Canada's Drug Agency
L'Agence des médicaments du Canada

Procedures for Reimbursement Reviews

May 2024

Record of Updates

Version	Date	Summary of revisions
21	May 5, 2024	• Document renamed as Procedures for Reimbursement Reviews. • Revised process for posting of patient group and clinician group input.
20	Jan. 25, 2024	• Revised criteria for the submission of cost-minimization analyses. • Revised description of attendees for reconsideration meetings. • Duration of pipeline meetings extended to 90 minutes. • Clarification added to the confidentiality guidelines for applications received prior to January 2, 2024.
19	Nov. 30, 2023	• Revised confidentiality guidelines. • Clarification of pharmacoeconomic requirements.
18	Sept. 28, 2023	• Clarification regarding requirements for sponsor summary of clinical evidence. • New application requirement to include responses to requests for deviation from the pharmacoeconomic requirements within the application materials. • Revised procedures for reconsideration meetings to include optional attendance by the participating drug programs. • Updates to section on reassessment through the Therapeutic Review or Streamlined Drug Class Review Processes
17	Jun. 8, 2023	• New instructions and application templates for industry pipeline meetings. • New information in the list of studies included in the clinical review provided to the sponsor.

16	Apr. 20, 2023	• New instructions for invitations to observe Health Canada meetings.
		• Revised timing for calls for patient and clinician group input.
		• Clarification regarding requirements for sponsor summary of clinical evidence.
		• Revisions made based on recommendations from the Procedural Review Panel:
		  ○ Clarification on the objectives of the reimbursement review process.
		  ○ Clarification on the nature of the descriptions provided for recommendation options.
		• Revised Appendix 2 to provide further clarity and guidance for those who wish to make a request for a procedural review.

15	Feb. 16, 2023	• Revised instructions for filing and receiving documents. • New application requirement for RIS files with economic references. • Revised process and updated template for ethics review. • Clarification about biosimilar eligibility. • Clarification within the confidentiality guidelines that correspondence between CDA-AMC and the sponsor regarding the drug under review may be shared with authorized recipients.
14	Nov. 10, 2022	• Clarification of pharmacoeconomic requirements.
13	Sept. 1, 2022	• Clarification regarding timing for notification following withdrawal from Health Canada. • New information will not be accepted after draft reports issued to sponsor. • Revised naming and eligibility criteria of the Interim Plasma Protein and Related Product review process.
12	Mar. 31, 2022	• New clinical evidence template for sponsors. • Clarification regarding reconsideration process. • Clarification of pharmacoeconomic requirements. • Revised confidentiality guidelines.
11	Dec. 16, 2021	• New rapid provisional funding algorithm process introduced.

10	Nov. 25, 2021	• New complex review process introduced. • New instructions for notifying CDA-AMC when the pause-the-clock process has been implemented during the regulatory review. • Revised process for pre-submission meetings. • Clarifications and revisions to pharmacoeconomic requirements.
9	Sept. 16, 2021	• Opportunity for sponsor to review stakeholder feedback for confidential information. • Revised process regarding new information during the reconsideration phase. • Revisions to pharmacoeconomic requirements. • Revised process for incorporating patient group and clinician group input into reports. • Feasibility of adoption listed as a reimbursement condition category.
8	Jun. 17, 2021	• Clarification regarding requests for reconsideration filed by the drug programs. • New application requirement for the status of the drug in other jurisdictions.
7	Apr. 29, 2021	• Additional details on pharmacoeconomic requirements for a cost-minimization analysis. • Clarification regarding the drug programs to be included in the budget impact analysis. • Clarification regarding timelines for the calls for patient and clinician group input. • Revision to the procedural review process. • Reformatted checklists.
6	Mar. 24, 2021	• Revisions to pharmacoeconomic requirements.
5	Feb. 25, 2021	• Revised timelines for posting clinician group input.
4	Jan. 14, 2021	• Revised instructions for submitting advance notification and pre-submission meeting request forms to CDA-AMC. • Clarification of pharmacoeconomic submission requirements.
3	Dec. 3, 2020	• Document renamed as *Procedures for CADTH Reimbursement Reviews*. • Revisions to checklists and file structures for tailored reviews to reflect that the reimbursement status of comparators is no longer located as an appendix of the tailored review submission template.
2	Oct. 29, 2020	• Clinician groups will not be asked to review and validate the summary of input that is prepared by CDA-AMC. • Clarification that the reimbursement status of comparators template must be filed as a Microsoft Word document.
1	Sept. 30, 2020	• Original version posted.

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Abbreviations

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

1. Introduction

1.1 Purpose of This Document

This document outlines the procedures for Canada's Drug Agency – L'Agence des médicaments du Canada (CDA-AMC) reimbursement review processes, including those used for oncology drugs, non-oncology drugs, and plasma protein and related products reviewed through the interim process. Selected novel products that are likely to pose substantial system-wide implementation challenges may be reviewed through the *Process for Drugs with Expanded Health System Implications*.

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

1.2 Procedures for Time-limited Reimbursement Recommendations

Effective September 28, 2023, CDA-AMC has introduced a new process for time-limited reimbursement recommendations. For complete details, please consult the *Procedures for Time-limited Reimbursement Recommendations*. If you have questions, please contact us at requests@cadth.ca.

1.3 Overview of Reimbursement Review Process

1.3.1 Drug Review Process

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

1.3.2 Expert Committees

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

1.3.3 Advisory Committees

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

1.4 Communications for Reimbursement Reviews

1.4.1 Stakeholder Inquiries

Stakeholders are asked to use requests@cadth.ca for inquiries related to CDA-AMC's reimbursement review processes. Inquiries should not be addressed directly to the program director or other CDA-AMC staff as this can disrupt the routine tracking and triaging of inquiries (and these types of disruptions can result in a lengthier time for obtaining a response).

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

Table 1: Contact Information

Type of inquiry	Where to direct your inquiry
General inquiries regarding procedures and processes	**Email:** requests@cadth.ca **Mail:** Canada's Drug Agency 600-865 Carling Avenue Ottawa, ON K1S 5S8
Filing documents	Pharmaceutical Submissions SharePoint Site
Inquiries regarding an active review	**Email:** formulary-support@cadth.ca
Inquiries regarding application fees	**Email:** accountsreceivable@cadth.ca

1.4.2 Communications

All communications for drug review programs are issued in a single email newsletter once per week (typically on Thursday). The newsletter includes the following announcements and opportunities:

- calls for patient group input
- calls for clinician group input
- opportunities for feedback draft recommendations
- opportunities for feedback draft provisional algorithms
- notice of final recommendation
- notice of final provisional funding algorithm

- procedural updates and clarifications
- consultation opportunities
- other news regarding drug review programs.

2. Eligibility

2.1 Submission Eligibility

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

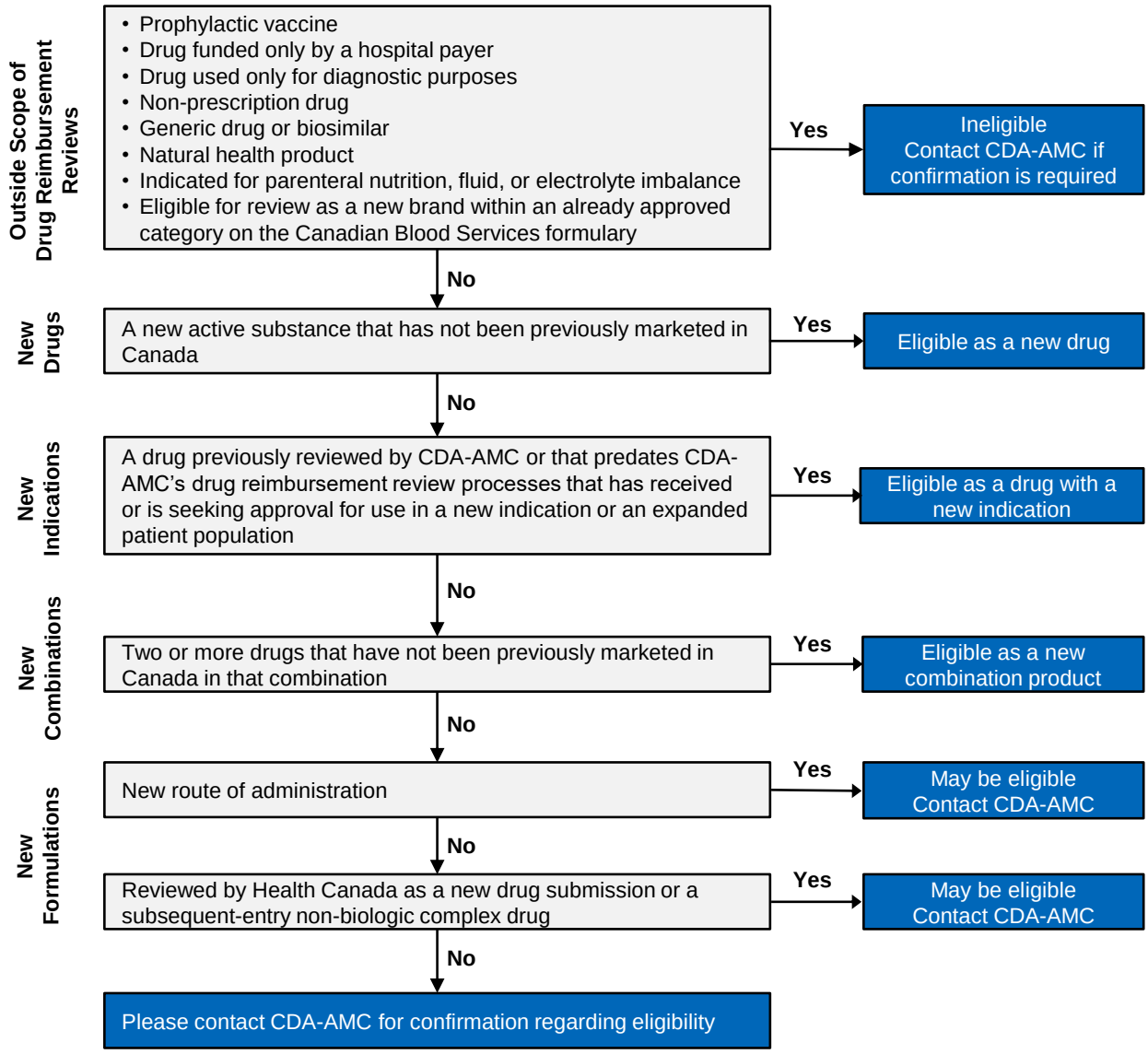
A sponsor or the drug programs may file an application for an eligible drug that has received or has a pending Notice of Compliance (NOC) or Notice of Compliance with conditions (NOC/c) for the indication(s) to be reviewed. In selected instances, CDA-AMC may undertake the review of a drug for an unapproved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

Table 2: Eligibility for Reimbursement Review Processes

Product type	Description
New drug	• A new active substance that has not been previously marketed in Canada • A drug consisting of a single active substance previously reviewed through one of the reimbursement review processes only as an active substance in a combination product • A new salt of a marketed product. • A drug for which eligibility for review has been confirmed in consultation with the drug programs on a case-by-case basis.
Drug with a new indication	• A drug previously reviewed through the reimbursement review process that has received or is seeking approval from Health Canada for use in a new indication. • A drug marketed before the establishment of the reimbursement review processes that has received or is seeking approval from Health Canada for use in a new indication. • A drug previously reviewed through the reimbursement review process that has received or is seeking approval from Health Canada for use in a new age group of patients.
New combination product	• Two or more drugs that have not been previously marketed in Canada in that combination.
New formulation of an existing drug	• New formulations of existing drugs that have a different route of administration than formulation(s) previously reviewed through the reimbursement review process.
Subsequent-entry products for non-biological complex drugs	• A subsequent-entry non-biological complex drug is a medicinal product that demonstrates a high degree of similarity to an already authorized product (i.e., a reference product that has been approved for use in Canada); due to the complex nature of the product, demonstrating bioequivalence may not be possible.

Figure 1: Drugs Eligible for the Reimbursement Review Processes

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



2.1.1 New Drugs

A new drug, for reimbursement review submission purposes, typically includes one of the following:

- a new active substance that has not been previously marketed in Canada, regardless of when the NOC or NOC/c was issued
- a drug consisting of a single active substance previously reviewed through one of the reimbursement review processes only as an active substance in a combination product

- a new salt of a marketed product
- a drug for which eligibility for review has been confirmed in consultation with the drug programs on a case-by-case basis.

2.1.2 New Indications

A drug with a new indication is:

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

2.1.3 New Combination Products

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

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

2.1.4 New Formulations of Existing Drugs

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

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

New parenteral products or formulations (e.g., IV, intramuscular, subcutaneous dosage forms) are not considered line extensions of one another, as they have different routes of administration and, as a result,

there may be potential differences in pharmacokinetics and pharmacodynamics, as well as differences in cost. Sponsors should submit a completed eligibility request form to requests@cadth.ca for guidance on whether a submission is required for a new parenteral formulation.

2.1.5 Plasma Protein and Related Products

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

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

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

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

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

2.1.6 Subsequent-Entry Products for Non-Biological Complex Drugs

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

2.1.7 Eligible Drugs That Have Become Genericized

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

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

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

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

- Similar products are not currently listed by the drug programs (e.g., different salts of the active substance).
- The manufacturer of the branded product has confirmed that it does not intend to file the product for a reimbursement review 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 a manufacturer may be advised that a submission is not required, it does not preclude the manufacturer from electing to file a submission provided the product meets the eligibility criteria for a new drug, a drug with a new indication, or a new combination product. Manufacturers with questions regarding the reimbursement review processes may contact requests@cadth.ca any time.

2.1.8 Biosimilars

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

programs. Sponsors that have questions regarding whether or not a biosimilar is eligible for review are asked to complete an eligibility request form and submit it to requests@cadth.ca.

2.2 Resubmission Eligibility

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

2.2.1 New Information

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

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

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

Table 3: Summary of New Information Required for Resubmissions

Basis of resubmission	Supporting information that must be filed
New clinical information supporting improved efficacy or safety	• One or more new studies that address specific issues identified by the expert 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	• New pharmacoeconomic evaluation • New budget impact analysis

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

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

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

2.2.2 Eligibility Assessment for Resubmissions and Reassessments

Prior to filing a resubmission or a reassessment, sponsors are required to have its eligibility assessed by CDA-AMC. Sponsors must provide the following information to requests@cadth.ca for evaluation:

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

The information provided by the sponsor will be screened to determine if:

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

Members of the expert committee and/or clinical experts may be consulted to determine if the new information filed by the sponsor meets the eligibility criteria. However, the final decision regarding whether a resubmission or reassessment will be eligible for review will be determined by CDA-AMC. The assessment of eligibility will typically be completed within 10 business days. Sponsors will be notified if additional time is required to complete the assessment.

