted?

At the beginning of the procedural review, the pERC Chair or program staff has the option to provide a provisional response as part of the procedural review process.

As may be required throughout the procedural review, CADTH may request additional information from the party who made the request, pERC, or other parties that participated in the review of the drug through the pCODR process. CADTH may also engage additional expertise, as required.

Senior CADTH staff will determine the outcomes of the procedural review, which are outlined in section 8. This determination will be communicated in writing to the party who made the request, the participating drug programs, and pERC. It is important to note that the outcome of the procedural review may or may not result in a change to the pERC Final Recommendation.

The participating drug programs do not implement the pERC Final Recommendation while a procedural review is being conducted. CADTH will issue a Notification to Implement a pERC Final Recommendation, indicating that the recommendation can be implemented.

8. What are the possible outcomes of a procedural review?

After review of the procedural review request has been conducted, senior CADTH staff may determine that:

1. The procedures were correctly applied by CADTH and no changes are required to the pERC Final Recommendation. A Notification to Implement the pERC Final Recommendation should be issued by CADTH.
2. Steps in the pCODR review process must be revisited and/or the submission must be re-deliberated by pERC at the next possible pERC meeting. A re-deliberation may result in the pERC Final Recommendation being maintained or being changed.
 - If the pERC Final Recommendation is maintained following the re-deliberation, a Notification to Implement the pERC Final Recommendation will be issued by CADTH.
 - If the pERC Final Recommendation is changed following the re-deliberation, a new pERC Final Recommendation will be publicly posted and a Notification to Implement the pERC Final Recommendation will be issued by CADTH.

If steps in the pCODR review process must be revisited and/or the recommendation re-deliberated, the submission receives priority placement on the pERC meeting agenda at which it will be re-deliberated and work on the submission would be prioritized within the pCODR process.

9. How are decisions on procedural reviews communicated?

High-level details of any submitted procedural review request will be publicly posted on the CADTH website.

If there are no grounds for a procedural review, this will be determined within 15 business days of the submitted date of an application for a procedural review, and it will be communicated on the CADTH website that the pERC Final Recommendation can be implemented.

When a pERC Final Recommendation can be implemented, CADTH will issue a Notification to Implement a pERC Final Recommendation and this will be communicated on the CADTH website.

The party who made the request will be informed by CADTH in writing of the following key procedural review decisions:

- After a procedural review request has been submitted, if the procedural review request has been accepted or not accepted.
- If accepted, whether the submission or resubmission will be re-deliberated by pERC or if a Notification to Implement a pERC Final Recommendation will be issued without a re-deliberation of the submission or resubmission.

The details and outcomes of the procedural review will be communicated in the pERC Final Recommendation.

10. How long does the procedural review process take?

A decision on whether or not to conduct a procedural review will take place within 15 business days of the submitted date of an application for a procedural review. The duration of the procedural review may vary, depending on the complexity and nature of the request.

Appendix 4: Suggested Reporting Format for Economics

Table 14: Disaggregated Clinical Outcomes and Costs

Parameter	Drug under Review	Comparator #1	Comparator #2 (add as required)
Discounted LYs			
Total LYs			
By Health State			
Health state 1			
Health state 2			
Discounted QALYs			
Total QALYs			
By Health State			
Health state 1			
Health state 2			
Incremental QALYs generated within trial period			
Incremental QALYs generated after trial period			
Discounted Costs			
Total Costs			
Drug			
Administration			
Other resource costs			
Health state/event			
Add others (as required)			

LYs = life-years; QALY = quality-adjusted life-years

Table 15: Presentation of Sequential ICURs

Treatment	Cost	QALYs	Incremental cost per QALY gained	
			Versus Reference	Sequential ICUR
Reference (Intervention A)				
Intervention B				
Intervention C				
Intervention D				

ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-years

Table 16: Disaggregated Costs in Budget Impact Analysis

Parameter	Drug Under Review	Comparator #1	Comparator #2 (add as required)
Drug program perspective			
Drug Acquisition Costs			
Premedication costs			
Concomitant medication costs			
Drug costs related to adverse events			
Drug costs related to subsequent treatment			
Dispensing Fee			
Mark-up costs			
Total cost			

Table 17: Presentation of Budget Impact Analysis Results

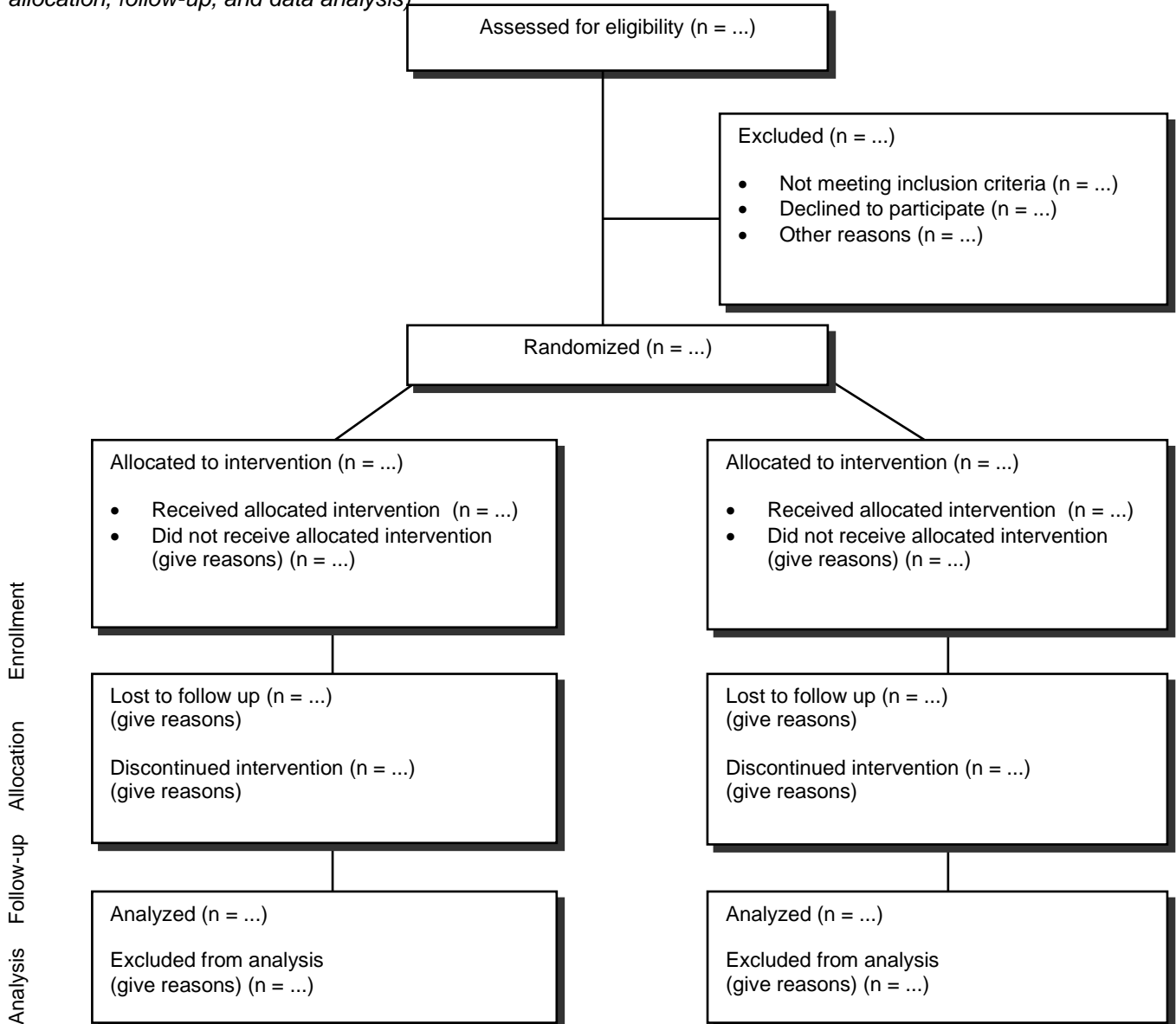
Costs (\$)	Year 0 (Baseline Year)	Year 1	Year 2	Year 3
Reference scenario				
Drug Under Review	–	–	–	–
Intervention A				
Intervention B				
Total costs				
New drug scenario				
Drug Under Review				
Intervention A				
Intervention B				
Total costs				
Budget impact				
3-year budget impact				

Appendix 5: CONSORT Reporting Standard for Patient Flow

Note: This is an example of the type of information that is required. It can be provided in a different format as long as all of the information shown in the flowchart below is provided.

CONSORT Flowchart

Flow Diagram of the progress through the phases of a randomized trial (i.e., enrolment, intervention allocation, follow-up, and data analysis)



For Reference: Schulz KF, Altman DG, Moher D, CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. *PLoS Med* [Internet]. 2010 [cited 2010 Apr 21];7(3):e1000251. Available from: <http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1000251>

Appendix 6: Checklists for Preparing Applications

Sponsors may use the checklists used by CADTH, as provided in this appendix, to help ensure that all submission or resubmission requirements for a CADTH Pan-Canadian Oncology Drug Review have been included.

A. Submission Requirements for a Standard Review Filed on a Pre-NOC Basis

Requirement	Specific Items and Criteria	Included
General Information		
Signed cover letter	• Clear description of submission filed	<input type="checkbox"/>
	• The indication(s) to be reviewed by CADTH	<input type="checkbox"/>
	• Requested reimbursement conditions, if applicable	<input type="checkbox"/>
	• Names and contact information for primary and backup contacts	<input type="checkbox"/>
Pre-submission information form	• Updated pre-submission information form • Supporting references for specified listing when requested by sponsor	<input type="checkbox"/>
Product monograph	• A copy of the most recent draft product monograph	<input type="checkbox"/>
Declaration letter	• Completed declaration letter template	<input type="checkbox"/>
Non-disclosable information	• Summary table listing non-disclosable information	<input type="checkbox"/>
Health Canada Documentation		
NOC	• A placeholder document indicating the anticipated NOC date for the indications(s) to be reviewed by CADTH	<input type="checkbox"/>
Clarimails/Clarifaxes	At time of filing: • Summary table of clinical Clarimails/Clarifaxes up to time of filing	<input type="checkbox"/>
	• Copies of all Clarifaxes and responses to the point of the NOC or NOC/c being issued by Health Canada.	<input type="checkbox"/>
	Ongoing basis until NOC or NOC/c is issued: • Revised clinical Clarimail/Clarifax summary table(s)	<input type="checkbox"/>
Screening acceptance letter	• A copy of the Screening Acceptance Letter	<input type="checkbox"/>
Efficacy, Effectiveness, and Safety Information		
Common technical document	• 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 2.7.6	<input type="checkbox"/>
	• Or a statement indicating section(s) were not required by Health Canada	<input type="checkbox"/>
Clinical studies	• Reference list of key clinical issues studies (published and unpublished)	<input type="checkbox"/>
	• Copies of studies addressing key clinical issues	<input type="checkbox"/>
Study protocol	• A copy of the study protocol for the pivotal study(ies)	<input type="checkbox"/>
Statistical analysis plan	• A copy of the statistical analysis plan for the pivotal study(ies)	<input type="checkbox"/>
Clinical study reports	• Complete clinical study reports for all pivotal studies as well as other studies that address key clinical issues (if submission is filed on or after March 2, 2020)	<input type="checkbox"/>

Requirement	Specific Items and Criteria	Included
CONSORT diagrams	<ul style="list-style-type: none"> Diagrams following CONSORT reporting standards or similar diagrams, documenting flow of patients through studies 	<input type="checkbox"/>
Table of studies	<ul style="list-style-type: none"> Completed table of studies template 	<input type="checkbox"/>
Search strategy	<ul style="list-style-type: none"> Search strategies used to locate published studies 	<input type="checkbox"/>
Editorials and errata	<ul style="list-style-type: none"> Reference list of editorial articles and errata (or document stating none found) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Copies of editorial articles and errata 	<input type="checkbox"/>
New data	<ul style="list-style-type: none"> Reference list of new data (or statement that none available) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Copies of new data available 	<input type="checkbox"/>
Validity of outcome measures	<ul style="list-style-type: none"> Reference list (or statement that none available) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Copies of validity of outcome measure references available 	<input type="checkbox"/>
Indirect comparison	<ul style="list-style-type: none"> Copies of any indirect comparisons used in pharmacoeconomic evaluation 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Indirect comparison technical report 	<input type="checkbox"/>
Provisional algorithm	<ul style="list-style-type: none"> Place in therapy template 	
	<ul style="list-style-type: none"> A reference list (or statement that none available) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Copies of studies that address sequencing of therapies 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Copy of the search strategy for sequencing of therapies 	<input type="checkbox"/>
Economic Information		
Pharmacoeconomic evaluation: technical report	<ul style="list-style-type: none"> Pharmacoeconomic evaluation for the full population identified in the indication(s) to be reviewed by CADTH 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Scenario analysis of the population identified in the reimbursement request (if different from the population in the full indication) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Economic evaluation is a cost-utility analysis 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Base case reflects the public health care payer perspective 	<input type="checkbox"/>
	<ul style="list-style-type: none"> 1.5% discount rate on costs and QALYs 	<input type="checkbox"/>
	<ul style="list-style-type: none"> All relevant comparators have been included 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Submitted price per smallest dispensable unit used 	<input type="checkbox"/>
	<ul style="list-style-type: none"> All results are presented probabilistically 	<input type="checkbox"/>
	<ul style="list-style-type: none"> All ICERs reported sequentially if more than one comparator is presented 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Results are presented in disaggregated format 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Treatment effect measures should generally not use composite endpoints 	<input type="checkbox"/>
	<ul style="list-style-type: none"> If relevant, a graph with Kaplan-Meier curve and parametric distributions for each relevant outcome 	<input type="checkbox"/>
	<ul style="list-style-type: none"> If relevant, companion diagnostic test information incorporated 	<input type="checkbox"/>
<ul style="list-style-type: none"> Alignment between the pharmacoeconomic evaluation technical report and the economic model 	<input type="checkbox"/>	
Economic model	<ul style="list-style-type: none"> Model is programmed in Excel 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model is fully unlocked and executable, and all code is provided 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model functions in a standalone environment and does not require access to a web-based platform 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Probabilistic analyses runs without error 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Results of the probabilistic analysis are stable (congruence test provided) 	<input type="checkbox"/>

Requirement	Specific Items and Criteria	Included
	<ul style="list-style-type: none"> Where there are multiple comparators, the model runs treatments simultaneously and results of all comparators are presented 	<input type="checkbox"/>
	<ul style="list-style-type: none"> 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 	<input type="checkbox"/>
Supporting documentation	<ul style="list-style-type: none"> Model user guide 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Indirect comparison technical report 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Unpublished studies or analyses used to inform the pharmacoeconomic evaluation 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Document summarizing key sources of information for the companion diagnostic test 	<input type="checkbox"/>
Budget Impact Analysis		
Budget impact analysis: technical report	<ul style="list-style-type: none"> Base case reflects pan-Canadian (national) perspective (excluding Quebec) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Base case reflects the Health Canada-approved (proposed) indication 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Scenario analysis of the reimbursement request population (if different from the Health Canada-approved (proposed) indication) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Base case analysis uses a one-year baseline period and three-year forecast period. 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Analyses presented deterministically 	<input type="checkbox"/>
	<ul style="list-style-type: none"> All relevant comparators included 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Submitted price per smallest dispensable unit used 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Report includes at minimum decision problem, methods, assumptions and results 	<input type="checkbox"/>
Budget impact model	<ul style="list-style-type: none"> Model is programmed in Excel 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model is fully unlocked and executable and all code provided 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model functions in a standalone environment and does not require access to a web-based platform 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model is flexible and allows assessment for each individual drug program 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Input values specific to the individual drug program 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Breakdown of costs by perspective reported within the submitted model 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Alignment between the technical report and the model 	<input type="checkbox"/>
Supporting documentation	<ul style="list-style-type: none"> Reference list of all supporting documentation used and/or cited in BIAs 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Unpublished studies or analyses used to inform the budget impact analysis 	<input type="checkbox"/>
Epidemiologic Information		
Disease prevalence and incidence	<ul style="list-style-type: none"> Disease prevalence and incidence with specified breakdown (if available) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Document is referenced 	<input type="checkbox"/>
Reimbursement status of comparators	<ul style="list-style-type: none"> A completed template summarizing the reimbursement status of all appropriate comparators (for all submissions filed on or after March 2, 2020). 	<input type="checkbox"/>
Pricing and Distribution Information		
Price and distribution method	<ul style="list-style-type: none"> Submitted unit pricing to four decimal places 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Method of distribution 	<input type="checkbox"/>
Companion Diagnostic(s)		

Requirement	Specific Items and Criteria	Included
Companion diagnostics	• Reference list	<input type="checkbox"/>
	• Articles that highlight the clinical utility of the companion diagnostic(s)	<input type="checkbox"/>
	• Disclosable price for the companion diagnostic(s)	<input type="checkbox"/>
Category 2 Requirements		
Signed cover letter	• A clear description of the documents being filed	<input type="checkbox"/>
	• The date the NOC or NOC/c was received	<input type="checkbox"/>
	• Intention to provide any remaining category 2 requirements	<input type="checkbox"/>
NOC	• A copy of the NOC or NOC/c, dated and signed by Health Canada, as soon as it has been issued.	<input type="checkbox"/>
Product monograph	• Draft product monograph with tracked clinical and label review changes up to time of Health Canada approval	<input type="checkbox"/>
	• Clean and dated version of Health Canada–approved product monograph	<input type="checkbox"/>

ICER = incremental cost-effectiveness ratio; NOC = Notice of Compliance; NOC/c = Notice of Compliance with conditions.