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

The request will be examined to determine whether the issue(s) raised change the conclusions regarding the eligibility of the resubmission or reassessment. Members of the expert committee and/or clinical experts (as required) may be consulted. The final decision regarding whether a resubmission or reassessment is eligible for review will be determined by CDA-AMC. The reconsideration will typically be completed within 10

business days, and sponsors will be notified if additional time is required to complete the assessment. The sponsor will be apprised in writing of the final decision regarding eligibility of the resubmission. The results of the resubmission or reassessment eligibility assessment may be posted on the website.

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

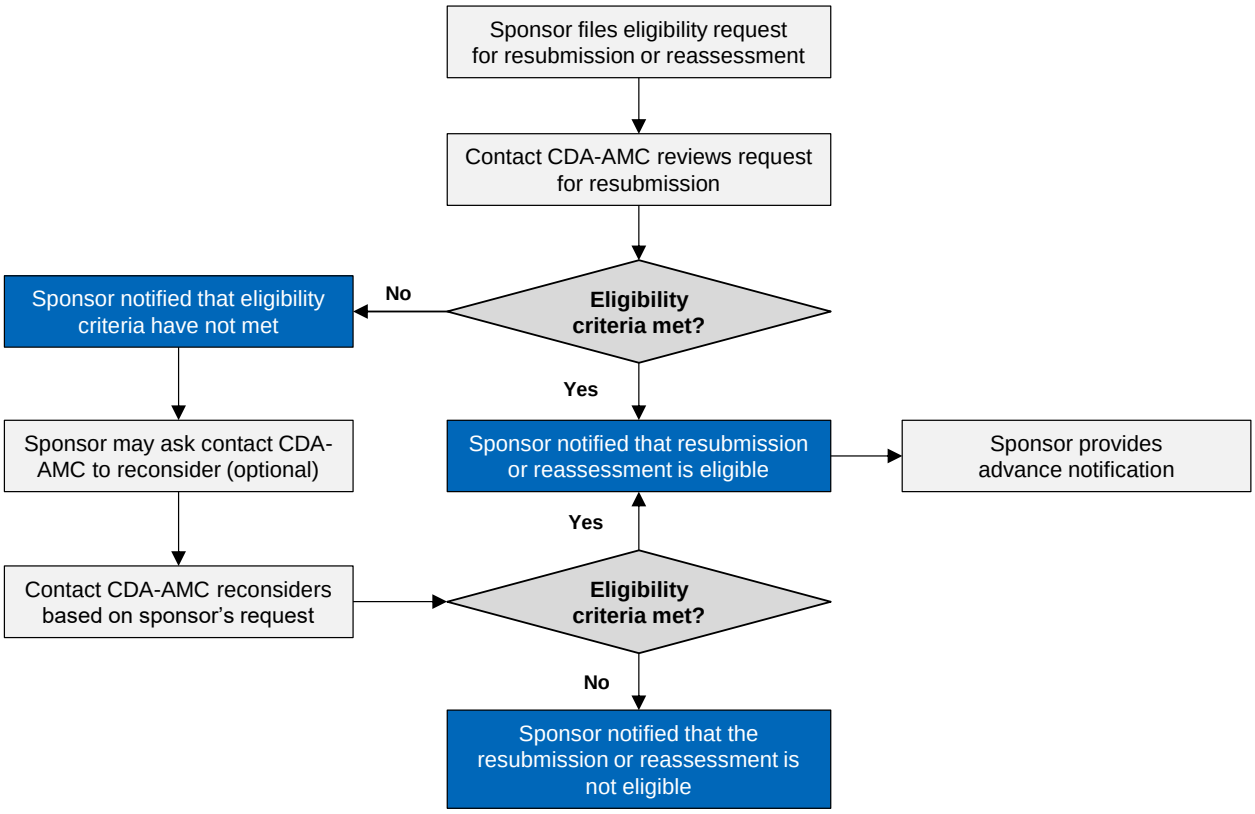
After receiving confirmation that the proposed resubmission or reassessment is eligible for review through a reimbursement review process, sponsors are required to provide advance notification in accordance with section 4.3.

2.2.3 Volume of Resubmissions and Reassessments

To ensure fair access to the reimbursement review processes for new drug submissions, the number of resubmissions and reassessments that can be made and/or initiated within a period of time may be limited. This decision will be made based on the availability of resources and will be communicated to stakeholders via a *Pharmaceutical Reviews Update*.

Figure 2: Assessing the Eligibility of Resubmissions

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



2.3 Reassessment Eligibility

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

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

Table 4: Potential Triggers for Reassessment

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

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

2.3.1 Standard Reassessments

The standard reassessment process is used when there is uncertainty regarding the comparative safety, clinical effectiveness, and/or cost-effectiveness of a single drug. The standard reassessment process requires the sponsor to file new clinical and/or economic information. Sponsors can initiate the standard reassessment process in a proactive or reactive manner.

- **Proactive reassessments** can be initiated by sponsors that are interested in pursuing revisions to any of the conditions associated with a previous reimbursement recommendation, provided they have new evidence that can support the revisions.
- **Reactive reassessments** can be initiated by sponsors that have received a formal request for reassessment on behalf of the drug programs.

Similar to the resubmission process, sponsors that wish to proactively have a drug considered through the standard reassessment process will be required to submit an eligibility form and copies of one or more new studies that support the requested revisions to the reimbursement criteria for the drug. The information provided by the sponsor will be assessed using the same approach that is currently used for resubmissions and will confirm eligibility with the sponsor. After receiving confirmation that the proposed reassessment is eligible for review, sponsors would be required to provide advance notification for the pending reassessment in accordance with procedures specified in section 4.3.

2.3.2 Request for Advice

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

recommendations. All requests for advice will relate to a drug that has previously been reviewed through the reimbursement review process and for which a final recommendation has been issued.

To initiate the request for advice process, a formal request must be received from the drug programs or pCPA that provides a clear description of the issues that are of interest to the drug programs. Drug manufacturers and tumour groups are not permitted to initiate the request for advice process.

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

2.4 Market Authorization Status

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

2.4.1 Pre-NOC Submissions

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

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

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

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

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

2.4.2 Post-NOC Submissions

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

2.4.3 Submissions for Unapproved Indications

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

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

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

2.5 Sponsor Eligibility

2.5.1 Industry Sponsors

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

2.5.2 Tumour Groups and Drug Programs

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

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

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

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

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

2.6 Declining to File a Submission

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

- Jurisdictions determine that they require a recommendation to inform their reimbursement decisions.
- A letter will be issued to the manufacturer on behalf of the Pharmaceutical Advisory Committee FWG or PAG informing it that the drug is eligible for review through the reimbursement review processes and that the drug programs would like a submission to be filed.
- The manufacturer will have 30 business days to respond to the letter indicating whether 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 "CDA-AMC is unable to recommend reimbursement as a submission was not filed by the manufacturer" statement will be issued on the website:
    - a manufacturer indicates that it is not planning to file a submission at this time
    - a manufacturer fails to respond to the FWG or PAG chair within the requested 30 business day period
    - a manufacturer indicated that a submission would be filed but did not provide advance notification with the anticipated filing date within 12 months of receiving the request from the FWG or PAG chair.
- These statements will be issued on the basis that a submission was not filed by the manufacturer and will not be discussed by the expert committees.
- The procedure will only apply to submissions and not to resubmissions.
- If a statement has been issued on the basis that a submission was not filed, the manufacturer may file a submission at any point in the future in accordance with the reimbursement review procedures. This would result in a reimbursement recommendation being issued for the drug and the previous statement being removed from the website.
- The participating jurisdictions can continue to file drug program–initiated submissions provided the requirements can been addressed (e.g., provision of an economic model and pharmacoeconomic evaluation).

3. Application Types

3.1 Submissions

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

- A **standard review** consists of a clinical report being prepared based on the sponsor's completed summary of clinical evidence template, source documentation provided by the sponsor, and stakeholder input; and an economic report based on an appraisal of the sponsor-provided pharmacoeconomic evaluation.

- A **tailored review** consists of an appraisal of the clinical evidence and pharmacoeconomic evaluation filed by the sponsor using a tailored review template. Eligibility must be confirmed prior to filing the submission by sending a completed tailored review application form to requests@cadth.ca. The form will be reviewed, and the sponsor will typically be notified within 10 business days.

- A **complex review** is conducted in a manner similar to a standard review but involves greater consultation with clinical experts (e.g., convening a pan-Canadian panel of specialists), greater consideration of non-randomized studies, a more detailed examination of potential implementation issues, and may include an additional review and consideration of potential ethical issues. Eligibility for review through the complex review process will be confirmed at the time of accepting the file for review.

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

The output of the review of a submission will be a recommendation document advising the drug programs on whether the drug under review should be reimbursed and under what conditions reimbursement should be considered.

3.2 Resubmissions

A **resubmission** is conducted when new evidence is available for a drug that has previously been reviewed for the indication of interest and for which a final recommendation has been issued. Resubmissions are typically limited to drugs that were not recommended for reimbursement by our expert committee and are not currently reimbursed by the drug programs for the indication of interest. Eligibility must be confirmed prior to filing the resubmission by sending a completed eligibility form to requests@cadth.ca. CDA-AMC will

review the form and provide confirmation to the sponsor, typically within 10 business days of receiving the form.

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

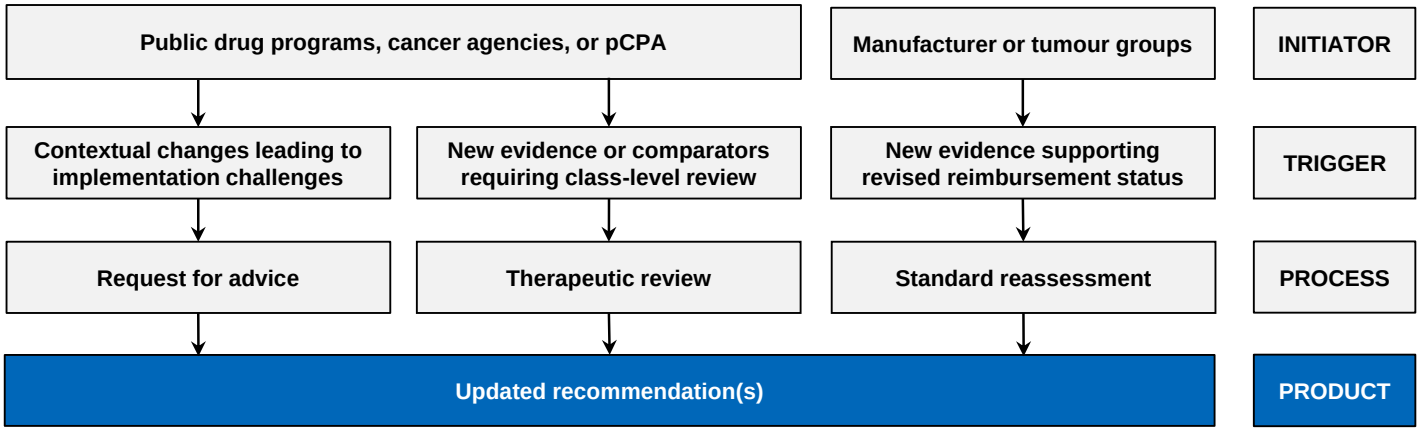
3.3 Reassessments

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

- A standard reassessment is conducted to address questions related to the comparative clinical benefit and/or cost-effectiveness of a single drug that is currently reimbursed by the drug programs for the indication(s) of interest. Eligibility must be confirmed prior to filing by sending a completed eligibility form to requests@cadth.ca. The form will be reviewed, and the sponsor will typically be notified within 10 business days.
- A request for advice is conducted to address changes in contextual factors that may affect the ability of the drug programs to implement existing recommendations. Contextual information can include regulatory actions, changes in clinical practice, or other forms of information that have introduced implementation questions or challenges for the jurisdictions.
- A therapeutic review is conducted where there are questions regarding the comparative safety, clinical effectiveness, and cost-effectiveness of multiple drugs.

Figure 3: Reimbursement Review Reassessment Processes

Alt text: Figure summarizes reimbursement review reassessment processes.



pCPA = pan-Canadian Pharmaceutical Alliance.

Table 5: Types of Reimbursement Reviews Conducted

Process	Eligibility	Output	Eligible requestors	Typical Timelines to Draft Recommendation	Application fee
Standard review	• Submissions for new drugs, drugs with new indications, and selected new combination products	• Reimbursement recommendation • Review reports • Stakeholder input	• Industry sponsors • Tumour groups • Drug programs	≤180 calendar days	Schedule A
Tailored review[a]	• Submissions for new combination products or new formulations of existing drugs that CDA-AMC has designated as tailored reviews • Submissions for subsequent-entry non-biologic complex drugs	• Reimbursement recommendation • Review reports • Stakeholder input	• Industry sponsors • Tumour groups • Drug programs	≤180 calendar days	Schedule C
Complex review	• Submissions for cell and gene therapies; products that are first-in-class; reviewed through one of Health Canada's expedited pathways (i.e., priority review or advance consideration under NOC/c); and have an undefined place in therapy	• Reimbursement recommendation • Review reports • Stakeholder input	• Industry sponsors • Tumour groups • Drug programs	≤180 calendar days	Schedule E
Resubmission[a]	• Drugs that are not reimbursed and have previously been reviewed by CDA-AMC and for which a final recommendation has been issued	• Updated reimbursement recommendation • Review reports • Stakeholder input	• Industry sponsors • Tumour groups • Drug programs	≤180 calendar days	Schedule A
Standard reassessment[a]	• Drugs that are currently reimbursed and there is uncertainty regarding safety, clinical effectiveness, and cost-effectiveness • Sponsors seeking revisions to existing reimbursement criteria on the basis of new clinical or economic evidence	• Updated reimbursement recommendation • Review reports • Stakeholder input	• Industry sponsors • Tumour groups • Drug programs	≤180 calendar days	Schedule A

Process	Eligibility	Output	Eligible requestors	Typical Timelines to Draft Recommendation	Application fee
Request for advice	• Changes in contextual information that may affect the ability to implement existing CDA-AMC recommendations	• Updated recommendation • Review report(s) • Stakeholder input	• Drug programs • pCPA	90 to 150 calendar days	Not applicable
Therapeutic review	• Uncertainty regarding the comparative safety, clinical effectiveness, and/or cost-effectiveness of multiple drugs	• Therapeutic review recommendations • Updated reimbursement recommendations (if required) • Review reports • Stakeholder input	• Drug programs • pCPA	12 months	Not applicable

pCPA = pan-Canadian Pharmaceutical Alliance.