B. Submission Requirements for a Standard Review Filed on a Post-NOC Basis

Requirement	Specific Items and Criteria	Included
General Information		
Signed cover letter	• Clear description of submission filed	<input type="checkbox"/>
	• The indication(s) to be reviewed by CADTH	<input type="checkbox"/>
	• Requested reimbursement conditions, if applicable	<input type="checkbox"/>
	• Names and contact information for primary and backup contacts	<input type="checkbox"/>
Pre-submission information form	• Updated pre-submission information form • Supporting references for specified listing when requested by sponsor	<input type="checkbox"/>
Product monograph	• A copy of the most current version of the Health Canada–approved product monograph	<input type="checkbox"/>
Declaration letter	• Completed declaration letter template	<input type="checkbox"/>
Non-disclosable information	• Summary table listing non-disclosable information	<input type="checkbox"/>
Health Canada Documentation		
NOC	• A copy of the NOC or NOC/c granted for the indication(s) to be reviewed	<input type="checkbox"/>
	• Letter of Undertaking (only if NOC/c granted)	<input type="checkbox"/>
Clarimails/Clarifaxes	• Summary table of any clinical Clarimails/Clarifaxes up to the time of NOC or NOC/c being issued	<input type="checkbox"/>
Efficacy, Effectiveness, and Safety Information		
Common technical document	• 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 2.7.6	<input type="checkbox"/>
	• Or a statement indicating which section(s) were not required by Health Canada	<input type="checkbox"/>
Clinical studies	• Reference list of key clinical issues studies (published and unpublished)	<input type="checkbox"/>
	• Copies of studies addressing key clinical issues	<input type="checkbox"/>
Study protocol	• A copy of the study protocol for the pivotal study(ies)	<input type="checkbox"/>
Statistical analysis plan	• A copy of the statistical analysis plan for the pivotal study(ies)	<input type="checkbox"/>
Clinical study reports	• Complete clinical study reports for all pivotal studies as well as other studies that address key clinical issues (if submission is filed on or after March 2, 2020)	<input type="checkbox"/>
CONSORT diagrams	• Diagrams following CONSORT reporting standards or similar diagrams, documenting flow of patients through studies	<input type="checkbox"/>
Table of studies	• Completed table of studies template	<input type="checkbox"/>
Search strategy	• Search strategies used to locate published studies	<input type="checkbox"/>

Requirement	Specific Items and Criteria	Included
Editorials and errata	<ul style="list-style-type: none"> Reference list of editorial articles and errata (or document stating none found) Copies of editorial articles and errata 	<input type="checkbox"/>
New data	Reference list of new data (or statement that none available)	<input type="checkbox"/>
	Copies of new data available	<input type="checkbox"/>
Validity of outcome measures	Reference list (or statement that none available)	<input type="checkbox"/>
	Copies of validity of outcome measure references available	<input type="checkbox"/>
Indirect comparison	Copies of any indirect comparisons used in pharmacoeconomic evaluation	<input type="checkbox"/>
	Indirect comparison technical report	<input type="checkbox"/>
Provisional algorithm	Place in therapy template	
	A reference list (or statement that none 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"/>
Economic Information		
Pharmacoeconomic evaluation: technical report	Pharmacoeconomic evaluation for the full population identified in the 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"/>
	Economic evaluation is a cost-utility analysis	<input type="checkbox"/>
	Base case reflects public health care payer perspective	<input type="checkbox"/>
	1.5% discount rate on costs and QALYs	<input type="checkbox"/>
	All relevant comparators have been included	<input type="checkbox"/>
	Submitted price per smallest dispensable unit used	<input type="checkbox"/>
	All results are presented probabilistically	<input type="checkbox"/>
	All ICERs reported sequentially if more than one comparator is presented	<input type="checkbox"/>
	Results are presented in disaggregated format	<input type="checkbox"/>
	Treatment effect measures should generally not use composite endpoints	<input type="checkbox"/>
	If relevant, a graph with Kaplan-Meier curve and parametric distributions for each relevant outcome	<input type="checkbox"/>
	If relevant, companion diagnostic test information incorporated	<input type="checkbox"/>
	Alignment between the pharmacoeconomic evaluation technical report and the economic model	<input type="checkbox"/>
Economic model	Model is programmed in Excel	<input type="checkbox"/>
	Model is fully unlocked and executable, and all code is provided.	<input type="checkbox"/>
	Model functions in a standalone environment and does not require access to a web-based platform	<input type="checkbox"/>
	Probabilistic analyses runs without error	<input type="checkbox"/>
	Results of the probabilistic analysis are stable (congruence test provided)	<input type="checkbox"/>
	Where there are multiple comparators, the model runs treatments simultaneously and results of all comparators are presented	<input type="checkbox"/>

Requirement	Specific Items and Criteria	Included
	<ul style="list-style-type: none"> 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. 	<input type="checkbox"/>
Supporting documentation	<ul style="list-style-type: none"> Model user guide 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Indirect comparison technical report 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Unpublished studies or analyses used to inform the pharmacoeconomic evaluation 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Document summarizing key sources of information for the companion diagnostic test 	<input type="checkbox"/>
Budget Impact Analysis		
Budget impact analysis: technical report	<ul style="list-style-type: none"> Base case reflects pan-Canadian (national) perspective (excluding Quebec) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Base case reflects the Health Canada-approved indication 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Scenario analysis of the reimbursement request population (if different from the Health Canada-approved indication) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Base case analysis uses a one-year baseline period and three-year forecast period 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Analyses presented deterministically 	<input type="checkbox"/>
	<ul style="list-style-type: none"> All relevant comparators included 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Submitted price per smallest dispensable unit used 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Report includes at minimum decision problem, methods, assumptions and results 	<input type="checkbox"/>
Budget impact model	<ul style="list-style-type: none"> Model is programmed in Excel 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model is fully unlocked and executable and all code provided 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model functions in a standalone environment and does not require access to a web-based platform 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model is flexible and allows assessment for each individual drug program 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Input values specific to the individual drug program 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Breakdown of costs by perspective reported within the submitted model 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Alignment between the technical report and the model 	<input type="checkbox"/>
Supporting documentation	<ul style="list-style-type: none"> Reference list of all supporting documentation used and/or cited in BIAs 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Copies of all supporting documentation used and/or cited in the BIAs 	<input type="checkbox"/>
Epidemiologic Information		
Disease prevalence and incidence	<ul style="list-style-type: none"> Disease prevalence and incidence with specified breakdown (if available) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Document is referenced 	<input type="checkbox"/>
Reimbursement status of comparators	<ul style="list-style-type: none"> A completed template summarizing the reimbursement status of all appropriate comparators (for all submissions filed on or after March 2, 2020). 	<input type="checkbox"/>
Pricing and Distribution Information		
Price and distribution method	<ul style="list-style-type: none"> Submitted unit pricing to four decimal places 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Method of distribution 	<input type="checkbox"/>

Requirement	Specific Items and Criteria	Included
Companion Diagnostic(s)		
Companion diagnostics	• Reference list	<input type="checkbox"/>
	• 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"/>

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

C. Submission Requirements for a Cell or Gene Therapy Filed on a Pre-NOC Basis

Requirement	Specific Items and Criteria	Included
General Information		
Signed cover letter	• Clear description of submission filed	<input type="checkbox"/>
	• The indication(s) to be reviewed by CADTH	<input type="checkbox"/>
	• Requested reimbursement conditions, if applicable	<input type="checkbox"/>
	• Names and contact information for primary and backup contacts	<input type="checkbox"/>
Pre-submission information form	• Updated pre-submission information form • Supporting references for specified listing when requested by sponsor	<input type="checkbox"/>
Product monograph	• A copy of the most recent draft product monograph	<input type="checkbox"/>
Declaration letter	• Completed declaration letter template	<input type="checkbox"/>
Non-disclosable information	• Summary table listing non-disclosable information	<input type="checkbox"/>
Health Canada Documentation		
NOC	• A placeholder document indicating the anticipated NOC date for the indications(s) to be reviewed by CADTH	<input type="checkbox"/>
Clarimails/Clarifaxes	At time of filing: • Summary table of clinical Clarimails/Clarifaxes up to time of filing	<input type="checkbox"/>
	• Copies of all Clarifaxes and responses to the point of the NOC or NOC/c being issued by Health Canada.	<input type="checkbox"/>
	Ongoing basis until NOC or NOC/c is issued: • Revised clinical Clarimail/Clarifax summary table(s)	<input type="checkbox"/>
Screening acceptance letter	• A copy of the Screening Acceptance Letter	<input type="checkbox"/>
Efficacy, Effectiveness, and Safety Information		
Common technical document	• 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 2.7.6	<input type="checkbox"/>
	• Or a statement indicating which section(s) were not required by Health Canada	<input type="checkbox"/>
Clinical studies	• Reference list of key clinical issues studies (published and unpublished)	<input type="checkbox"/>
	• Copies of studies addressing key clinical issues	<input type="checkbox"/>
Study protocol	• A copy of the study protocol for the pivotal study(ies)	<input type="checkbox"/>
Statistical analysis plan	• A copy of the statistical analysis plan for the pivotal study(ies)	<input type="checkbox"/>
Clinical study reports	• Complete clinical study reports for all pivotal studies as well as other studies that address key clinical issues (if submission is filed on or after March 2, 2020)	<input type="checkbox"/>
CONSORT diagrams	• Diagrams following CONSORT reporting standards or similar diagrams, documenting flow of patients through studies	<input type="checkbox"/>
Table of studies	• Completed table of studies template	<input type="checkbox"/>
Search strategy	• Search strategies used to locate published studies	<input type="checkbox"/>