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

4. Pre-submission Procedure

4.1 Pre-submission Meetings

4.1.1 Purpose

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

4.1.2 Timing of Pre-submission Meetings

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

4.1.3 Requesting a Pre-submission Meeting

To request a pre-submission meeting, sponsors are required to complete a pre-submission meeting request form and upload it to the *Pharmaceutical Submissions SharePoint* site in the "Pre-Submission Meeting" folder.

4.1.4 Briefing Paper and Meeting Materials

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

The completed template along with a draft version of the pre-submission meeting slides (in .ppt form) must be uploaded to the *Pharmaceutical Submissions SharePoint* site in the "Pre-Submission Meeting" folder. The briefing paper and pre-submission meeting slides must be filed no later than 10 business days prior to the scheduled date of the meeting. Failure to provide these documents within this time frame may result in postponement of the meeting.

4.1.5 Attendees

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

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

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

4.1.6 Meeting Logistics and Agenda

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

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

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

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

Pre-submission meetings will be recorded for internal purposes. The recordings are not distributed.

In the pre-submission phase, all sponsors will be required to specify whether or not the drug under review is expected to meet the time-limited recommendation eligibility criteria regarding the regulatory review status, the evidence-generation plans, and that the sponsor is willing to comply with the reassessment process for a time-limited recommendation.

4.2 Pipeline Meetings

4.2.1 Purpose

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

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

4.2.2 Frequency of Pipeline Meetings

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

4.2.3 Requesting a Pipeline Meeting

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

4.2.4 Briefing Paper and Meeting Materials

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

The completed template along with a draft version of the meeting slides (in .ppt form) must be uploaded to the Pharmaceutical Submissions SharePoint site in the Pipeline Meeting folder. The briefing paper and slides must be filed no later than 10 business days before the scheduled date of the meeting. Failure to provide these documents within this time frame may result in meeting postponement.

4.2.5 Attendees

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

4.2.6 Meeting Logistics and Agenda

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

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

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

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

Pipeline meetings will be recorded for internal purposes. The recordings are not distributed.

4.3 Advance Notification Procedure

4.3.1 Advance Notification Form

a) Filing the Advance Notification Form

Sponsors are required to provide a minimum of 30 business days advance notice for anticipated submissions and resubmissions. All sponsors are encouraged to provide as much notice as possible to facilitate resource planning and budgeting for the pharmaceutical review programs (≥ 120 calendar days is preferred). Sponsors who provided less than 30 business days' notice will be required to revise the anticipated filing date to meet the minimum requirement. To fulfill the advance notification requirement, sponsors must complete the advance notification template in its entirety and upload to the Pharmaceutical Submissions SharePoint site in the "Advance Notification" folder. The 30–business day notification period will be counted from the date of receipt of the advance notification template to the targeted filing date for all anticipated applications.

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

For resubmissions and reassessments, sponsors are required to receive confirmation from CDA-AMC that the proposed resubmission is eligible for review, before providing advance notification (refer to section 0). The eligibility assessment and advance notification processes must occur sequentially to ensure that the patient engagement process is only initiated for resubmissions and reassessments that are eligible for review by CDA-AMC.

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

Table 6: Advance Notification Process

Advance notification process	Days prior to anticipated filing date
Preferred advance notification	≥ 120 calendar days
Minimum mandatory advance notification	30 business days
Confirmation of anticipated filing date	30 business days[a]
Call for patient and clinician group input issued	29 business days

[a] Required only if more than 30 business days' advance notice was provided.

b) Revisions to the Anticipated Filing Date

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

c) Posting Information about a Pending Application

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

4.3.2 Proposed Place in Therapy for Oncology Drugs

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

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

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

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

4.4 Health Canada Information Sharing

4.4.1 Consenting to Information Sharing

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

Sponsors must indicate on the advance notification form (i.e., received ≥ 30 business days in advance of the submission filing date) whether they have consented or will be consenting to participate in the information-sharing process with Health Canada.

To promote alignment of regulatory and reimbursement reviews, sponsors should consent to information sharing at the time of, or prior to, submission filing with Health Canada. This may help to minimize the time between issuance of market authorization and the reimbursement recommendation. If the sponsor is unwilling to participate in the information-sharing process with Health Canada, CDA-AMC will continue to request information directly from the sponsor.

A secure portal will be used to exchange documents between Health Canada and CDA-AMC.

In the interest of transparency, CDA-AMC will indicate whether a sponsor has consented to participate in the information-sharing process (if applicable).

4.4.2 Invitations to Health Canada Pre-Submission and Pipeline Meetings

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

d) Sending an Initial Request

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

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

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

Review the confidentiality guidelines in Appendix 1 of the *Procedures for Reimbursement Reviews* to understand how sponsor-provided information is managed.

e) Sending the Meeting Invitations

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

f) Uploading Meeting Materials

Sponsors are provided with a secure portal (the Pharmaceutical Submissions SharePoint site) to upload confidential meeting materials for pre-submission meetings and pipeline meetings. Please follow the instructions outlined in the *Pharmaceutical Submissions SharePoint Site Set-Up Guide* for details on requesting access to the site. Meeting materials must be uploaded to the Pharmaceutical Submissions SharePoint site in the location assigned for the meeting. Sponsors should request access to the Pharmaceutical Submissions SharePoint site 10 business days prior to the intended date of uploading the meeting materials. If this timeline cannot be met, please contact support@cadth.ca as soon as possible to ensure the meeting materials can be submitted without delay.

g) Participation in the Meetings

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

5. Application Requirements

This section provides details regarding the documentation that must be filed and accepted for before a reimbursement review will be initiated.

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

Confidentiality guidelines have been developed to protect confidential information obtained through reimbursement review processes (Appendix 1). These confidentiality guidelines ensure that appropriate steps and procedures are in place to protect confidential information, and that this information will be handled in a consistent manner. CDA-AMC will comply with these confidentiality guidelines when handling information as part of the reimbursement review processes. A sponsor will be deemed to have consented to the confidentiality guidelines when it files an application, or when it supplies other information to CDA-AMC. A sponsor will maintain the confidentiality of documents shared with it by CDA-AMC. The confidentiality guidelines will constitute an agreement between CDA-AMC and the sponsor.

Table 7: Submission Requirements

Section	Specific items and criteria	Reimbursement Review Type		
		Standard	Tailored	Complex
General information	Application overview template	Required	Required	Required
	Signed cover letter	Required	Required	Required
	Executive summary template	Required	Required	Required
	Product monograph	Required	Required	Required
	Completed declaration letter template	Required	Required	Required
	Completed regulatory and HTA status template	Required	Required	Required
	Request for deviation response letter or statement that a deviation was not requested	Required	N/A	Required
Submission template	Completed tailored review submission template	N/A	Required	N/A
	Complete sponsor summary of clinical evidence template	Required	N/A	Required
	RIS file with references	Required	Not required	Required
Health Canada documentation	NOC or NOC/c and Letter of Undertaking, or a document specifying the anticipated NOC date	Required	Required	Required
	Table of Clarimails or Clarifaxes	Required	Required	Required
Efficacy, effectiveness, and safety information	Common Technical Document sections 2.5, 2.7.1, 2.7.3, 2.7.4, and 5.2, or a statement indicating any section(s) that are not available	Required	Required	Required
	Clinical study reports for pivotal and key studies	Required	Required	Required
	Reference list, copies of key studies, and errata	Required	Required	Required
	Table of studies	Required	Required	Required
	Reference list and copies of editorial articles	Required	Not required	Required
	Reference list and copies of new data	Required	Not required	Required
	Reference list and copies of articles for validity of outcome measure	Required	Not required	Required
	Indirect comparison with full technical report	May be required	Not required	May be required
Economic information	Pharmacoeconomic evaluation for the full population identified in the approved Health Canada indication(s) to be reviewed	Required	Not required	Required
	Unlocked and fully executable economic model	Required	Not required	Required
	Economic model supporting documentation	Required	Not required	Required
	Completed checklist of economic requirements	Required	Required	Required
	RIS file with economic references	Required	Not required	Required

Section	Specific items and criteria	Reimbursement Review Type		
		Standard	Tailored	Complex
Budget impact analysis	Aggregate pan-Canadian budget impact report	Required	Required	Required
	Aggregate pan-Canadian budget impact model	Required	Required	Required
	Supporting documentation used in BIA	Required	Required	Required
Epidemiologic information	Disease prevalence and incidence data	Required	Required	Required
	Number of patients accessing a new drug	May be required	May be required	May be required
Pricing and distribution information	Submitted price per smallest dispensable unit to 4 decimal places	Required	Required	Required
	Method of distribution	Required	Required	Required
Reimbursement status	Reimbursement status of all relevant comparators	Required	Required	Required
Provisional algorithm[a]	Place in therapy template	Required	Not required	Required
	Reference list and copies of studies	Required	Not required	Required
Companion diagnostics	Reference list and articles highlighting clinical utility	May be required	May be required	May be required
	Disclosable price	May be required	May be required	May be required
Implementation	Completed implementation plan template	Not required	Not required	Required for cell and gene therapies
Pre-NOC letter	Letter for sending NOC or NOC/c	Required	Required	Required

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

[a] Required only in applications for oncology drugs.

Table 8: Resubmission and Reassessment Requirements

Section	Specific items and criteria	Resubmissions		Standard reassessment
		New clinical and cost	New cost only	
General information	Application overview template	Required	Required	Required
	Signed cover letter	Required	Required	Required
	Executive summary template	Required	Required	Required
	Product monograph	Required	Required	Required
	Completed declaration letter	Required	Required	Required
	Completed regulatory and HTA status template	Required	Required	Required
	Request for deviation response letter or statement that a deviation was not requested	Required	Required	Required
Efficacy, effectiveness, and safety information	Common Technical Document sections 2.5, 2.7.1, 2.7.3, 2.7.4, and 5.2, or a statement indicating any section(s) that are not available	Required	Required	Not required
	Clinical study reports for pivotal and/or key studies	Required	Not required	Required

Section	Specific items and criteria	Resubmissions		Standard reassessment
		New clinical and cost	New cost only	
	Reference list, copies of studies, and errata	Required	Not required	Required
	Reference list and copies of articles for validity of outcome measure	Required	Not required	Required
	Reference list and copies of editorial articles	Required	Not required	Required
	Table of studies	Required	Required	Required
	Indirect comparison with full technical report	May be required	May be required	May be required
Submission template	Complete sponsor summary of clinical evidence template	Required	May be required	Required
Epidemiologic information	Disease prevalence and incidence data	Required	Required	Required
	Number of patients accessing a new drug	May be required	May be required	Not required
Reimbursement status	Reimbursement status of all relevant comparators	Required	Required	Required
	Reimbursement status of the drug under review	Required	Required	Required
Economic information	New pharmacoeconomic evaluation for the full population identified in the approved Health Canada indication(s) to be reviewed	Required	Required	Not required
	Updated pharmacoeconomic evaluation(s) addressing: population covered under current reimbursement criteria; and population covered under proposed reimbursement criteria (if applicable)	Not required	Not required	Required
	Unlocked and fully executable economic model	Required	Required	Required
	Economic model supporting documentation	Required	Required	Required
	Completed checklist of economic requirements	Required	Required	Required
	RIS file with economic references	Required	Required	Required
Budget impact analysis	Aggregate pan-Canadian budget impact report	Required	Required	Required
	Aggregate pan-Canadian budget impact model	Required	Required	Required
	Supporting documentation used in BIA	Required	Required	Required
Pricing and distribution information	Submitted price per smallest dispensable unit to 4 decimal places	Required	Required	Required
	Method of distribution	Required	Required	Required
Provisional algorithm[a]	Place in therapy template	Required	Required	Required
	Reference list and copies of studies	Required	Required	Required
Companion diagnostics	Reference list and articles highlighting clinical utility	May be required		
	Disclosable price	May be required		
Implementation	Updated implementation plan template	May be required		

BIA = budget impact analysis.

[a] Required only in applications for oncology drugs.

5.1 General Information

5.1.1 Application Overview Template

A completed application overview template.

5.1.2 Signed Cover Letter

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

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

5.1.3 Executive Summary

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

5.1.4 Product Monograph

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

Sponsors must provide immediate notification, 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 CDA-AMC of any changes to the product monograph could result in a temporary suspension of the review.

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

Table 9: Requirements for Filing Product Monograph

NOC status	Application requirements
Pre-NOC	• At the time of filing the submission: a copy of the most recent draft product monograph showing the company, drug brand, and non-proprietary names that correspond to the anticipated NOC • As soon as available: ▪ a copy of the draft product monograph showing, in tracked changes, all 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, 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	• A copy of the most current version of the Health Canada–approved product monograph

NOC = Notice of Compliance.

5.1.5 Declaration Letter

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

5.1.6 Regulatory and HTA Status in Other Jurisdictions

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

5.1.7 Request for Deviation from Pharmacoeconomic Requirements

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

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

5.2 Sponsor Submission Templates

5.2.1 Clinical Evidence Template for Standard and Complex Reviews

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

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

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

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

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

Section 5: This section allows the sponsor to summarize evidence from additional studies that address important gaps in the evidence presented in sections 2 to 3 of the template. Prior to completing Section 5, sponsors must clearly identify the gaps in the evidence that has been provided in each of the preceding sections. Examples of gaps in the evidence include the following:

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

It is recommended that studies presented within section 5 should be derived from a systematic literature review to minimize the risk of evidence selection bias. The information provided by the sponsor in section 5 will be considered and a case-by-case determination will be made if the additional evidence will be included

in the clinical report. The inclusion of evidence from section 5 in the clinical report will be determined solely by CDA-AMC based on the following factors:

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

5.2.2 RIS File with References for Standard and Complex Reviews

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

5.2.3 Submission Templates for Tailored Reviews

A completed tailored review submission template.

5.3 Health Canada Documentation

5.3.1 Health Canada NOC or NOC/c

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

Table 10: Requirements for Filing an NOC

NOC status	Application requirements
Pre-NOC	• 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, dated and signed by Health Canada, must be sent as soon as it is available (i.e., on the day of, or next business day after, receipt from Health Canada). • If the drug receives an NOC/c for the indication(s) being reviewed: 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 CDA-AMC as soon as it is available.
Post-NOC	• A copy of the NOC or NOC/c for the indication(s) for which the drug is to be reviewed. • 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.