Requirement	Specific Items and Criteria	Included
Editorials and errata	<ul style="list-style-type: none"> Reference list of editorial articles and errata (or document stating none found) Copies of editorial articles and errata 	<input type="checkbox"/>
New data	<ul style="list-style-type: none"> Reference list of new data (or statement that none available) Copies of new data available 	<input type="checkbox"/>
Validity of outcome measures	<ul style="list-style-type: none"> Reference list (or statement that none available) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Copies of validity of outcome measure references available 	<input type="checkbox"/>
Indirect comparison	<ul style="list-style-type: none"> Copies of any indirect comparisons used in pharmacoeconomic evaluation 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Technical report 	<input type="checkbox"/>
Provisional algorithm	<ul style="list-style-type: none"> Place in therapy template 	
	<ul style="list-style-type: none"> A reference list (or statement that none available) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Copies of studies that address sequencing of therapies 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Copy of the search strategy for sequencing of therapies 	<input type="checkbox"/>
Economic Information		
Pharmacoeconomic evaluation: technical report	<ul style="list-style-type: none"> Pharmacoeconomic evaluation for the full population identified in the indication(s) to be reviewed by CADTH 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Scenario analysis of the population identified in the reimbursement request (if different from the population in the full indication) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Economic evaluation is a cost-utility analysis 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Base case reflects public health care payer perspective 	<input type="checkbox"/>
	<ul style="list-style-type: none"> 1.5% discount rate on costs and QALYs 	<input type="checkbox"/>
	<ul style="list-style-type: none"> All relevant comparators have been included 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Submitted price per smallest dispensable unit used 	<input type="checkbox"/>
	<ul style="list-style-type: none"> All results are presented probabilistically 	<input type="checkbox"/>
	<ul style="list-style-type: none"> All ICERs reported sequentially if more than one comparator is presented 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Results are presented in disaggregated format 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Treatment effect measures should generally not use composite endpoints 	<input type="checkbox"/>
	<ul style="list-style-type: none"> If relevant, a graph with Kaplan-Meier curve and parametric distributions for each relevant outcome. 	<input type="checkbox"/>
	<ul style="list-style-type: none"> If relevant, companion diagnostic test information incorporated 	<input type="checkbox"/>
<ul style="list-style-type: none"> Alignment between the pharmacoeconomic evaluation technical report and the economic model 	<input type="checkbox"/>	
Economic model	<ul style="list-style-type: none"> Model is programmed in Excel 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model is fully unlocked and executable, and all code is provided. 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model functions in a standalone environment and does not require access to a web-based platform 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Probabilistic analyses runs without error 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Results of the probabilistic analysis are stable (congruence test provided) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Where there are multiple comparators, the model runs treatments simultaneously and results of all comparators are presented 	<input type="checkbox"/>
	<ul style="list-style-type: none"> 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. 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model user guide 	<input type="checkbox"/>

Requirement	Specific Items and Criteria	Included
Supporting documentation	• Indirect comparison technical report	<input type="checkbox"/>
	• Unpublished studies or analyses used to inform the pharmacoeconomic evaluation	<input type="checkbox"/>
	• Document summarizing key sources of information for the companion diagnostic test	<input type="checkbox"/>
Budget Impact Analysis		
Budget impact analysis: technical report	• Base case reflects pan-Canadian (national) perspective (excluding Quebec)	<input type="checkbox"/>
	• Base case reflects the Health Canada-approved (proposed) indication	<input type="checkbox"/>
	• Scenario analysis of the reimbursement request population (if different from the Health Canada-approved (proposed) indication)	<input type="checkbox"/>
	• Base case analysis uses a one-year baseline period and three-year forecast period	<input type="checkbox"/>
	• Analyses presented deterministically	<input type="checkbox"/>
	• All relevant comparators included	<input type="checkbox"/>
	• Submitted price per smallest dispensable unit used	<input type="checkbox"/>
	• Report includes at minimum decision problem, methods, assumptions and results	<input type="checkbox"/>
Budget impact model	• Model is programmed in Excel	<input type="checkbox"/>
	• Model is fully unlocked and executable and all code provided	<input type="checkbox"/>
	• Model functions in a standalone environment and does not require access to a web-based platform	<input type="checkbox"/>
	• Model is flexible and allows assessment for each individual drug program	<input type="checkbox"/>
	• Input values specific to the individual drug program	<input type="checkbox"/>
	• Breakdown of costs by perspective reported within the submitted model	<input type="checkbox"/>
	• Alignment between the technical report and the model	<input type="checkbox"/>
Supporting documentation	• Reference list of all supporting documentation used and/or cited in BIAs	<input type="checkbox"/>
	• Unpublished studies or analyses used to inform the budget impact analysis	<input type="checkbox"/>
Reimbursement status of comparators	• A completed template summarizing the reimbursement status of all appropriate comparators (for all submissions filed on or after March 2, 2020).	<input type="checkbox"/>
Epidemiologic Information		
Disease prevalence and incidence	• Disease prevalence and incidence with specified breakdown (if available)	<input type="checkbox"/>
	• Document is referenced	<input type="checkbox"/>
Pricing and Distribution Information		
Price and distribution method	• Submitted unit pricing to four decimal places	<input type="checkbox"/>
	• Method of distribution	<input type="checkbox"/>
Implementation plan	• Completed implementation plan template	<input type="checkbox"/>
Companion Diagnostic(s)		
Companion diagnostics	• Reference list	<input type="checkbox"/>
	• 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"/>
Category 2 Requirements		
Signed cover letter	• A clear description of the documents being filed	<input type="checkbox"/>

Requirement	Specific Items and Criteria	Included
	<ul style="list-style-type: none"> The date the NOC or NOC/c was received 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Intention to provide any remaining category 2 requirements 	<input type="checkbox"/>
NOC	<ul style="list-style-type: none"> A copy of the NOC or NOC/c, dated and signed by Health Canada, as soon as it has been issued. 	<input type="checkbox"/>
Product monograph	<ul style="list-style-type: none"> Draft product monograph with tracked clinical and label review changes up to time of Health Canada approval 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Clean and dated version of Health Canada–approved product monograph 	<input type="checkbox"/>

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

D. Submission Requirements for a Cell or Gene Therapy Filed on a Post-NOC Basis

Requirement	Specific Items and Criteria	Included
General Information		
Signed cover letter	• Clear description of submission filed	<input type="checkbox"/>
	• The indication(s) to be reviewed by CADTH	<input type="checkbox"/>
	• Requested reimbursement conditions, if applicable	<input type="checkbox"/>
	• Names and contact information for primary and backup contacts	<input type="checkbox"/>
Pre-submission information form	<ul style="list-style-type: none"> • Updated pre-submission information form • Supporting references for specified listing when requested by sponsor 	<input type="checkbox"/>
Product monograph	• A copy of the most current version of the Health Canada–approved product monograph	<input type="checkbox"/>
Declaration letter	• Completed declaration letter template	<input type="checkbox"/>
Non-disclosable information	• Summary table listing non-disclosable information	<input type="checkbox"/>
Health Canada Documentation		
NOC	• A copy of the NOC or NOC/c granted for the indication(s) to be reviewed	<input type="checkbox"/>
	• Letter of Undertaking (only if NOC/c granted)	<input type="checkbox"/>
Clarimails/Clarifaxes	• Summary table of any clinical Clarimails/Clarifaxes up to the time of NOC or NOC/c being issued	<input type="checkbox"/>
Efficacy, Effectiveness, and Safety Information		
Common technical document	• 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 2.7.6	<input type="checkbox"/>
	• Or a statement indicating which section(s) were not required by Health Canada	<input type="checkbox"/>
Clinical studies	• Reference list of key clinical issues studies (published and unpublished)	<input type="checkbox"/>
	• Copies of studies addressing key clinical issues	<input type="checkbox"/>
Study protocol	• A copy of the study protocol for the pivotal study(ies)	<input type="checkbox"/>
Statistical analysis plan	• A copy of the statistical analysis plan for the pivotal study(ies)	<input type="checkbox"/>
Clinical study reports	• Complete clinical study reports for all pivotal studies as well as other studies that address key clinical issues (if submission is filed on or after March 2, 2020)	<input type="checkbox"/>
CONSORT diagrams	• Diagrams following CONSORT reporting standards or similar diagrams, documenting flow of patients through studies	<input type="checkbox"/>
Table of studies	• Completed table of studies template	<input type="checkbox"/>
Search strategy	• Search strategies used to locate published studies	<input type="checkbox"/>