5.3.2 Clarimails or Clarifaxes

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

Table 11: Requirements for Filing Clarimails/Clarifaxes

NOC status	Application requirements
Pre-NOC	• 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; including the date of each Clarimail/Clarifax, the topic for clarification, a brief summary of the response, and the date of the response must be included • On an ongoing basis up to the point of the NOC or NOC/c being issued, the sponsor must provide revised summary tables to reflect any additional Clarimails/Clarifaxes as aforementioned
Post-NOC	• 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; including the date of each Clarimail/Clarifax, the topic for clarification, a brief summary of the response, and the date of the response must be included.

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

5.4 Efficacy, Effectiveness, and Safety Evidence

5.4.1 Common Technical Document

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

Table 12: Common Technical Document Module Sections

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

5.4.2 Clinical Study Reports

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

5.4.3 Publications or Manuscripts for Key Clinical Studies

The requirements for including publications or manuscripts for key clinical studies are summarized in Table 13. For the clinical studies requirements, the preference is for any unpublished data to be submitted in

manuscript format; however, if the data are unavailable in manuscript format, the information should be provided in accordance with the CONSORT 2010 Statement Checklist, using clearly labelled sections (i.e., title, abstract, introduction, methods, results, discussion, other information).

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

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

Review type	Application requirements
Submission	• Copies of the published and unpublished studies that address key clinical issues for the drug under review. • Copies of any supplemental appendices that are associated with published studies. • Copies of any errata related to any of the published studies provided (or a placeholder document with a statement confirming that there are no errata). • A reference list with all of the published and unpublished studies (including any errata) that address key clinical issues for the drug under review.
Resubmission based on new clinical information	• Copies of the published and unpublished studies that address key clinical issues for the drug under review, including all new clinical information that addresses specific issues identified by the expert committee in the final recommendation document. • Copies of any supplemental appendices that are associated with published studies. • Copies of any errata related to any of the published studies provided (or a placeholder document with a statement confirming that there are no errata). • A reference list with all the published and unpublished studies (including any errata) that address key clinical issues for the drug under review. The studies in the list must be presented as follows: ▪ All new clinical information that addresses specific issues identified by the expert committee in the final recommendation document. ▪ Key clinical studies that were included in the initial submission and/or previous resubmissions filed.
Standard reassessment	• A reference list of the published and unpublished studies included in the submission; the list should specifically identify the new clinical information that supports the sponsor's request for the reassessment (e.g., revised reimbursement criteria). • Copies of any errata related to any of the published studies provided (or a placeholder document with a statement confirming that there are no errata).

5.4.4 Table of Studies

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

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

5.4.5 Editorials

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

5.4.6 New Data

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

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

5.4.7 Validity of Outcome Measures

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

5.5 Indirect Comparisons

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

5.6 Pharmacoeconomic Submission

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

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

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

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

When multiple indications and/or populations are relevant, CDA-AMC will assess whether the review constitutes multiple submissions or may require multiple application fees. Please refer to the *Fee Schedule for Pharmaceutical Reviews* for details.

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

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

Only 1 type of economic evaluation can be included in an application. For example, the following will not be accepted:

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

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

5.6.1 Type of Analysis: Cost-utility Analysis

a) Pharmacoeconomic Evaluation: Technical Report

Target Population

For submissions and resubmissions:

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

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

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

Comparators

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

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

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

Perspective

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

Discounting

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

Effectiveness

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

Costs and Resource Use

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

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

Analysis

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

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

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

Reporting

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

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

A suggested reporting format is presented in Appendix 4.

Companion Diagnostics

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

b) Economic Model

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

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

The probabilistic analysis must run all interventions that are being compared against each other simultaneously or be conducted in a way that ensures the same input parameter values are considered

within each simulation and report the analysis results sequentially as relevant (per guidance in the analysis section above).

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

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

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

5.6.2 Type of Analysis: Cost-Minimization Analysis

a) Pharmacoeconomic Evaluation: Technical Report

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

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

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

- 1 or more indirect comparisons that allow for the comparison of the drug under review to relevant comparator(s).

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

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

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

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

Target Population

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

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

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

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

Comparators

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

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

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

Perspective

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

Discounting

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

Costs and Resource Use

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

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

Analysis

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

Reporting

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

A suggested reporting format is presented in Appendix 4.

b) Cost Calculations

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

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

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

If the analysis is probabilistic:

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

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

5.6.3 Budget Impact Analysis

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

a) BIA: Technical Report

Target Population

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

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

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

Perspective

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

Time Horizon

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

Costs and Resource Use

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

Reporting

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

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

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

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

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

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

b) Budget Impact Model

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

The budget impact model must be programmed in Excel.

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

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

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

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

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

5.6.4 Supporting Material

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

- A user guide for the economic model to ensure clarity on how to modify input parameters and how to run the economic model for the base case and all scenario analyses; within the user guide, please note the expected model run time.
- The full technical report of the indirect treatment comparison(s), if 1 or more indirect treatment comparison is used to inform model parameters in the submitted economic evaluation.
- Technical reports of any unpublished studies or analyses used to inform parameters or assumptions in either the pharmacoeconomic evaluation or BIA (this includes but is not limited to data from utility studies, patient registries, Clinical Study Reports, expert opinion, market research information, epidemiological data on disease incidence and/or prevalence); the technical report(s) must be easily identified (i.e., provided separately to published studies or reports), and provide details of how input parameter values were derived, including a description of the study or dataset, the analysis plan, and results of the analyses; any modification or transformation of the results for use in the economic model must be described.
- Supporting documentation (i.e., references), numbered according to their respective number in the reference list, used to inform the methods, assumptions, and inputs in the economic evaluation and the BIA reports and models
- A RIS file with all references that are used in the pharmacoeconomic evaluation technical report and BIA technical report is required. The preferred format is a single RIS file, but separate RIS files for the pharmacoeconomic evaluation technical report and BIA technical report will be accepted.

- A document clarifying any key source(s) and assumption(s) of the relevant inputs for the companion diagnostic (e.g., articles, studies), if there is a companion diagnostic test associated with the drug under review.

Deviations from any of the requirements within the economic evaluation section must be discussed with and accepted 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.

5.7 Epidemiologic Information

5.7.1 Disease Prevalence and Incidence

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

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

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

5.7.2 Patients Accessing a New Drug

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

5.8 Reimbursement Status of Comparators

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

5.9 Pricing and Distribution Information

5.9.1 Submitted Price

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

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

The submitted price is the price per smallest dispensable unit that is submitted and that must not be exceeded for any of the drug programs following completion of the reimbursement review process. Only 1 price (anticipated or current market price) to 4 decimal places per smallest dispensable unit is to be submitted per drug that is to be reviewed (i.e., only 1 price for all indications undergoing review concurrently).

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

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

5.9.2 Method of Distribution

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

5.10 Provisional Algorithm for Oncology Drugs

a) Proposed Place in Therapy Template

A completed proposed place in therapy template with the following information:

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

b) Studies for Studies Addressing the Sequencing of Therapies

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

5.11 Companion Diagnostics

5.11.1 Clinical Utility of Companion Diagnostic

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

5.11.2 Price of Companion Diagnostic

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

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

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

5.13 Additional Information Requests

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

5.13.1 Economic Information

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

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

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

5.13.2 Health Canada Clinical Reviewer Report(s)

CDA-AMC may request copies of all Health Canada clinical reviewer reports (*Pharmaceutical Safety and Efficacy Assessment* or *Biologics Safety and Efficacy Assessment Report*) pertaining to the evaluation of pivotal safety and efficacy clinical trials — including those associated with any previous negative decision received during any review iteration — for the indication to be reviewed. If the *Pharmaceutical Safety and Efficacy Assessments* or *Biologics Safety and Efficacy Assessment Reports* are unavailable from Health

Canada at the time the request is received, the sponsor should provide the reports as soon as they are available (i.e., on the day of, or the business day after, receipt from Health Canada).

5.13.3 Health Canada Clarifaxes and Clarimails

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

5.13.4 Clinical Study Reports and Periodic Safety Update Reports

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

6. Stakeholder Engagement

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

6.1 Sponsor Engagement

6.1.1 Communications Between CDA-AMC and the Sponsor

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

Direct contact between a sponsor and expert committee members (in their capacity as members of the expert committees) or the review team is not permitted during the review process. Direct approaches in any form to committee members or the review team may be viewed as introducing conflict of interest and may create an appearance of bias or unfairness. Direct contact by a sponsor with 1 or more members of the review team may result in a significant delay in the review process because additional steps may be required to obtain an unbiased recommendation on the product.

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

6.1.2 Pre-Submission Phase

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

6.1.3 Review Phase

During the review phase, the sponsor may be requested to provide additional information and/or clarification that is required to complete the review. These requests will be provided in writing sponsors are encouraged to respond in a timely manner to avoid potential delays with the review timelines. Additional details regarding these requests are provided in section 5.13.

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

6.1.4 Recommendation Phase

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

6.2 Patient Engagement

6.2.1 Role of Patient Groups

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

Table 14: Key Milestones for Patient Group Engagement

Milestones	Description
Call for patient group input	The call for patient input is issued 29 business days before the anticipated date of filing the application and will be open for 35 business days from the date the call for input is issued in the weekly update.
Posting complete patient group input[a]	All patient group input will be posted on the website (this typically occurs approximately 2 weeks after call for input closes).
Commentary on recommendations	Patient groups will have 10 business days to review and comment on the draft recommendations during the stakeholder feedback period.

[a] This will include all conflict of interest declarations.

6.2.2 Patient Group Input and Feedback

a) Call for Patient Input

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

Open calls for patient input are available via:

- Website (as a pending drug submission and an open call for patient input).
- Weekly Summary newsletter that summarizes all notifications and is sent to subscribers every Thursday.
- Social media platforms including X (@CDA_AMC) and Facebook (@CDA.AMC).

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

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

b) Submitting Patient Input

Patient input is submitted by patient groups. Individual patients or caregivers who wish to provide input are encouraged to work with a patient group that represents their condition to prepare a group submission. Patient input from individual patients and caregivers will only be accepted when there is no patient advocacy group representing patients with a condition for which a drug under review is indicated. Individual patients and caregivers who wish to submit input for a drug review should first contact CDA-AMC (at requests@cadth.ca) to confirm the absence of a relevant patient group. Upon confirmation that no relevant patient group exists, interested individuals will be provided with the individual patient and caregiver template for completion. The process for providing input, and how the input is used and posted, remains the same as that for patient groups, with minor modifications, as applicable, for an individual patient or caregiver.

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

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

c) How Patient Group Input Is Used

All patient group input received for the drug under review is collated. The complete patient group input is posted and included in the committee briefing materials. The public and patient members on the expert committees present the patient input at the outset of the deliberations (section 9.2), and a summary of the patient input discussion is included in the recommendation documents. A summary of input is also included in the report(s).

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

d) Posting Patient Group Input

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

The patient group submissions for each drug are consolidated for posting on the website. Posting typically occurs approximately 2 weeks after call for input closes. The conflict of interest information will be included in the posted material.

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

e) Feedback on Draft Recommendations

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

6.3 Clinician Engagement

6.3.1 Clinician Group Input and Feedback

a) Role of Clinician Groups

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

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

Table 15: Key Milestones for Clinician Group Engagement

Milestones	Description
Call for clinician group input	The call for clinician group input is issued 29 business days before the anticipated date of filing the application and will be open for 35 business days from the date the call for input is issued in the weekly update.
Posting complete clinician group input[a]	All clinician group input will be posted on the website (this typically occurs approximately 2 weeks after call for input closes).
Commentary on recommendations	Clinician groups will have 10 business days to review and comment on the draft recommendations during the stakeholder feedback period.

[a] This will include all conflict of interest declarations

b) Call for Clinician Input

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

Open calls for clinician input are available via:

- Website (as a pending drug submission and an open call for patient input).
- Weekly Summary newsletter that summarizes all notifications and is sent to subscribers every Thursday.
- social media platforms including X (@CDA_AMC) and Facebook (@CDA.AMC).

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

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

c) Submitting Clinician Group Input

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

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

d) Posting Clinician Group Input

The information will be posted for the drug under review after the call for clinician input is closed. The clinician group submissions for each drug are consolidated for posting on the website. Posting typically occurs approximately 2 weeks after call for input closes. The conflict of interest information will be included in the posted material.

e) Feedback on Draft Recommendations

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

6.3.2 Clinical Experts on the Review Team

a) Role of Clinical Experts

All reimbursement review teams include at least 1 clinical specialist with expertise in the diagnosis and management of the condition for which the drug is indicated. Clinical experts are a critical part of the review team and are involved in all phases of the review process (e.g., assisting in the critical appraisal of clinical evidence, interpreting the clinical relevance of the results, and providing guidance on the potential place in therapy). In addition, the clinical experts are invited to attend expert committee meetings to address any issues raised by the committee.

The number of clinical specialists is increased depending on the complexity of the drug under review. In addition to including multiple core clinical specialists in the review team, clinical panels for selected drugs with higher levels of complexity may be established (refer to section 6.3.2b).

Lower complexity drugs include all tailored reviews as well as standard reviews that are follow-on products within established drug class, are reviewed through Health Canada's standard review pathway, and have a generally well-defined place in therapy. These reviews will typically include 1 to 2 clinical specialists as part of the review team but do not require a clinical panel.

Higher complexity products include cell and gene therapies as well as standard reviews for products that are often first-in-class, are reviewed through one of Health Canada's expedited review pathways (i.e., priority review or advance consideration under NOC/c policy) and have an undefined place in therapy. These reviews

will typically include 2 to 3 clinical specialists as part of the review team and a panel with additional clinical specialists may be convened.

Table 16: Key Functions of Clinical Experts

Phase	Role in the reimbursement review process
Review phase	• Assisting in the critical appraisal of clinical evidence • Interpreting the clinical relevance of the results • Providing guidance on the potential place in therapy • Reviewing and advising on the appraisal and interpretation sections of the clinical report • Advising on the assumptions used in the pharmacoeconomic analysis to assist in critical appraisal and to inform reanalyses • Advising on implementation issues raised by jurisdictions
Recommendation phase	• Attending expert committee meetings to address any issues raised by the committee • Providing input on requests for reconsideration
Implementation phase	• As part of an implementation advice panel, experts may advise on outstanding implementation issues and further develop and refine reimbursement conditions • Advising on treatment sequencing within a particular indication for oncology drugs

b) Clinical Panels

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

These panels will be used to characterize unmet therapeutic needs, assist in identifying and communicating situations where there are gaps in the evidence that could be addressed through the collection of additional data, promote the early identification of potential implementation challenges, gain further insight into the clinical management of patients living with a condition, and explore the drug's potential place in therapy (e.g., potential reimbursement conditions).

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

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

members of its expert committee will also attend the clinical panel meetings. Refer to section 6.3.2d for details on joint engagement with INESSS.

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

c) Input From Clinical Experts

CDA-AMC engages with the clinical experts (with or without a supplemental clinical panel) before the expert committee meeting to ensure that the committee has this information available to inform their deliberation and recommendation. The input from the clinical experts will be made available to the sponsor for review and commentary before the expert committee meeting. CDA-AMC will aim to integrate the input of the clinical experts into the review report(s) before it is sent to the sponsor for review and commentary.

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

Any feedback from the sponsor regarding the input from the clinical experts will be reviewed and addressed and the experts (as required). If deemed appropriate, the review report(s) will be revised.

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

d) CDA-AMC and INESSS Joint Engagement

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

- similar submission timelines to CDA-AMC and INESSS
- challenges in generating robust evidence due to the rarity of the condition
- potential for challenging implementation issues
- perceived ethical challenges for decision-makers
- high acquisition costs and/or substantial budget impact.

CDA-AMC and INESSS will collaborate to establish the clinical panels, interact with the clinical experts on the panels, and summarize input and key information from the clinical panellists. Otherwise, the 2 agencies

independently complete all other phases of their respective review process, including the deliberation and recommendation phases.

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

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

e) Clinical Experts Interested in Participating

Clinical experts who are interested in participating in the reimbursement review process can register by completing a web form with contact information and details about their areas of expertise and interest. The information provided by registrants will be reviewed and selected individuals may be contacted to discuss their potential participation in the review. Any interested clinicians are encouraged to register for potential involvement in future opportunities, including initiatives through the Optimal Use and Therapeutic Review processes.

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

- expertise regarding the diagnosis and management of the condition for which the drug is indicated
- conflict of interest declaration
- availability to commit to the review timelines
- regional representation (particularly for clinical panels).

6.4 Drug Program Engagement

6.4.1 Role of the Drug Programs

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

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

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

6.4.2 Drug Program Input

a) Pre-submission Phase

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

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

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

- the advance notification form
- the sponsor's completed proposed place in therapy template (for oncology drugs)
- an updated rotational schedule for lead jurisdictions.

b) Review Phase

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

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

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

c) Recommendation Phase

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

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

Table 17: Key Milestones for Drug Program Engagement

Milestones	Description
Timing of drug program input	Drug programs will provide input early in the review phase (i.e., 10 to 15 business days after the file has been accepted for review)
Documents provided	Advance notification documentation followed by the complete application filed by the sponsor
Format for drug program input	A standardized template is provided for completion by the lead jurisdiction; the initial draft will be discussed and finalized at the next scheduled PAG or FWG meeting
Posting drug program input	Drug program input will be incorporated into the review report(s) and posted publicly
Role at expert committee meeting	Lead jurisdiction would present a summary of the implementation issues identified by the drug programs and respond to inquiries from the committee members
Commentary on recommendations	Clinician groups will have 10 business days to review and comment on the draft recommendations during the stakeholder feedback period; the drug programs are eligible to file a request for reconsideration
Implementation phase	Drug programs may request that an implementation advice panel be convened and participate in the process

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

7. Application and Screening Procedure

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

7.1 Application Filing

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

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

Requirements must be filed using the Pharmaceutical Submissions SharePoint site. The sponsor must upload 1 copy of all requirements to the corresponding review using the Pharmaceutical Submissions SharePoint site, per the file folder and file format specified in Appendix 6. Requirements must be filed using the Pharmaceutical Submissions SharePoint site during business hours (between 8:00 a.m. and 4:00 p.m. Eastern time). If filed outside of business hours, the next business day will be considered the date of transmittal.

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

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

7.2 Application Screening

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

- The Pharmaceutical Submissions SharePoint site logs the date and time that the requirements are received.
- Applications are accepted on an ongoing basis and are screened in the order they are received.
- The date of receipt is considered day zero for the purpose of calculating the 10–business day targeted time frame for initial screening of requirements.
- If the filed requirements are deficient or require revision, a notice is sent to the sponsor advising what information needs to be included or revised to be accepted for review. Rescreening of the requirements is completed as soon as possible after receipt but may take up to 5 business days.
- On day 10 of the screening period, a letter is sent to the sponsor advising whether the requirements have been accepted for review.
- Following an acceptance for review, the sponsor must also provide the requirements to all of the drug programs that require copies (refer to *Contact Information and Requirements for Drug programs* for details).

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

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

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

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

7.4 Application Fees for Reimbursement Reviews

All applications filed by manufacturers are subject to an application fee. For details please consult the *Fee Schedule for Pharmaceutical Reviews*.

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

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

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

Any sponsors that are uncertain about the application fees are encouraged to contact requests@cadth.ca early in the pre-submission phase to seek guidance.

7.5 Ordering and Initiation of Reviews

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

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

Prior to initiating the review of an application, CDA-AMC will:

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

7.6 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 CDA-AMC Conflict of Interest Policy. Except for the review manager(s), the names of the review team members, including members of clinical expert panels (if applicable), will not be disclosed to the sponsor.

7.7 Targeted Time Frames and Tracking

7.7.1 Target Timeframes

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

Table 18: Targeted Timelines for the Reimbursement Review Processes

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

[a] The timing required to prepare the draft reports for a request for advice depends on the complexity of the request and the amount of effort required to address the request.

[b] Sponsors will be sent responses and the revised reports 8 business days prior to the expert committee meeting.

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

[d] In the case of a disagreement expressed by the sponsor regarding redactions made in the review report(s), additional time may be required to resolve the disagreement in consultation with the sponsor. This additional time could delay publication of the review report(s)

7.7.2 New Information Filed in the Review Phase

a) Before Draft Reports Sent to Sponsor

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

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

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

b) After Draft Reports Sent to Sponsor

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

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

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

7.7.3 Pausing the Clock During Health Canada Review

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

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

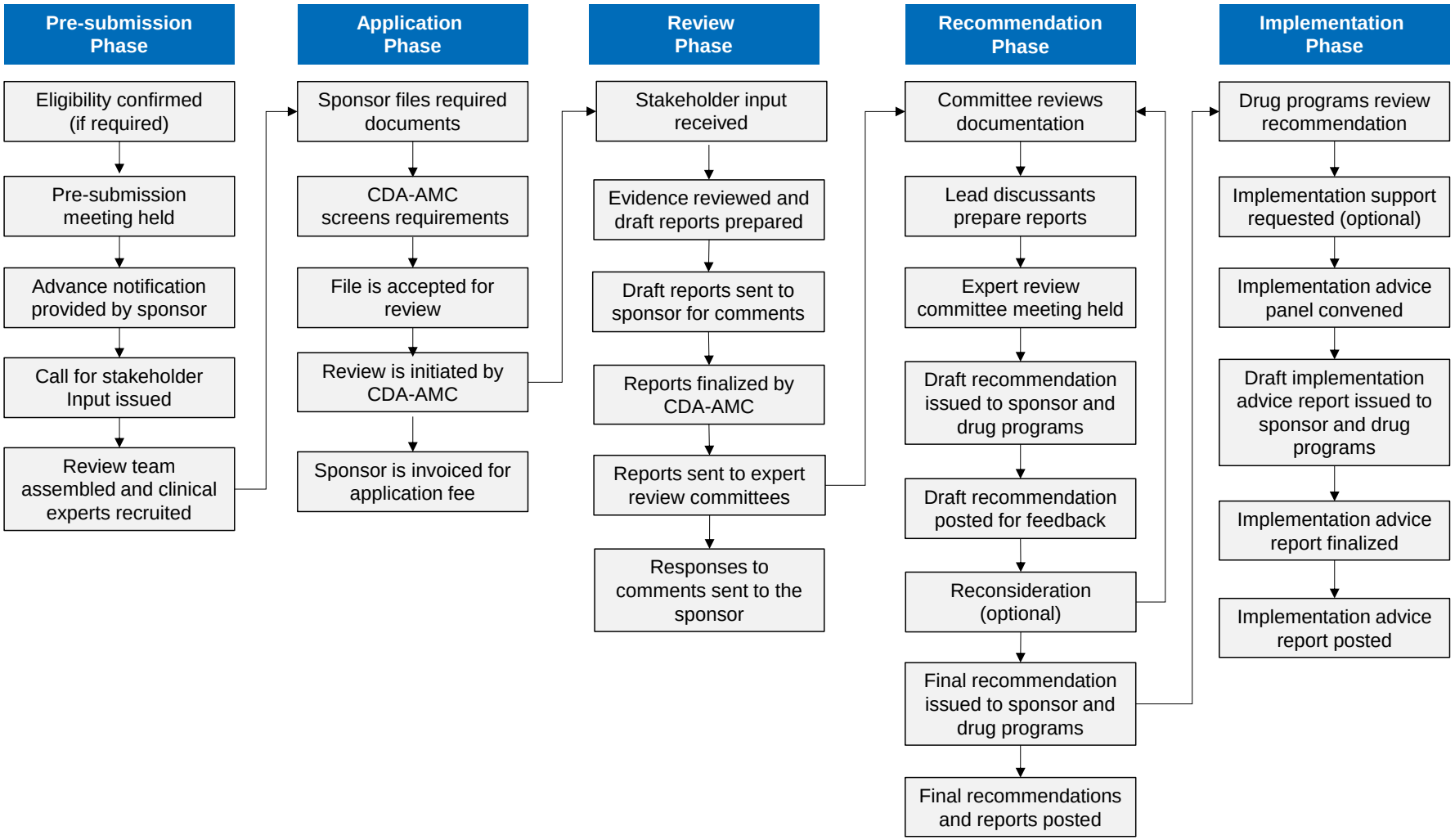
CDA-AMC will review the issues being discussed between the sponsor and Health Canada and determine the following:

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

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

Figure 4: Overview of Reimbursement Review Processes

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



8. Review Procedure

8.1 Review of Submissions

8.1.1 Standard Reviews

a) Clinical Review

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

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

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

The clinical report is prepared in accordance with a template and is finalized in accordance with section 8.3.

b) Economic Review

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

The economic review is conducted in line with the *Guidelines for the Economic Evaluation of Health Technologies: Canada*. CDA-AMC reviews the sponsor's pharmacoeconomic report and economic model, and critically appraises the sponsor's methods, inputs, and assumptions. As part of this appraisal, this entails:

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

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

8.1.2 Complex Reviews

a) Clinical Review

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

b) Economic Review

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

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

Sponsors will be required to complete a template with key details about their plans to implement the drug in the Canadian system. The drug programs will be asked to review and comment on the completed implementation plan template filed by the sponsor. Their feedback on the implementation plan could help provide early identification of potential access issues within the different jurisdictions, potential issues with administration or distribution mechanisms (e.g., need for specialty clinics), and/or challenges with diagnostic, prognostic, monitoring or other, testing requirements. This will approach will allow CDA-AMC and the drug programs to efficiently reflect on potential implementation issues and corresponding mitigation strategies.

d) Ethics Review

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

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

The ethics report is prepared in accordance with a template and is finalized in accordance with section 8.3.

8.1.3 Tailored Reviews

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

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

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

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

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

8.1.4 Plasma Protein Product Reviews

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

8.1.5 Companion Diagnostics

For submissions that include companion diagnostics, the reimbursement review process will include the following additional considerations.

a) Clinical Evidence

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

b) Economic Evidence

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

c) Patient Input

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

d) Clinician Input

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

e) Jurisdictional Input

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

8.2 Review of Resubmissions and Reassessments

8.2.1 Resubmissions and Standard Reassessments

The length of time required to conduct the review of a resubmission or reassessment will be determined based primarily on the following considerations:

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

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

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

8.2.2 Requests for Advice

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

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

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

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

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

The review report is finalized in accordance with section 8.3.

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

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

- *Therapeutic Review Framework and Process*
- *Procedures for Streamlined Drug Class Reviews*

8.3 Review Report(s)

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

8.3.1 Sponsor Review of Draft Reports

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

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

- 10 pages for commentary on draft reports for standard and tailored reviews
- 11 pages for commentary on draft reports for cell and gene therapy reviews (10 pages is allotted for commentary on the clinical and economic reports and one additional page is allotted for commentary on the draft ethics report).

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

As described in section 7.7.2, no new economic model may be filed after the draft review reports have been sent for sponsor review and comment. Any sponsor who wishes to file a revised economic model after receiving the draft review reports will be required to formally withdraw and refile their application in accordance with section 11.2.

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

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

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

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

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

8.3.2 Identification of Confidential Information

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

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

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

- a completed identification of confidential information form
- a copy of the review report(s) with confidential information highlighted in yellow.
- a copy of the stakeholder feedback document, with confidential information highlighted in yellow.

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

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

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

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

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

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

[a] This is a target of 8 business days. Extensions may be required depending on the nature, complexity, and clarity of the redaction requests.

9. Recommendation Procedure

9.1 Expert Committees

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

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

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

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

9.2 Expert Committee Meetings

9.2.1 Meeting Preparation

a) Meeting Agenda

The expert committee meeting agenda is set by CDA-AMC and the committee chair.

b) Committee Briefing Materials

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

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

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

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

9.2.2 Attendance

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

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

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

9.2.3 Meeting Minutes

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

9.3 Deliberative Framework and Processes

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

9.3.1 Recommendations Framework

a) Recommendation Options

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

Table 20: Description of Recommendations

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

Note: Scenarios described in this table are meant to be illustrative and are not exhaustive.
Existing treatment options may include best supportive care and non-pharmaceutical health technologies or procedures.
[a] An appropriate comparator is typically a drug reimbursed by one or more drug programs for the indication under review. However, the choice of appropriate comparator(s) in the review is made on a case-by-case basis, considering input from jurisdictions and clinical experts.

b) Reimbursement Conditions

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

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

Table 21: Examples of Commonly Used Reimbursement Conditions

Reimbursement conditions	Description
Initiation criteria	Provides guidance on the appropriate reimbursement criteria for initiating treatment with the drug under review. Commonly used patient characteristics include: • severity of the condition • treatment history (e.g., inability to use, intolerance, or inadequate response to appropriate comparator[s]) • comorbidities • subtypes of the condition (e.g., based on genotypic and/or phenotypic characteristics).
Renewal criteria	Provides guidance on how and when patients who are receiving the drug should be assessed to determine if they are benefiting from the treatment. Commonly used criteria include: • minimum treatment response for continuation of therapy • type and timing of the clinical assessment(s) that should be used to evaluate the response to treatment.
Discontinuation criteria	Provides guidance on when reimbursement of the drug under review should be discontinued. These conditions can be used to identify the drug in patients who are longer responding and/or benefiting from treatment. Commonly used criteria include: • need for an invasive intervention (e.g., organ transplant or ventilation) • initiation of a different therapy for the condition • disease progression.
Prescribing criteria	Provides guidance on the appropriate setting for the treatment. Commonly used criteria include: • that prescribing and/or administration should be limited to clinicians or health care teams with a particular area of expertise • restrictions on dosage strength and frequency of administration • restrictions on combination use with other drugs.
Pricing conditions	Provides guidance on cost considerations for the drug under review. Commonly used criteria include: • a reduction in price (i.e., cost-effectiveness must be improved) • that the cost of the drug under review does not exceed the cost of appropriate comparator(s) • that the cost of the drug under review should provide cost savings compared with appropriate comparator(s).