Requirement	Specific Items and Criteria	Included
Editorials and errata	• Reference list of editorial articles and errata (or a document stating none found)	<input type="checkbox"/>
	• Copies of editorial articles and errata	<input type="checkbox"/>
New data	• Reference list of new data (or statement that none available)	<input type="checkbox"/>
	• Copies of new data available	<input type="checkbox"/>
Validity of outcome measures	• Reference list (or statement that none available)	<input type="checkbox"/>
	• Copies of validity of outcome measure references available	<input type="checkbox"/>
Indirect comparison	• Copies of any indirect comparisons used in pharmacoeconomic evaluation	<input type="checkbox"/>
	• Technical report	<input type="checkbox"/>
Provisional algorithm	• Place in therapy template	
	• A reference list (or statement that none 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"/>
Economic Information		
Pharmacoeconomic evaluation: technical report	• Pharmacoeconomic evaluation for the full population identified in the indication(s) to be reviewed by CADTH	<input type="checkbox"/>
	• Treatment effect measures should generally not use composite endpoints	<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"/>
	• Economic evaluation is a cost-utility analysis	<input type="checkbox"/>
	• Public health care payer perspective	<input type="checkbox"/>
	• 1.5% discount rate on costs and QALYs	<input type="checkbox"/>
	• All relevant comparators have been included	<input type="checkbox"/>
	• Submitted price per smallest dispensable unit used	<input type="checkbox"/>
	• All results are presented probabilistically	<input type="checkbox"/>
	• All ICERs reported sequentially if more than one comparator is presented	<input type="checkbox"/>
	• Results are presented in disaggregated format	<input type="checkbox"/>
	• Treatment effect measures generally should not use composite endpoint data	<input type="checkbox"/>
	• If relevant, a graph with Kaplan-Meier curve and parametric distributions for each relevant outcome.	<input type="checkbox"/>
	• If relevant, companion diagnostic test information incorporated	<input type="checkbox"/>
• Alignment between the pharmacoeconomic evaluation technical report and the economic model	<input type="checkbox"/>	
Economic model	• Model is programmed in Excel	<input type="checkbox"/>
	• Model is fully unlocked and executable, and all code is provided.	<input type="checkbox"/>
	• Model functions in a standalone environment and does not require access to a web-based platform	<input type="checkbox"/>
	• Probabilistic analyses runs without error	<input type="checkbox"/>
	• Results of the probabilistic analysis are stable (congruence test provided)	<input type="checkbox"/>

Requirement	Specific Items and Criteria	Included
	<ul style="list-style-type: none"> Where there are multiple comparators, the model runs treatments simultaneously and results of all comparators are presented 	<input type="checkbox"/>
	<ul style="list-style-type: none"> 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. 	<input type="checkbox"/>
Supporting documentation	<ul style="list-style-type: none"> Model user guide 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Indirect comparison technical report 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Unpublished studies or analyses used to inform the pharmacoeconomic evaluation 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Document summarizing key sources of information for the companion diagnostic test 	<input type="checkbox"/>
Budget Impact Analysis		
Budget impact analysis: technical report	<ul style="list-style-type: none"> Base case reflects pan-Canadian (national) perspective (excluding Quebec) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Base case reflects the Health Canada-approved indication 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Scenario analysis of the reimbursement request population (if different from the Health Canada-approved indication) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Base case analysis uses a one-year baseline period and three-year forecast period. 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Analyses presented deterministically 	<input type="checkbox"/>
	<ul style="list-style-type: none"> All relevant comparators included 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Submitted price per smallest dispensable unit used 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Report includes at minimum decision problem, methods, assumptions and results 	<input type="checkbox"/>
Budget impact model	<ul style="list-style-type: none"> Model is programmed in Excel 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model is fully unlocked and executable and all code provided 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model functions in a standalone environment and does not require access to a web-based platform 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model is flexible and allows assessment for each individual drug program 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Input values specific to the individual drug program 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Breakdown of costs by perspective reported within the submitted model 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Alignment between the technical report and the model 	<input type="checkbox"/>
Supporting documentation	<ul style="list-style-type: none"> Reference list of all supporting documentation used and/or cited in BIAs 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Unpublished studies or analyses used to inform the budget impact analysis 	<input type="checkbox"/>
Reimbursement status of comparators	<ul style="list-style-type: none"> A completed template summarizing the reimbursement status of all appropriate comparators (for all submissions filed on or after March 2, 2020). 	<input type="checkbox"/>
Epidemiologic Information		
Disease prevalence and incidence	<ul style="list-style-type: none"> Disease prevalence and incidence with specified breakdown (if available) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Document is referenced 	<input type="checkbox"/>
Pricing and Distribution Information		

Requirement	Specific Items and Criteria	Included
Price and distribution method	• Submitted unit pricing to four decimal places	<input type="checkbox"/>
	• Method of distribution	<input type="checkbox"/>
Implementation plan	• Completed implementation plan template	<input type="checkbox"/>
Companion Diagnostic(s)		
Companion diagnostics	• Reference list	<input type="checkbox"/>
	• 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"/>

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

E. Requirements for All Resubmission Types

Section	Specific Items and Criteria	Included
General Information		
Signed cover letter	• Clear description of resubmission being filed	<input type="checkbox"/>
	• The indication(s) to be reviewed	<input type="checkbox"/>
	• Requested reimbursement conditions, if applicable	<input type="checkbox"/>
	• Rationale for the resubmission	<input type="checkbox"/>
	• Names and contact information for primary and backup contacts	<input type="checkbox"/>
Pre-submission information form	<ul style="list-style-type: none"> • Updated pre-submission information form • Supporting references for specified listing when requested by sponsor 	<input type="checkbox"/>
Product monograph	• A copy of the most current version of the Health Canada–approved product monograph	<input type="checkbox"/>
Declaration letter	• Completed declaration letter template	<input type="checkbox"/>
Non-disclosable information	• Summary table listing non-disclosable information	<input type="checkbox"/>
New and Updated Efficacy and/or Safety Information		
New clinical studies	• Reference lists of all new clinical studies included in the resubmission that were not provided in the initial submission, or a previous resubmission	<input type="checkbox"/>
	• Copies of all new clinical information	<input type="checkbox"/>
Confirmatory studies for drugs with NOC/c	• Status of confirmatory studies for drug with NOC/c	<input type="checkbox"/>
	• Most recent interim analysis of confirmatory studies for drug with NOC/c	<input type="checkbox"/>
CONSORT diagrams	• Diagrams following CONSORT reporting standards or similar diagrams, documenting flow of patients through studies	<input type="checkbox"/>
Table of studies	• An updated tabulated list of all published and unpublished clinical studies using the provided table of studies template	<input type="checkbox"/>
Search strategy	• Search strategies used to locate published studies	<input type="checkbox"/>
Provisional algorithm	• Place in therapy template	<input type="checkbox"/>
	• A reference list (or statement that none 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"/>
New and Updated Economic Information		
Pharmacoeconomic evaluation: technical report	• Pharmacoeconomic evaluation for the full population identified in the indication(s) to be reviewed by CADTH	<input type="checkbox"/>
	• Treatment effect measures should generally not use composite endpoints	<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"/>
	• Economic evaluation is a cost-utility analysis	<input type="checkbox"/>
	• Base case reflects public health care payer perspective	<input type="checkbox"/>
	• 1.5% discount rate on costs and QALYs	<input type="checkbox"/>
	• All relevant comparators have been included	<input type="checkbox"/>
	• Submitted price per smallest dispensable unit used	<input type="checkbox"/>
• All results are presented probabilistically	<input type="checkbox"/>	

Section	Specific Items and Criteria	Included
	<ul style="list-style-type: none"> All ICERs reported sequentially if more than one comparator is presented 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Results are presented in disaggregated format 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Treatment effect measures generally should not use composite endpoint data 	<input type="checkbox"/>
	<ul style="list-style-type: none"> If relevant, a graph with Kaplan-Meier curve and parametric distributions for each relevant outcome. 	<input type="checkbox"/>
	<ul style="list-style-type: none"> If relevant, companion diagnostic test information incorporated 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Alignment between the evaluation report and the economic model 	<input type="checkbox"/>
Economic model	<ul style="list-style-type: none"> Model is programmed in Excel 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model is fully unlocked and executable, and all code is provided. 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model functions in a standalone environment and does not require access to a web-based platform 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Probabilistic analyses runs without error 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Results of the probabilistic analysis are stable (congruence test provided) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Where there are multiple comparators, the model runs treatments simultaneously and results of all comparators are presented 	<input type="checkbox"/>
	<ul style="list-style-type: none"> 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. 	<input type="checkbox"/>
Supporting documentation	<ul style="list-style-type: none"> Model user guide 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Indirect comparison technical report 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Unpublished studies or analyses used to inform the pharmacoeconomic evaluation 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Document summarizing key sources of information for the companion diagnostic test 	<input type="checkbox"/>
Budget Impact Analysis		
Budget impact analysis: technical report	<ul style="list-style-type: none"> Base case reflects pan-Canadian (national) perspective (excluding Quebec) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Base case reflects the Health Canada-approved indication 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Scenario analysis of the reimbursement request population (if different from the Health Canada-approved indication) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Base case analysis uses a one-year baseline period and three-year forecast period. 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Analyses presented deterministically 	<input type="checkbox"/>
	<ul style="list-style-type: none"> All relevant comparators included 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Submitted price per smallest dispensable unit used 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Report includes at minimum decision problem, methods, assumptions and results 	<input type="checkbox"/>
Budget impact model	<ul style="list-style-type: none"> Model is programmed in Excel 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model is fully unlocked and executable and all code provided 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model functions in a standalone environment and does not require access to a web-based platform 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Model is flexible and allows assessment for each individual drug program 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Input values specific to the individual drug program 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Breakdown of costs by perspective reported within the submitted model 	<input type="checkbox"/>

Section	Specific Items and Criteria	Included
	<ul style="list-style-type: none"> Alignment between the technical report and the model 	<input type="checkbox"/>
Supporting documentation	<ul style="list-style-type: none"> Reference list of all supporting documentation used and/or cited in BIAs 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Unpublished studies or analyses used to inform the budget impact analysis 	<input type="checkbox"/>
Reimbursement status of comparators	<ul style="list-style-type: none"> A completed template summarizing the reimbursement status of all appropriate comparators (for all resubmissions filed on or after March 2, 2020). 	<input type="checkbox"/>
Reimbursement status of drug under review	<ul style="list-style-type: none"> List reimbursement decisions for the drug under review 	<input type="checkbox"/>
Pricing and Distribution Information		
Price and distribution method	<ul style="list-style-type: none"> Submitted unit pricing to four decimal places 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Method of distribution 	<input type="checkbox"/>
Companion Diagnostic(s)		
Companion diagnostics	<ul style="list-style-type: none"> Reference list and copies of articles that highlight the clinical utility of the companion diagnostic(s) 	<input type="checkbox"/>
	<ul style="list-style-type: none"> Disclosable price for the companion diagnostic(s) 	<input type="checkbox"/>

Appendix 7: Electronic File Structure and Naming Format

Instructions for Sponsors

Please carefully review the following electronic file structure and naming convention before assembling the submission or resubmission requirements. If you have any questions, please email requests@cadth.ca with the complete details of your question(s).