Feasibility of Adoption into the Health System	Provides an assessment of the ease with which the drug can be adopted into the overall health care and cancer care systems. Feasibility of adoption may be noted in the following scenarios: • Economic feasibility may be noted when there are concerns regarding the affordability of the drug under review based on the budget impact assessment. • Organizational feasibility may be noted when there are concerns regarding the ability of the health system to adopt the drug under review based on an assessment of health system enablers and barriers to implementation, as identified by the participating drug programs, inclusive of all elements: operational, capital, human resources, legislative, and regulatory requirements.

c) Considerations for Significant Unmet Need

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

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

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

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

Consideration	Description
Considerations for significant unmet need	
Rarity of condition	• The drug under review is approved by Health Canada for the treatment of a rare disease. Specifically, the condition for which the drug is indicated has the following characteristics: ▪ is life-threatening, seriously debilitating, or both serious and chronic in nature. ▪ affects a relatively small number of patients (incidence of fewer than 5 in 10,000, but typically closer to 1 in 100,000) ▪ is often genetically based, onset at birth or early childhood, and leads to a shortened lifespan ▪ places a heavy burden on caregivers and the health care system ▪ is difficult to study because of the small patient population.
Population	• Need is identified on a population or subpopulation basis and not on an individual basis.
Absence of alternatives	• There is an absence of clinically effective drug or non-drug alternative treatments. • Substantial morbidity and mortality exist despite the available drug or non-drug alternative treatments.
Factors that contribute to uncertainty of clinical benefit	
Clinical data	• Limited number of clinical studies • Small sample sizes (e.g., due to rare disease that affects a relatively small number of patients [incidence of fewer than 5 in 10,000, but typically closer to 1 in 100,000]) • Absence of comparator groups • Alternative or adaptive trial designs for rare diseases • Short study durations or follow-up • Inability to distinguish disease severity in heterogeneous manifested rare diseases • Limited to surrogate end points • Insufficient evidence on meaningful clinical end points • Greater uncertainty in statistical analyses

9.3.2 Drafting Recommendations

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

a) Submissions and Resubmissions

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

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

b) Reassessments

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

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

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

9.3.3 Voting on Recommendations

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

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

9.3.4 Deferring a Recommendation

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

9.4 Draft Recommendations

9.4.1 Issuing the Draft Recommendation

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

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

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

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

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

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

Table 23: Target Timelines for Issuing and Posting Draft Recommendations

Key milestones	Description
Issuance to sponsor and drug programs	Draft recommendation issued 8 to 10 business days after the expert review committee meeting
Sponsor identifies confidential information	Sponsor has 2 business days to identify any confidential information in the draft recommendation using the template
Redaction of confidential information	Confidential information redacted 1 business day after receipt of the completed template from the sponsor
Sponsor validates redactions	Sponsor has 1 business day to validate the redactions in the recommendation after receipt from CDA-AMC
Posting on CDA-AMC's website	The draft recommendation will be posted on the day of the next scheduled issuance of Weekly Summary
Stakeholder feedback period	The stakeholder feedback period will be 10 business days after the draft recommendation is posted on the website

9.4.2 Feedback on the Draft Recommendation

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

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

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

Table 24: Stakeholders Eligible to Provide Feedback on Draft Recommendations

Source	Scope of feedback
Sponsor	• Provide feedback on the draft recommendation • File a request for reconsideration of the draft recommendation
Manufacturer (if not the sponsor)	• Provide feedback on the draft recommendation • File a request for reconsideration of the draft recommendation
Drug programs	• Provide feedback on the draft recommendation • File a request for reconsideration of the draft recommendation
Patient group(s)	• Provide feedback on the draft recommendation
Clinician group(s)	• Provide feedback on the draft recommendation

9.5 Request for Reconsideration

9.5.1 Eligibility

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

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

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

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

9.5.2 Reconsideration Options

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

- **Major revisions:** Requests for major revisions will typically be focused on the recommendation category (e.g., do not reimburse) or involve revisions that would result in changes to the patient population that would be eligible for reimbursement with the drug under review (e.g., expansion of the patient population addressed in the initiation criteria).
- **Minor revisions:** Requests for minor revisions will typically be focused on any of the following: reimbursement conditions within the patient population for whom reimbursement of the drug under review has been recommended (e.g., renewal criteria, pricing conditions, or administration criteria); implementation guidance; or reasons for recommendation. Requests for minor revisions that would alter the patient population (e.g., expand the population or the criteria related to the identification of appropriate patients) will not be accepted and the request will have to be refiled as a request for major revisions.
- **Editorial revisions:** Requests to revise the text in the recommendation to provide additional clarity and details regarding the recommendation, evidence that was considered, the deliberative process, or reasons for recommendation.

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

Table 25: Reconsideration Options

	Major revisions	Minor revisions	Editorial revisions
Criteria	Reconsideration requests that are focused on the recommendation category (e.g., do not reimburse); or requests that would result in changes to the patient population that would be eligible for reimbursement with the drug under review (e.g., expansion of the patient population address in the initiation criteria).	Reconsideration requests that are focused on any of the following: reimbursement conditions within the patient population for whom reimbursement of the drug under review has been recommended (e.g., renewal criteria, pricing conditions, or administration criteria); implementation guidance; or reasons for recommendation.	Requests to revise the text in the recommendation to provide additional clarity and details regarding the recommendation, evidence that was considered, the deliberative process, or reasons for recommendation.
Deliberation	All requests for major revisions to the recommendation will be addressed through discussion and deliberation with the full expert committee with additional support from clinical experts.	The majority of requests for minor revisions will be addressed through discussion and deliberation with a subpanel of the expert review committee with additional support from clinical experts, as required.	CDA-AMC staff and the expert committee chair will address the majority of requests for editorial revisions. Other committee members may be consulted, as required.
Outcomes	Should the recommendation be substantially revised following deliberation on the reconsideration request, another draft recommendation for stakeholder feedback. A final recommendation will be issued if the committee upheld the existing recommendation or made only minor revisions to the recommendation.	To expedite the review timelines, another draft recommendation is not issued following deliberations on a request for minor revisions. A final recommendation will be issued whether the committee decided to uphold the existing recommendation or make minor revisions to the recommendation.	These will be limited to editorial revisions or corrections that do not impact the reimbursement recommendation.
Timelines	Requests for major revisions to a recommendation will typically require 2 to 3 months to address.	Requests for minor revisions to a recommendation will typically require 1 month to address.	A final recommendation will be issued in accordance with standard timelines (i.e., typically no delays).
Eligibility	Due the resources required to address these requests and the implications for timelines, only those stakeholders that will be directly involved in the negotiations for the drug under review are permitted to file these requests (i.e., the sponsor and the drug programs).		All stakeholders that are eligible to provide feedback on reimbursement recommendations may request editorial revisions.

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

9.5.3 Filing a Request for Reconsideration

a) Request for Major or Minor Revisions

A request for major or minor revisions is filed by the sponsor using the reconsideration request template and by the participating drug programs using a dedicated feedback form. The completed template must be received by CDA-AMC during the stakeholder feedback period.

b) Request for Editorial Revisions

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

9.5.4 Patient and Clinician Group Feedback

Reconsiderations result in a significant extension of the overall review timelines (typically 2 to 3 months) and have important resource implications for CDA-AMC, as well as for sponsors. As such, only those stakeholders that will be directly involved in the negotiations for the drug under review are permitted to file requests for reconsideration (i.e., the sponsor and the drug programs). This helps provide greater predictability in the review timelines for sponsors, minimize the overall review timelines for decision-makers and patients, and help to avoid delays to accessing new medications.

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

9.5.5 Examination of Request for Reconsideration

a) Assessment and Timelines

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

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

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

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

b) New Information

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

- the application was accepted through the complex review process
- the new information has been provided to try and address an important clear gap in the evidence that has been identified by the expert committee
- the sponsor confirms in writing that the new information was not available during the review phase of the reimbursement review process (i.e., it could not have been included in the initial application without substantially delaying the overall review process and was not available at the time of providing comments on the draft reports)

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

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

c) Timelines for Expert Committee Meeting

The sponsor will be notified regarding the target expert committee meeting date for the reconsideration. The following factors are considered when establishing the timelines for reviewing a request for reconsideration:

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

9.5.6 Reconsideration Meeting

a) Purpose

The reconsideration meeting provides the sponsor an opportunity to elaborate on the issues that were raised in their request for reconsideration that was filed. These meetings are not offered for a situation where the request for reconsideration has been filed by the participating drug programs. In such cases, CDA-AMC provides the complete written request for reconsideration to the sponsor and provides an opportunity for direct input and commentary on the request. CDA-AMC cannot facilitate a meeting between the sponsor and representatives of the public drug programs.

b) Attendance

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

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

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

c) Meeting Logistics and Agenda

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

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

d) Summary of the Discussion

The sponsor is required to prepare a draft summary of the discussion using the template provided by CDA-AMC. The summary must not exceed 2 pages and must be submitted to CDA-AMC in accordance with the deadlines provided at the meeting. Delays in providing the summary could impact the target expert committee meeting. CDA-AMC staff will review and finalize the summary (revising as required to ensure clarity). Expert committee members will be provided with the meeting materials and the summary of the meeting.

9.5.7 Requests for Reconsideration Filed by the Drug Programs

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

9.5.8 Addressing the Reconsideration Request

a) Request for Major Revisions

The committee briefing materials to address the reconsideration request, include but are not limited to:

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

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

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

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

Either a final recommendation or a revised draft recommendation will be issued to the sponsor and drug programs 8 to 10 business days following the expert committee meeting.

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

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

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

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

b) Request for Minor Revisions

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

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

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

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

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

9.6 Final Recommendations

9.6.1 Issuing the Final Recommendation

The final recommendation will be issued in the following circumstances:

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

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

9.6.2 Posting the Final Recommendation

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

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

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

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

Table 26: Target Timelines for Issuing and Posting Final Recommendations

Key milestones	Description
Final recommendation issued to sponsor and drug programs	**No reconsideration:** The final recommendation is issued 8 to 10 business days after the end of the stakeholder feedback period.
	Following reconsideration: The final recommendation is issued 8 to 10 business days after the expert committee meeting where the recommendation was upheld following a request for reconsideration.
Sponsor identifies confidential information	The sponsor has 2 business days to identify any confidential information in the final recommendation using the CDA-AMC template.
Redaction of confidential information	Confidential information will be redacted 1 business day after receipt of the completed template from the sponsor.
Sponsor validates redactions	The sponsor has 1 business day to validate redactions in the recommendation after receipt from CDA-AMC.
Posting on website	The final recommendation will be posted on the website 7 business days after the redactions have been validated by the sponsor.

10. Temporary Suspension of a Review

10.1 Suspension Due to Incomplete Information

If CDA-AMC is unable conduct a thorough review and/or an appraisal due to incomplete information, CDA-AMC, in its sole discretion, may temporarily suspend a review in the following manner:

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

10.2 Suspension Following an NOD or NON

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

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

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

For drugs that undergo temporary suspension because of an NOD or NON, the following information would be required for the suspension to be lifted:

- a summary of the issue and how the sponsor has or is planning to resolve the issue (please note that details are not required and should not be provided to CDA-AMC for any issues related to the quality review by Health Canada [e.g., chemistry, manufacturing, and controls])
- any new clinical data filed with Health Canada to address the issue.

- advance notification of a minimum of 6 weeks from the sponsor when the issue is likely to be resolved and the anticipated date that an NOC or NOC/c may be issued by Health Canada.

Depending on the availability of resources, CDA-AMC 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

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

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

11. Withdrawal From the Reimbursement Review Processes

11.1 Withdrawal Procedure

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

- The sponsor voluntarily requests withdrawal from the CDA-AMC process.
- The sponsor has withdrawn from the Health Canada review process.
- Health Canada has withdrawn market authorization.
- Health Canada has issued a Notice of Deficiency — Withdrawal or Notice of Non-Compliance.

- Health Canada has issued a Notice of Non-Compliance or Notice of Deficiency, and the sponsor has not or will not consent to the information-sharing process.
- CDA-AMC determines that temporary suspension following the issuance of a Notice of Deficiency or Notice of Non-Compliance is not appropriate.

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

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

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

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

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

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

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

11.2 Refiling After Withdrawal

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

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

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

12. Implementation Advice for a Recommendation

Effective February 2024, CDA-AMC has introduced the *Procedures for Implementation Advice for Health Technologies* that supersede the implementation advice for a recommendation that was previously described within this section the *Procedures for Reimbursement Reviews*). If you have questions, please contact us at requests@cadth.ca.

13. Provisional Funding Algorithm for Oncology Drugs

13.1 Purpose and Eligibility

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

CDA-AMC will initiate the development of a provisional funding algorithm in the following instances:

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

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

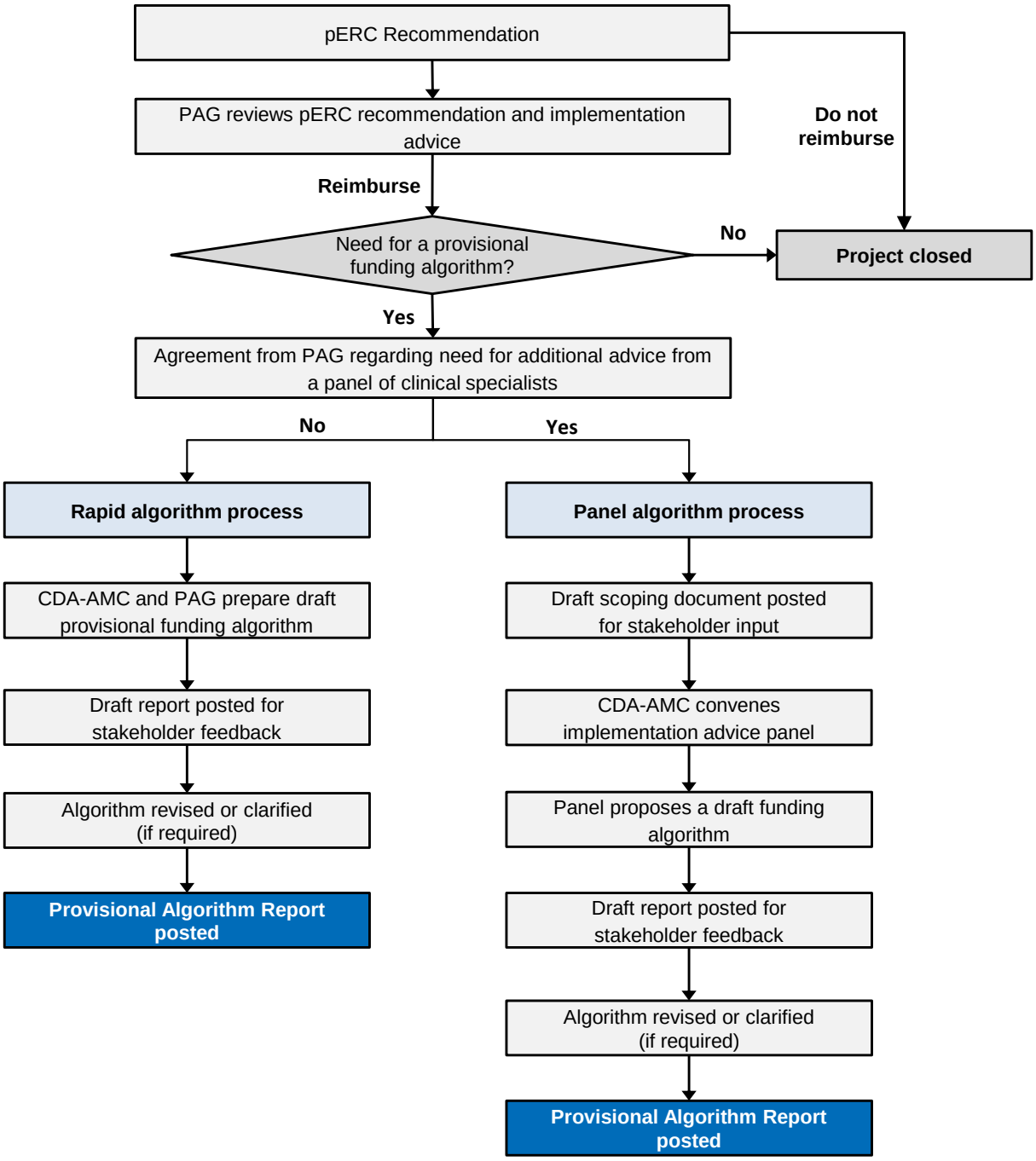
13.2 Algorithm Processes

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

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

Figure 5: Funding Algorithm Processes

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



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

13.3 Targeted Time Frames and Tracking

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

Table 27: Targeted Timelines for the Provisional Funding Algorithm Processes

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

N/A = Not Applicable.
[a] The actual timelines may depend on the scheduling of Provincial Advisory Group meetings.
[b] The time frame will be extended if there is the need for an additional panel meeting.

13.4 Panel Algorithms

13.4.1 Stakeholder Engagement

a) Industry Engagement

All manufacturers (i.e., DIN holders) whose products may be directly impacted by the provisional algorithm may provide input into the review being conducted. For drug manufacturers other than the sponsor for the drug under review, the opportunity to participate in the implementation advice process will only apply in situations where CDA-AMC has been asked to directly comment on one or more of that manufacturer's product(s). CDA-AMC will post a scoping document with the following information:

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

Upon notification that the algorithm is being developed by CDA-AMC, all manufacturers with products that fall within the scope of the provisional algorithm will have 10 business days to provide written input to CDA-AMC regarding their perspective on the treatment algorithm and the place in therapy for their product(s). This input must be shared using the template provided by CDA-AMC and must not contain any confidential information (as all information included in the template will be considered disclosable by CDA-AMC). Once CDA-AMC has drafted the provisional algorithm report, the manufacturer(s) will be provided with an opportunity to review and provide comments (as described in section 13.4.3).

b) Drug Program Engagement

The participating drug programs will be engaged throughout all phases of the provisional algorithm process. To help ensure that the issues are clearly addressed by the panel and to help expedite the overall process, representatives from CAPCA, pCPA, and/or the drug programs will have the opportunity to participate in panel meetings. Once CDA-AMC has drafted the provisional algorithm report, the drug programs(s) will be provided with an opportunity to review and provide comments (as described in section 13.4.3).

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

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

c) Patient and Clinician Group Engagement

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

13.4.2 Implementation Panel and Deliberative Process

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

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

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

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

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

13.4.3 Provisional Funding Algorithm Reports

a) Scoping Document and Call for Input

CDA-AMC will notify all stakeholders that an implementation advice panel is being convened to discuss the sequencing of treatments for a particular indication. CDA-AMC will post a document detailing the scope of the implementation advice panel and will communicate that the call for stakeholder input is open. All stakeholders will have 10 business days to provide written input to CDA-AMC regarding their perspective on the treatment algorithm and the place in therapy for their product(s). No requests for extensions will be granted. This input must be provided using the template and must not contain any confidential information (all information included in the template will be considered disclosable).

b) Draft Provisional Algorithm Report

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

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

c) Final Provisional Algorithm Report

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

13.5 Rapid Algorithms

13.5.1 Stakeholder Engagement

a) Industry Engagement

At the outset of the review, CDA-AMC will attempt to notify all manufacturers (i.e., DIN holders) whose products may be directly impacted by the provisional funding algorithm that the review is being undertaken. For drug manufacturers other than the sponsor for the drug under review, the opportunity to participate in the implementation advice process will only apply in situations where CDA-AMC has been asked to directly comment on one or more of that manufacturer's product(s).

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

b) Drug Program Engagement

The participating drug programs will be engaged throughout all phases of the provisional funding algorithm process. To help ensure that the issues are clearly addressed by the panel and to help expedite the overall process, representatives from CAPCA, pCPA, and/or the drug programs will have the opportunity to participate in panel meetings. Once CDA-AMC has drafted the provisional funding algorithm report, the drug programs(s) will be provided with an opportunity to review and provide comments (as described in section 13.4.3).

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

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

c) Patient and Clinician Group Engagement

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

13.5.2 Development of the Algorithm

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

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

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

13.5.3 Provisional Funding Algorithm Reports

a) Draft Provisional Algorithm Report

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

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

b) Final Provisional Algorithm Report

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

14. Other Implementation Support Activities

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

15. Request for Procedural Review

Implementing a procedural review mechanism is an important cornerstone for ensuring an accountable and ethical review process that aligns with CDA-AMC's foundational values for decision-making. The grounds for a procedural review relate only to whether CDA-AMC failed to act in accordance with its procedures in conducting the reimbursement review and issuing the final recommendation. A procedural review is not an opportunity to reopen issues that the expert committee has decided on or to circumvent existing feedback mechanisms (e.g., request for a reconsideration). This procedure also does not cover fairness in the colloquial sense; for instance, that it is "unfair" that a recommendation is issued to not reimburse a treatment. Unsubstantiated allegations of general unfairness (for example, the alleged inability to understand a conclusion or the applicant simply disagrees with the views or conclusions in the final recommendation) will not be accepted as valid grounds for a procedural review. Please refer to Appendix 2 for detailed procedural review process requirements.

16. Document Management

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

Appendix 1: Confidentiality Guidelines

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

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

A. Definition of Confidential Information

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

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

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

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

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

Item	Redactable	Rationale
General Information		
Changes to the indication during the review of a submission filed on a pre-NOC basis.	Not redacted	The indication and/or sponsor's requested reimbursement conditions will not be considered confidential by CDA-AMC once this information has been posted on the CDA-AMC website (e.g., at the time of issuing the call for stakeholder input). If the indication and/or sponsor's requested reimbursement conditions are revised during the review of a submission filed on a pre-NOC basis, the originally filed information will not be considered confidential by CDA-AMC once it has been published on the CDA-AMC website.
Changes to the dosing, dosage forms, or dosage strengths during the review of a submission filed on a pre-NOC basis.	Redactable	Changes relating to the recommended dosing, dosage forms, or dosage strengths (e.g., strengths filed for review on a pre-NOC basis, but not approved by Health Canada) may be considered redactable if the information is not publicly available.
Clinical Data		
Methods used to conduct a study or to analyze data from a study.	Not redacted	Methods information is required to understand how model inputs are derived.
Clinical data that are available in the public domain.	Not redacted	Information that is publicly available is not considered confidential information by CDA-AMC.
Clinical data not yet in the public domain but either: • awaiting publication, including in a journal OR • will be released into the public domain by regulatory authorities	Not redacted	To avoid redaction of data that will subsequently be available and when publishing in committee papers will not jeopardise publication elsewhere. The International Committee of Medical Journal Editors (ICMJE) recommendations on overlapping publications state that it 'does not consider results or data contained in assessment reports published by health technology assessment agencies, medical regulators, medical device regulators, or other regulatory agencies to be duplicate publication'.

Clinical data that has not been made publicly available and for which there is no plan for the data to become publicly available.	Redactable, except for minimum reporting requirements.	In recognition that there will be unpublished clinical data that will be confidential. However, to allow transparent reporting of decision making, CDA-AMC has outlined minimum reporting requirements for data which is likely to be fundamental to committee decision making (see Table 29). Clinical data should be treated as clinical data without a publication plan if: • there is clinical data awaiting first public presentation at a congress that is scheduled to take place after documentation from CDA-AMC would be released to the public, and • this data is not awaiting publication in a journal or within marketing authorisation documentation.
Data from real-world evidence studies that has not been made publicly available and for which there is no plan for the data to become publicly available.	Redactable (if collected by company then minimum summary information should be provided). The confidentiality requirements of third-party sources of data will be adhered to.	See the above rationale for clinical data that has not been made publicly available and for which there is no publication plan.
Company's indirect comparison that has not been made publicly available and for which there is no plan for the data to become publicly available	Redactable, except for minimum summary information.	Assessing the benefit of a technology compared with its comparators and the uncertainty around these comparisons is fundamental to committee decision making. CDA-AMC has outlined the minimum reporting requirements for indirect comparisons outcomes to allow transparent reporting of committee decision making (see Table 29).

Critical appraisal of clinical studies and indirect comparisons (for example, of the validity of methodology and assessment of bias and uncertainty).	Not redacted	Critical appraisal is not considered to be confidential information and will not be redacted. This applies to critical appraisals carried out by both the sponsor and CDA-AMC.
Data derived from clinical opinion.	Not redacted	Clinical opinion may vary, and it is vital to have transparent discussion. This includes the outcome of expert elicitation. Clinical expert opinion is not considered to be confidential information and will not be redacted.
References	Not redacted	Referencing is required to understand where inputs and assumptions are derived and does not predicate inputs that are considered confidential.
Pharmacoeconomic Evaluation		
Description of methods used to conduct the economic evaluation.	Not redacted	Methods of economic evaluations are not considered confidential, as they are required to understand what was submitted.
Weighted distribution of comparator and/or subsequent treatments.	Not redacted	Methods of economic evaluations are not considered confidential. The definition of the comparator is critical to understand the results of the economic model. • Where distributions/data are based on public sources of information or expert opinion, this information will not be redacted. • If the input(s) is based on clinical trial information that is not publicly available, then this information is redactable. • If the input(s) is based on alternate data source (e.g., claims data), AND no supporting reference is provided, the input(s) are not redactable. Evidence of the use of commercial in confidence information must be provided to CDA-AMC (i.e., a detailed technical report outlining the data used and methods to derive the inputs) to be considered redactable.
Clinical inputs that are in the public domain.	Not redacted	Information that is publicly available is not considered confidential information by CDA-AMC.
Data from clinical studies that are not in the public domain.	Redactable	If the data are from clinical studies and the results are not in the public domain, then this information is redactable.

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

References	Not redacted	Referencing is required to understand where inputs and assumptions are derived and does not predicate inputs that are considered confidential.
Budget Impact Analysis		
Description of design of the budget impact analysis.	Not redacted	A description of the methods is required to understand the model.
Estimates for population size, market share, displacement of comparators, and resource assumptions that are based on published information.	Not redacted	Information that is publicly available is not considered confidential information by CDA-AMC.
Estimates for population size, market share, displacement of comparators, and resource assumptions that are based on unpublished information from the following sources: • Expert opinion • Assumption that is not supported by evidence (e.g., where no reference is provided, or stated as data on file with no reference provided).	Not redacted	Methods of budget impact analyses are not considered confidential. They are required to understand what is being conducted and measured.

Estimates for population size, market share, displacement of comparators, and resource assumptions that are based on unpublished information from market research obtained from a third party that cannot be publicly disclosed due to licensing agreements. This is exclusive of expert opinion.	Redactable	CDA-AMC considers information from these sources as confidential information and will redact when requested by the sponsor. However, to be considered redactable the sponsor must provide CDA-AMC with evidence that the information is commercial in confidence information (e.g., a detailed technical report outlining the data used and methods used to derive the inputs)
Sponsor's estimated budget impact (yearly and 3-year total).	Not redacted	Results from the sponsor's budget impact analysis are not considered to be confidential and will not be redacted. There may be rare situations where reporting of results may result in the ability to back-calculate confidential information exactly (e.g., when deterministic results are used). The burden of proof is on the sponsor to demonstrate how this can be done (to be included with the request for redaction).
CDA-AMC critical appraisal of the budget impact analysis.	Not redacted	CDA-AMC critical appraisal of the methods and data used in the pharmacoeconomic submission is not redacted.
CDA-AMC estimated budget impact (yearly and 3-year total).	Not redacted	CDA-AMC reanalyses are not considered to be confidential and will not be redacted.
Data which is commercially sensitive or allows back-calculation of data which is commercially sensitive.	May be redactable	Please see guidance on how this may be applied in Table 29.
References	Not redacted	Referencing is required to understand where inputs and assumptions are derived and does not predicate inputs that are considered confidential.
Time-Limited Recommendations		
Evidence-generation requirements for conditional regulatory approvals (i.e., NOC/c) described within the Qualifying Notice from Health Canada.	Not redacted	This information is required to ensure that stakeholders, including patients, understand: • the rationale for the time-limited recommendation • the type of evidence that will be generated to address the uncertainty the time frame for generating and submitted the evidence.