Filing Category 1 Requirements:

- All materials must be submitted using Collaborative Workspaces.
- Files should be submitted as zipped (.zip) files. The maximum file size is approximately 1GB. If there are several .zip files, the number of files should be noted in the additional comments box of the submission form (e.g., file 1 of 4). The root folder(s) should be clearly named with the brand or generic drug name and submission requirement.
- An email notification will be sent to the sponsor when the file has been submitted successfully.
- File names cannot exceed 64 characters or contain special characters; therefore, sponsors are required to use abbreviations as necessary.
- 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, 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 course of the review, sponsors must provide the requested information to CADTH using Collaborative Workspaces.
- The documents 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.
- File names cannot exceed 64 characters or contain special characters; therefore, sponsors are asked to use abbreviations as necessary.







A. Folder Structure for a Standard Review for an Oncology Drug

 Represents one folder  Represents one file (unlocked, searchable, and printable)

01_Brand Name_General Information






-  01.01_Brand Name_Signed Cover Letter
-  01.02_Brand Name_Updated Presub Info
-  01.03_Brand Name_Non-Disclosable Info Table (in Word format)
-  01.04_Brand Name_Product Monograph
-  01.05_Brand Name_Declaration Letter

02_Brand Name_Health_Canada_Information

-  02.01_Brand Name_HC NOC or NOC/c
-  02.02_Brand Name_Letter of Undertaking (if applicable)
-  02.03_Brand Name_Screening Acceptance Letter (if pre-NOC submission)
-  02.04_Brand Name_Table of Clarifaxes
-  02.05_Brand Name_Copies of Clarifaxes (if pre-NOC submission)
 -  02.05.01_Brand Name_Clarifax number_Date






03_Brand Name_Clinical Information

03.01 Brand Name_Common_Technical_Document

-  03.01.01_Brand Name_Section 2.5
-  03.01.02_Brand Name_Section 2.7.1
-  03.01.03_Brand Name_Section 2.7.3
-  03.01.04_Brand Name_Section 2.7.4
-  03.01.05_Brand Name_Section 2.7.6



03.02 Brand Name_Critical Studies

Note 1: Critical studies and all trials discussed in the clinical evidence portion of the submission should be included in this folder. Each trial should be a separate document. When feasible the trial should be numbered with the same number as listed in the reference list and the name should be short and concise. For example:


-  03.02.01_Smith et al.CMAJ.2007.pdf
-  03.02.02_Wong.BMJ.2008.pdf
-  03.02.03_manufacturer.unpublished.2010.pdf
-  03.02.04_Brown et al.poster.2010.pdf
-  03.02.05_Lee.[abstract].J Cardiology.2010.pdf

Note 2: If structured summaries of clinical information for disclosure are part of the submission, they should be included in this folder

03.03_Brand Name_CONSORT

-  03.03.01_Brand Name_CONSORT diagram (Study x)
-  03.03.02_Brand Name_CONSORT diagram (Study y)

03.04_Brand Name_New data generated after NDS

-  03.04.01_Brand Name_Smith et al. CMAJ 2007.pdf

03.05_Brand Name_Editorial articles and errata

-  03.05.01_Brand Name_Smith et al. CMAJ 2007.pdf

03.06_Brand Name_References supporting outcome measures

-  03.06.01_Brand Name_Smith et al. CMAJ 2007.pdf

-
- 03.07_Brand Name_Table_of_Studies
 - 03.07.01_Brand Name_Table of studies
 - 03.08_Brand Name_Statistical Analysis Plan
 - 03.08.01_Brand Name_Statistical Analysis Plan
 - 03.09_Brand Name_Study Protocol
 - 03.09.01_Brand Name_Study Protocol
 - 03.10_Brand Name_Search strategies
 - 03.10.01_Brand Name_Search strategy
 - 03.11_Indirect Comparison
 - 03.11.01_Brand Name_Indirect Comparison
 - 03.11.01_Brand Name_Technical report
 - 03.12_Clinical Study Reports (if filed on or after March 2, 2020)
 - 03.12.01_Brand Name_Trial Name
 - 04_Brand Name_Epidemiologic Information
 - 04.01_Brand Name_Disease Prevalence and Incidence
 - 05_Brand Name_Pharmacoeconomic Evaluation
 - 05.01_Brand Name_Pharmacoeconomic evaluation
 - 05.02_Brand Name_Economic model
 - 05.03_Brand Name_Economic model supporting documentation
 - 06_Brand Name_Reimbursement Status (if filed on or after March 2, 2020)
 - 06.01_Brand Name_Comparator Reimbursement Status
 - 07_Brand Name_Pricing and Distribution
 - 07.01_Brand Name_Pricing and Distribution
 - 08_Brand Name_BIA (if filed on or after March 2, 2020)
 - 08.01_BIA Report
 - 08.01.01_Brand Name_Pan-Canadian BIA Report
 - 08.02_BIA Model
 - 08.01.01_Brand Name_Pan-Canadian BIA Model
 - 08.03_BIA Supporting Documentation
 - 08.03.01_Brand Name_List of references
 - 08.03.02_Brand Name_Name of document
 - 09_Companion Diagnostic (if applicable)
 - 09.01_Clinical Utility
 - 09.01.01_Brand Name_List of References
 - 09.01.02_Brand Name_Author_Year
 - 09.02_Price
 - 09.02.01_Brand Name_Companion Diagnostic Price
 - 10_Brand Name_Provisional Algorithm
 - 10.01.01_Brand Name_Place In Therapy
 - 10.01.02_Brand Name_List of References
 - 10.01.03_Brand Name_Search Strategy
 - 10.01.04_Brand Name_Author_Year

Guidance for Submitting Additional Information Request:



AddInfo_YYYY-MM-DD






Note: Examples of additional information requested include but are not limited to

- HCReviewersReport_YYYY-MM-DD
- PSURs
- ClinicalStudyReport
- HCClarifax_YYYY-MM-DD
- Brand Name_Economic Model_[VERSION]_YYYY-MM-DD
- Brand Name_BIA_[VERSION]_YYYY-MM-DD
- Brand Name_UpdatedNon-DisclosableInfoTable_[VERSION]_YYYY-MM-DD





B. Folder Structure for an Oncology Cell or Gene Therapy Review

 Represents one folder  Represents one file (unlocked, searchable, and printable)


01_Brand Name_General Information

-  01.01_Brand Name_Signed Cover Letter
-  01.02_Brand Name_Updated Presub Info
-  01.03_Brand Name_Non-Disclosable Info Table (in Word format)
-  01.04_Brand Name_Product Monograph
-  01.05_Brand Name_Declaration Letter

02_Brand Name_Health_Canada_Information






-  02.01_Brand Name_HC NOC or NOC/c
-  02.02_Brand Name_Letter of Undertaking (if applicable)
-  02.03_Brand Name_Screening Acceptance Letter (if pre-NOC submission)
-  02.04_Brand Name_Table of Clarifaxes

02.05_Brand Name_Copies of Clarifaxes (if pre-NOC submission)

-  02.05.01_Brand Name_Clarifax number_Date






03_Brand Name_Clinical Information

03.01 Brand Name_Common_Technical_Document

-  03.01.01_Brand Name_Section 2.5
-  03.01.02_Brand Name_Section 2.7.1
-  03.01.03_Brand Name_Section 2.7.3
-  03.01.04_Brand Name_Section 2.7.4
-  03.01.05_Brand Name_Section 2.7.6



03.02 Brand Name_Critical Studies

Note 1: Critical studies and all trials discussed in the clinical evidence portion of the submission should be included in this folder. Each trial should be a separate document. When feasible the trial should be numbered with the same number as listed in the reference list and the name should be short and concise. For example:


-  03.02.01_Smith et al.CMAJ.2007.pdf
-  03.02.02_Wong.BMJ.2008.pdf
-  03.02.03_manufacturer.unpublished.2010.pdf
-  03.02.04_Brown et al.poster.2010.pdf
-  03.02.05_Lee.[abstract].J Cardiology.2010.pdf

Note 2: If structured summaries of clinical information for disclosure are part of the submission, they should be included in this folder (Brand Name_Clinical Information)


03.03_Brand Name_CONSORT

-  03.03.01_Brand Name_CONSORT diagram (Study x)
-  03.03.02_Brand Name_CONSORT diagram (Study y)

03.04_Brand Name_New data generated after NDS

-  03.04.01_Brand Name_Smith et al. CMAJ 2007.pdf

03.05_Brand Name_Editorial articles and errata

-  03.05.01_Brand Name_Smith et al. CMAJ 2007.pdf

03.06_Brand Name_References supporting outcome measures

-  03.06.01_Brand Name_Smith et al. CMAJ 2007.pdf

-
- 03.07_Brand Name_Table_of_Studies
 - 03.07.01_Brand Name_Table of studies
 - 03.08_Brand Name_Statistical Analysis Plan
 - 03.08.01_Brand Name_Statistical Analysis Plan
 - 03.09_Brand Name_Study Protocol
 - 03.09.01_Brand Name_Study Protocol
 - 03.10_Brand Name_Search strategies
 - 03.10.01_Brand Name_Search strategy
 - 03.11_Indirect Comparison
 - 03.11.01_Brand Name_Indirect Comparison
 - 03.11.01_Brand Name_Technical report
 - 03.12_Clinical Study Reports (if filed on or after March 2, 2020)
 - 03.12.01_Brand Name_Trial Name
 - 04_Brand Name_Epidemiologic Information
 - 04.01_Brand Name_Disease Prevalence and Incidence
 - 05_Brand Name_Pharmacoeconomic Evaluation
 - 05.01_Brand Name_Pharmacoeconomic evaluation
 - 05.02_Brand Name_Economic model
 - 05.03_Brand Name_Economic model supporting documentation
 - 06_Brand Name_Reimbursement Status (if filed on or after March 2, 2020)
 - 06.01_Brand Name_Comparator Reimbursement Status
 - 07_Brand Name_Pricing and Distribution
 - 07.01_Brand Name_Pricing and Distribution
 - 08_Brand Name_BIA (if filed on or after March 2, 2020)
 - 08.01_BIA Report
 - 08.01.01_Brand Name_Pan-Canadian BIA Report
 - 08.02_BIA Model
 - 08.01.01_Brand Name_Pan-Canadian BIA Model
 - 08.03_BIA Supporting Documentation
 - 08.03.01_Brand Name_List of references
 - 08.03.01_Brand Name_Name of document
 - 09_Brand Name_Implementation_Guidance
 - 09.01_Brand Name_Implementation Plan
 - 10_Companion Diagnostic (if applicable)
 - 10.01_Clinical Utility
 - 10.01.01_Brand Name_List of References
 - 10.01.01_Brand Name_Author_Year
 - 10.02_Price
 - 10.01.02_Brand Name_Companion Diagnostic Price
 - 11_Brand Name_Provisional Algorithm
 - 11.01.01_Brand Name_Place In Therapy
 - 11.01.02_Brand Name_List of References
-

- 11.01.03_Brand Name_Search Strategy
- 11.01.04_Brand Name_Author_Year

Guidance for Submitting Additional Information Request:

- AddInfo_YYYY-MM-DD
 - Note: Examples of additional information requested include but are not limited to
 - HCReviewersReport_YYYY-MM-DD
 - PSURs
 - ClinicalStudyReport
 - HCClarifax_YYYY-MM-DD
 - Brand Name_Economic Model_[VERSION]_YYYY-MM-DD
 - Brand Name_BIA_[VERSION]_YYYY-MM-DD
 - Brand Name_UpdatedNon-DisclosableInfoTable_[VERSION]_YYYY-MM-DD

C. Folder Structure for a Resubmission for an Oncology Drug

- Represents one folder ■ Represents one file (unlocked, searchable, and printable)
- 01_Brand Name_General Information
 - 01.01_Brand Name_Signed Cover Letter
 - 01.02_Brand Name_Updated Presub Info
 - 01.03_Brand Name_Non-Disclosable Info Table (in Word format)
 - 01.04_Brand Name_Product Monograph
 - 01.06_Brand Name_Declaration Letter
- 02_Brand Name_New_Information
 - 02.01_Brand Name_New Clinical Studies
 - 02.01.01_Brand Name_List of New Clinical Studies
 - 02.01.02_Brand Name_Trial Name_Author_Year
 - 02.02_Brand Name_Clinical Study Reports (if filed on or after March 2, 2020)
 - 02.01.01_Brand Name_Trial Name
 - 02.03_Brand Name_New Editorials and Errata
 - 02.03.01_Brand Name_List of Editorials and Errata
 - 02.03.03_Brand Name_Author_Year_Editorial
 - 02.03.03_Brand Name_Trial Name_Author_Year_Erratum
 - 02.04_Brand Name_CONSORT
 - 02.04.01_Brand Name_CONSORT diagram (Study x)
 - 02.04.02_Brand Name_CONSORT diagram (Study y)
 - 02.05_Brand Name_Trials (if applicable)
 - 02.05.01_Brand Name_Status of confirmatory trials
 - 02.05.01_Brand Name_Trial Name (please include most recent analysis)
 - 02.06_Brand Name_References supporting outcome measures
 - 03.06.01_Smith et al. CMAJ 2007.pdf
 - 02.07_Brand Name_Table_of_Studies
 - 02.07.01_Brand Name_Table of studies
 - 02.08_Brand Name_Search strategies
 - 03.10.01_Brand Name_Search strategy

-
- 02.09_Brand Name_Indirect Comparison (if applicable)
 - 03.11.01_Brand Name_Indirect Comparison
 - 03.11.01_Brand Name_Technical report
 - 02.10_Brand Name_Clinical Study Reports (if filed on or after March 2, 2020)
 - 03.12.01_Brand Name_Trial Name
 - 04_Brand Name_Epidemiologic Information
 - 04.01_Brand Name_Disease Prevalence and Incidence
 - 05_Brand Name_Pharmacoeconomic Evaluation
 - 05.01_Brand Name_Pharmacoeconomic evaluation
 - 05.02_Brand Name_Economic model
 - 05.03_Brand Name_Economic model supporting documentation
 - 06_Brand Name_Reimbursement Status (if filed on or after March 2, 2020)
 - 06.01_Brand Name_Comparator Reimbursement Status
 - 06.02_Brand Name_Reimbursement Status of Drug
 - 07_Brand Name_Pricing and Distribution
 - 07.01_Brand Name_Pricing and Distribution
 - 08_Brand Name_BIA (if filed on or after March 2, 2020)
 - 08.01_BIA Report
 - 08.01.01_Brand Name_Pan-Canadian BIA Report
 - 08.02_BIA Model
 - 08.01.01_Brand Name_Pan-Canadian BIA Model
 - 08.03_BIA Supporting Documentation
 - 08.03.01_Brand Name_List of references
 - 08.03.02_Brand Name_Name of document
 - 09_Brand Name_Provisional Algorithm
 - 09.01.01_Brand Name_Place In Therapy
 - 09.01.02_Brand Name_List of References
 - 09.01.03_Brand Name_Search Strategy
 - 09.01.04_Brand Name_Author_Year

Guidance for Submitting Additional Information Request:

- AddInfo_YYYY-MM-DD
- Note: Examples of additional information requested include but are not limited to
- HCReviewersReport_YYYY-MM-DD
 - PSURs
 - ClinicalStudyReport
 - HCClarifax_YYYY-MM-DD
 - Brand Name_Economic Model_[VERSION]_YYYY-MM-DD
 - Brand Name_BIA_[VERSION]_YYYY-MM-DD
 - Brand Name_UpdatedNon-DisclosableInfoTable_[VERSION]_YYYY-MM-DD

Appendix 8: Key Definitions

The following definitions shall apply to this document, unless otherwise stated.

Additional Information - any information that is requested by CADTH, Guidance Panel, pERC, and required to complete the review of the submission or resubmission, or to explain or clarify information related to the submission or resubmission. Providing this information does not affect the review queue; however, if there is a delay in providing it or if the quantity and complexity of the requested information is significant, there may be a consequent delay in completion of the review. In exceptional cases, PAG may request additional information on a submission which extends beyond the submitted scope of the review. Revision of review scope may be considered by CADTH in very limited instances, based on jurisdictional input, feasibility to conduct the revised review and clinical importance. All three criteria must be met for scope modification.

Biosimilar – a biologic drug (i.e., a drug derived from living sources versus a chemically synthesized drug) demonstrating 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). Similarity between a biosimilar and the reference product is established in accordance with Health Canada’s [Guidance Document: Information and Submission Requirements for Biosimilar Biologic Drugs](#), for the authorized indications.

Business Day - any day (other than a Saturday, Sunday, statutory holiday, or company holiday) on which CADTH is open for business.

Checkpoint Meeting – the meeting corresponding at which there is an opportunity to clarify information with the sponsor and to discuss the management of non-disclosable information included in the submission.

Clarifax - a Health Canada request for clarification from the sponsor.

Clinical Guidance Panel - Tumour-specific expert panels that ensure the review of each cancer drug draws from the most important, relevant and current clinical information. These panels submit a Clinical Guidance Report for use by the pERC in making recommendations.

Clinical Guidance Report - the report written by the Clinical Guidance Panel and other review team members after conducting the clinical review and that is provided to pERC for their deliberations on a submission or resubmission.

Companion Diagnostic Test - A companion diagnostic test is a medical device that provide 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.

Disclosable Information - has the meaning given to it in the *pCODR Disclosure of Information Guidelines*.

Disclosure of Information Guidelines – the guidelines adopted for the pCODR process to ensure the appropriate protection and disclosure of information obtained through the pCODR review process.

Drug - an active substance considered to be a drug under the Canadian *Food and Drugs Act* and *Food and Drug Regulations*, which is sold for human use (e.g., includes biosimilars, radiopharmaceuticals, among others).

Economic Guidance Panel – experts who assess the economic evidence provided by the sponsor for each cancer drug submission filed with CADTH. These panels submit an pharmacoeconomic report for use by the pERC in making its recommendations.

Economic report – the report written by the Economic Guidance Panel after conducting the economic review and that is provided to pERC for their deliberations on a submission or resubmission.

External Expert –an individual with appropriate qualifications and expertise required to provide some input on some aspect of a submission or resubmission during a pCODR review or at a pERC meeting when requested by the pERC Chair.

F/P/T – federal, provincial and territorial.

Final Recommendation - the recommendation made by the pERC at the pERC meeting identified in step 8 of the pCODR review process map or as a result of early conversion of an Initial Recommendation in step 7.4 of the pCODR review process map.

Guiding Principles – the eight guiding principles developed for the pCODR process by the participating drug programs that direct the way in which CADTH conduct its work with respect to the pCODR process and which are available on the CADTH website.

Initial Recommendation – the initial recommendation made by pERC. The Initial Recommendation is publicly posted for stakeholder feedback on the CADTH website.

Manufacturer - a drug manufacturer, also known as a pharmaceutical manufacturer.

Methods Team – individuals with methodological expertise in conducting systematic reviews.

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
- a biological substance previously approved for sale in Canada as a drug, but differing in molecular structure, nature of the source material, or manufacturing process.

New Indication – a condition or place in therapy for a drug that has not previously been reviewed by CADTH.

New Information - new clinical information (not previously submitted or published) in support of improved efficacy or safety or new cost information that significantly impacts the cost-effectiveness of the drug.

New Oncology Drug - a therapeutic substance for the active treatment of cancer 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
- a biological substance previously approved for sale in Canada as a drug, but differing in molecular structure, nature of the source material, or manufacturing process.

Non-Disclosable Information - has the meaning given to it in the *pCODR Disclosure of Information Guidelines*.

Notice of Compliance (NOC) - 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 (NOC/c) - 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.

Oncology drug with a new indication - a drug for the active treatment of cancer that was either previously reviewed by through the pCODR process or marketed prior to the establishment of the pCODR process and that has or has not received a NOC or NOC/c for a new indication(s) and:

- the drug has defined funding criteria by one or more drug plans / Provincial Cancer Agencies and the P/T Ministries of Health, PAG or Provincial Cancer Agencies have agreed that it should be submitted; or
- the drug is not funded by any of the Federal drug plans, P/T Ministries of Health / Provincial Cancer Agencies and the Federal drug plans, P/T Ministries of Health, PAG, or Provincial Cancer Agencies have agreed that it should be submitted; or
- the Federal drug plans, P/T Ministries of Health, PAG or Provincial Cancer Agencies have requested the review of the drug with New Indication(s).

PAG - Provincial Advisory Group provides operational, as well as some strategic advice, to ensure pERC recommendations are useful to drug funding decision makers. The PAG consists of appointed representatives from Federal drug plans, each of the provincial Ministries of Health and Provincial Cancer Agencies participating in the pCODR process.

Pharmaceutical Advisory Committee – Advisory body that provides provide strategic advice to CADTH on drug related issues and topics.

pERC - the pCODR Expert Review Committee (pERC) assesses the clinical evidence and cost effectiveness of new cancer drugs or a class of cancer drugs, and uses this information to make recommendations to the provinces and territories to guide their drug funding decisions. The pERC is an advisory body composed of up to 18 individuals with expertise in drug therapy / drug evaluation and patient members.

pERC brief – a brief prepared by CADTH that includes the information upon which pERC will deliberate when making an initial recommendation for a drug submission or a recommendation for a therapeutic review when available and relevant for a cancer drug class review conducted through the therapeutic review process.

pERC Chair -The pERC is led by a Chair who reports on pERC's activities to CADTH's President and Chief Executive Officer, as set out in the *pERC Terms of Reference*.

pERC Member- a member of the pCODR Expert Review Committee (pERC)

pERC Reconsideration Brief – a brief prepared by CADTH that includes the information upon which pERC will deliberate when reconsidering an initial recommendation and making a final recommendation for a drug submission or a recommendation for a therapeutic review when available and relevant for a cancer drug class review conducted through the therapeutic review process.

pERC Vice-Chair – the pERC member selected to be Vice-Chair of the pERC with responsibilities as set out in the *pERC Terms of Reference*.

pre-NOC submission - those submissions made to CADTH prior to authorization issued by Health Canada. The submission may be for a new drug or new indication for which Health Canada is highly likely to issue a NOC or NOC/c within 180 calendar days of the sponsor filing a submission with CADTH.

Pre-submission Information – the information required by CADTH during the pre-submission phase, as detailed in a Pre-submission Information Requirements Form, in order to optimize the submission planning and review process. Sponsors are requested to file this information at least 120 calendar days before the anticipated date of filing the complete submission. If the 120th day falls on a weekend or statutory holiday, the following business day will be applied.

Provincial Cancer Agencies – those provincially funded organizations or programs mandated with implementing a broad range of cancer-related health services, such as cancer control strategies, provision of care delivery, and cancer research and systems innovation.

Recommendation – an evidence-based recommendation made by pERC following deliberations on a submission or resubmission as set out in the pERC Deliberative Framework or a class of cancer drugs conducted through a therapeutic review process.

Reconsideration – the process identified in steps 7 and 8 of the pCODR review process map whereby stakeholders provide feedback on the Initial Recommendation and pERC considers the feedback and reconsiders its Initial Recommendation at a subsequent pERC meeting before making a Final Recommendation.

Record of Decisions – a written record of the decisions that are made by CADTH and other attendees at a meeting that is part of the pCODR review process.

Request for Advice – a written request made by the PAG or the Pharmaceutical Advisory Committee, through PAG, to the pERC for advice on specific therapeutic, clinical or pharmacoeconomic issues, or regarding a pERC Recommendation, which may result in a new Recommendation.

Request for Withdrawal – a written request by a sponsor to withdraw a submission or resubmission from the pCODR review process.

Resubmission – Manufacturers, provincially recognized clinician-based Tumour Groups and the PAG may file resubmissions when new information becomes available that was not provided in the original submission.

Review Team – the team established to complete the clinical and economic reviews of a submission or resubmission and composed of individuals with methodological expertise, members of the Clinical Guidance Panel, members of the Economic Guidance Panel and external experts as needed.

Sponsor - the person, corporation, or entity filing a submission or resubmission.

Submission - a submission to the CADTH pCODR process consisting of:

- a CD/DVD provided by the sponsor with supporting documentation, to have a drug funded by a Federal drug plan, P/T Ministry of Health or Provincial Cancer Agency participating in the pCODR process; or
- a request, together with supporting documentation, if any, made by the PAG, to consider the funding status of drugs already funded or previously reviewed for funding by one or more of the participating Federal drug plans, P/T Ministries of Health or Provincial Cancer Agencies, as required.

Submission Requirements - information that is required by CADTH to undertake the clinical and economic reviews of drugs and other information that is required by the Federal drug plans, P/T Ministries of Health or Provincial Cancer Agencies in making funding decisions. The requirements apply to submissions and resubmissions.

Tumour Groups - A clinical and/or research group, officially affiliated with a Provincial Cancer Agency or a P/T Ministry of Health, where medical/surgical cancer specialists, health care professionals and researchers with common interest/expertise in managing tumours related to a specific area of the body (e.g. breast or lung) work together to share information, make new discoveries and develop consistent protocols/best practices for treating patients.

Appendix 9: List of Templates

Various hyperlinked templates are provided throughout this document and are to be used when filing a submission or resubmission with CADTH. These templates are also available on the [CADTH website](#).

Pre-Submission Phase Forms

- [Pre-submission Information Requirements Form — Submissions](#)
- [Pre-submission Information Requirements Form — Resubmissions](#)
- [Proposed place in therapy template](#)
- [Resubmission eligibility form](#)
- [Submission eligibility form](#)
- [Request for deviation from economic requirements form](#)

Templates for Category 1 Requirements

- [Table of studies template](#)
- [Declaration letter template](#)
- [Reimbursement status of comparators template](#)
- [Implementation plan for a cell or gene therapy](#)
- [Non-disclosable information template](#)

Templates for Stakeholder Input

- [Patient Input Template for CADTH CDR and pCODR Programs](#)
- [Stakeholder Feedback on a pERC Initial Recommendation](#)
- [Verification of non-disclosable information template](#)
- [pCODR procedural review request form](#)
- [pCODR Conflict of Interest Disclosure Form](#)