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

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

Table 29: Standard Reporting and Minimum Reporting Requirements

Standard reporting requirements	Minimum reporting requirements
Baseline and patient characteristics of trial populations that will be subject to disclosure by Health Canada.	This data for the whole trial population should be reported in full because it is expected to be published within marketing authorization documentation.
Baseline and patient characteristics of all subgroups that are relevant to the sponsor's requested reimbursement criteria: This includes: • Data for the population covered by the marketing authorization, if the trial population is broader than that covered by the marketing authorization. • The subgroup for whom the sponsor is positioning the technology if this population is narrower than that covered by the full indication approved or under review by Health Canada.	For the subgroups, a description of any imbalances between treatment arms or differences between the subgroups and whole trial population should be provided.
Primary outcomes (including for that are relevant to the sponsor's requested reimbursement criteria, if relevant) at the data cut included in the economic model.	Primary outcomes at the data cut which inform the regulatory submission should be reported because they are typically published within marketing authorization documentation (e.g., Product Monograph; Summary Basis for Decision; Regulatory Decision Summary).
Relative treatment effect and measure of precision such as 95% confidence interval.	If data from a later data cut than what informed the marketing authorization are used in the economic model and is marked as confidential, then the unredacted data cut informing the marketing authorization should also be presented alongside the later data cut. Commentary should be provided on similarities or differences between the point estimates and confidence intervals from publicly available versus confidential data cuts. For subgroup data that will not be reported within marketing authorization documentation, an accompanying description of the direction of treatment effect and how the point estimate and measure of precision compare with the data for the whole population should be provided alongside the confidential information.

Kaplan–Meier data (including extrapolations), if relevant.	If Kaplan–Meier data from a later data cut than what informed the marketing authorization are used in the model and is marked as confidential, then the unredacted data cut informing the marketing authorization should also be presented alongside the later data cut. For overall survival extrapolation, the proportions of people alive at a range of time intervals over the time horizon should be provided to enable discussion of plausibility of this modelled outcome.
Secondary outcomes at the data cut that inform the modelling.	Follow the principles for the primary outcomes.
Adverse events including death.	The equivalent data to that reported in marketing authorization documentation is expected.
Indirect treatment comparison: • an overview of the methodological approach, including any matching of data or adjustments • number of patients included in studies • patient characteristics from included studies • commentary on potential heterogeneity or sources of bias • outcomes (for example, comparative efficacy) with measure of precision such as 95% credible interval, if relevant.	All methodology and critical appraisal should be reported. If there is a demonstrated reason why numerical outcomes are confidential then an accompanying statement of direction of treatment effect and commentary on the measure of precision should be provided. For example, the width of the credible intervals and if the credible intervals cross parity. For adjusted outcomes, an accompanying description of how these outcomes differ from unadjusted outcomes should be provided.
Utility values (by health state, intervention utility increments or decrements, and disutility for adverse events) which are used in the model.	Quality of life data collected in the trial may be redactable.

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

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

Weighted distribution of comparator and/or subsequent treatments	Not redacted	Methods of economic evaluations are not considered confidential. The definition of the comparator is critical to understand the results of the economic model. • Where distributions/data are based on public sources of information or expert opinion, this information will not be redacted. • If the input(s) is based on clinical trial information that is not publicly available, then this information is redactable. • If the input(s) is based on alternate data source (e.g., claims data), AND no supporting reference is provided, the input(s) are not redactable. Evidence of the use of commercial in confidence information must be provided to CDA-AMC (i.e., a detailed technical report outlining the data used and methods to derive the inputs) to be considered redactable.
Clinical inputs that are in the public domain	Not redacted	Information that is publicly available is not considered confidential information by CDA-AMC.
Data from clinical studies that are not in the public domain	Redactable	If the data are from clinical studies and the results are not in the public domain, then this information is redactable.
Data that are not in the public domain, but are derived from expert opinion or sponsor assumptions (e.g., the data are not from unpublished clinical studies)	Not redacted	If the input(s) is based on expert opinion or assumption, then it is not considered redactable. Any information that is listed as "assumption" or "data on file" will not be redacted unless a detailed technical report has been provided for this information to indicate the derivation methods of the input(s).
Submitted price for the drug under review	Not redacted	CDA-AMC does not accept confidential submitted prices for applications filed for review through its reimbursement review processes. The submitted price is disclosed in all applicable CDA-AMC reports.
Prices for comparators and companion diagnostic testing (if applicable)	Not redacted	CDA-AMC does not accept confidential submitted prices for applications filed for review through its reimbursement review processes. The prices of comparators and/or companion diagnostic testing are disclosed in all applicable CDA-AMC reports.
Results in the sponsor's economic evaluation (e.g., ICER, total or incremental LYs, total or incremental QALYs, total or incremental costs)	Not redacted	Results from the sponsor's economic evaluation are not considered to be confidential and will not be redacted. There may be rare situations where reporting of results may result in the ability to back-calculate confidential information exactly (e.g., when deterministic results are used). The burden of proof is on the sponsor to demonstrate how this can be done (to be included with the request for redaction).
CDA-AMC critical appraisal of the sponsor's economic evaluation	Not redacted	CDA-AMC appraisal of the methods and data used in the sponsor's pharmacoeconomic evaluation is not redacted.

CDA-AMC reanalyses of the economic evaluation (e.g., ICER, total or incremental LYs, total or incremental QALYs, total or incremental costs)	Not redacted	Results of the economic model, including CDA-AMC reanalyses, are not considered to be confidential and will not be redacted.
Model output (e.g., disaggregated health state, cost category results, health state distribution over time)	Not redacted	Results of the model, sponsor's results and CDA-AMC reanalyses are not redacted. There may be exception situations where reporting of results may result in the ability to back-calculate confidential information exactly (when deterministic results are used). The burden of proof is on the sponsor to demonstrate how this can be done (to be included with the request for redaction).
References	Not redacted	Referencing is required to understand where inputs and assumptions are derived and does not predicate inputs that are considered confidential.
Budget Impact Analysis		
Description of design of the budget impact analysis	Not redacted	A description of the methods is required to understand the model.
Estimates for population size, market share, displacement of comparators, and resource assumptions that are based on published information	Not redacted	Information that is publicly available is not considered confidential information by CDA-AMC.
Estimates for population size, market share, displacement of comparators, and resource assumptions that are based on unpublished information from the following sources: • Expert opinion • Assumption that is not supported by evidence (e.g., where no reference is provided, or stated as data on file with no reference provided)	Not redacted	Methods of budget impact analyses are not considered confidential. They are required to understand what is being conducted and measured.

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

B. Handling Confidential Information

1. Responsibilities of CDA-AMC

CDA-AMC will use reasonable care to prevent the unauthorized use, disclosure, publication, or dissemination of information received by CDA-AMC as part of the reimbursement review processes that has been designated confidential.

CDA-AMC will not disclose confidential information in and related to an application to any third party except as permitted by the confidentiality guidelines, or as required by law or by order of a legally qualified court or tribunal.

CDA-AMC will use the confidential information solely for the purpose of carrying out its responsibilities with respect to the reimbursement review processes.

2. Responsibilities of Sponsors

Information identified as confidential information within an application is expected to be kept to a minimum. It is not acceptable to mark an entire section as confidential. Sponsors should make sure that such information has not already been disclosed in documents posted by other Health Technology Assessment agencies and/or regulatory authorities.

It is the responsibility of the sponsor to clearly identify (using highlighting) any information that it considers to be confidential, and to list the confidential information and clearly state the reason(s) for its confidentiality in a summary table provided by CDA-AMC.

Care should be taken when submitting information relating to individuals. Personal identifiers and sensitive information will be removed.

3. Release of Sponsor's Information

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

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

For drugs selected for joint engagement with clinical specialists by CDA-AMC and INESSS, CDA-AMC may release any sponsor-supplied information received through the reimbursement review processes, including confidential information, to INESSS expert committee members who are participating in meetings with the panel of clinical experts.

While CDA-AMC is an independent not-for-profit organization and is therefore not subject to access to information legislation, some of the authorized recipients listed previously have their own confidentiality procedures and are subject to freedom of information and access to information legislation over which CDA-AMC has no control.

CDA-AMC does not accept confidential submitted prices for applications filed for review through the reimbursement review processes. The submitted price is disclosed in all applicable CDA-AMC reports, as well as the recommendation documents posted on the CDA-AMC website. The outputs of economic models (e.g., incremental cost-effectiveness ratios) are not considered confidential and will not be redacted. Please

refer to Table 28 and Table 29 which provides sponsors with guidance regarding what information that has been included in an application will and will not be considered redactable by CDA-AMC (or Table 30 for applications received prior to January 2, 2024).

CDA-AMC staff members are required, as a condition of employment, to comply with CDA-AMC's confidentiality requirements, code of conduct, and conflict of interest policy. All the previously described authorized recipients (except for staff of federal, provincial, and territorial government representatives, including their agencies and departments; CAPCA; and pCPA) are required to sign a confidentiality agreement requiring them to comply with these confidentiality guidelines.

4. Documents Shared with Authorized Recipients

The documents that CDA-AMC may share with authorized recipients include, but are not limited to:

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

CDA-AMC provides the following documents to the sponsor (of which the sponsor must keep confidential until it is published on the CDA-AMC website):

- draft CDA-AMC review report(s)
- CDA-AMC's responses to the sponsor's comments about draft review report(s)
- the draft recommendation (until posted on the CDA-AMC website)
- the final recommendation (until posted on the CDA-AMC website).

The documents that CDA-AMC may post on its website include:

- a tracking document indicating the status of the review, including for a submission filed on a pre-NOC basis
- CDA-AMC review report(s) (with confidential information redacted, if specified)

- a draft recommendation (with confidential information redacted, if specified)
- a final recommendation (with confidential information redacted, if specified).

5. Referring to Confidential Information in Public CDA-AMC Documents

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

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

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

C. Archiving of Documents Containing Confidential Information

CDA-AMC may retain copies of all documents associated with the review of a drug for as long as there may be a need to consult them. CDA-AMC will determine at its sole discretion if there is a need to consult this information.

CDA-AMC staff undertake regular reviews of archived material. Any material that CDA-AMC determines to be no longer required will be disposed of. Any extra copies of documents at the completion of the review will be destroyed.

Appendix 2: Procedural Review

A. Purpose

The purpose of this section is to define the steps CDA-AMC will take to determine whether the established process outlined in the Procedures for Reimbursement Reviews was followed in the development of the final recommendation issued by a CDA-AMC expert committee for a pharmaceutical review. This section provides guidance for those who wish to make a request for a procedural review or who are considering doing so. A party that participated in the process relating to the final recommendation at issue may make a request for a procedural review; refer to paragraph C1 for further information on eligibility requirements.

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

B. About Procedural Reviews

The ground for a procedural review relates only to whether the process was followed and not to the content or scientific issue that may or may not be included in the final recommendation (i.e., did CDA-AMC fail to act in accordance with its procedures in conducting the review and issuing the final recommendation). Such examples may include omitting an eligible stakeholder input, deviating from the published steps without providing notice, failing to manage expert committee conflict of interest declaration in accordance with CDA-AMC's conflict of interest policy, or the expert committee exceeds the scope of its mandate.

A procedural review is not an opportunity to reopen issues that CDA-AMC's expert committee has decided on or to circumvent existing feedback mechanisms (e.g., request for reconsideration). This procedure also does not cover fairness in the colloquial sense; for instance, that it is "unfair" that a recommendation is issued to not reimburse a treatment. Unsubstantiated allegations of general unfairness, for example the alleged inability to understand a conclusion or the applicant simply disagrees with the views or conclusions in the final recommendation, will not be accepted as a valid ground for a procedural review.

This procedure is not intended to address concerns related to the methodology used in the development of a CDA-AMC process or in the interpretation and use of data during the review. For example, it would not be unfair if the expert committee considered the relevant dataset and reached a view with which the applicant did not agree.

In addition, disagreement with CDA-AMC's approach to managing confidential information that was provided in the filed application dossier, including use or non-use in the review process, does not constitute grounds for a procedural review, provided processes were followed as outlined in the confidentiality guidelines (Appendix 1).

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

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

To promote transparency, processes for the development of the main types of CDA-AMC recommendations issued by a CDA-AMC expert committee are published on the CDA-AMC website. Parties are strongly encouraged to discuss their concerns about perceived deviations from the procedure with the CDA-AMC Pharmaceutical Reviews Directorate prior to filing a request for a procedural review by contacting CDA-AMC at requests@cadth.ca.

C. Procedure

1. Eligible Parties – Who Can File?

The following parties are eligible to submit a formal request to CDA-AMC for a procedural review:

- a sponsor that filed the submission or resubmission for the review in question (applies to reimbursement reviews)
- a company whose review was assessed as part of a therapeutic category or a class review in question (applies to therapeutic reviews)
- a patient group that provided input in response to a call by CDA-AMC for patient input for the review in question
- a clinician group that provided input in response to a call by CDA-AMC for clinician input for the review in question
- Formulary Working Group or Provincial Advisory Group members that engaged in the drug review reimbursement process.

Multiple parties, if eligible, may submit a request for a procedural review of a final recommendation issued by a CDA-AMC expert committee for a specific review but each of these parties may submit only 1 request per final recommendation review at issue within the 20-business day period. In cases where a request may be made by more than 1 eligible party and they are accepted for the same final recommendation review at issue, CDA-AMC will conduct the requests jointly for the purpose of the procedural review proceeding.

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

A formal request to CDA-AMC may be made for a procedural review related to a final recommendation issued by a CDA-AMC expert committee for a specific review. A procedural review cannot be lodged against other documents produced during the process (for example, the draft recommendation or draft report).

Formal request for a procedural review must be made in writing using the designated procedural review request form and must be received within 20 business days of the final recommendation in question being posted on the CDA-AMC website.

The completed procedural review request form must include the full name of the party making the request, the contact information of the party filing the prescribed request form, the name of the CDA-AMC final recommendation in question, the involvement of the party with the final recommendation in question, and the details of the alleged deviation from procedure, including all supporting documents.

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

Formal request using the designated Procedural Review Request form must be submitted to requests@cadth.ca.

3. Receipt of Request(s) for Procedural Reviews

Upon receipt of the Procedural Review Request form, CDA-AMC will acknowledge receipt of the request.

4. Screening the Procedural Review Request Form

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

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

If these conditions are met, CDA-AMC will notify the applicant in writing if the request has been accepted within 15 business days from the date of receipt of the prescribed request form by CDA-AMC.

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

5. Case Conference

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

If a request is accepted, a notice indicating that a procedural review is in progress will be co-located with the file in question on the CDA-AMC website. Efforts will be made to complete this step within 7 business days from the date that the request is accepted.

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

6. Procedural Review Panel and Proceeding

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

A panel will comprise the following members selected by CDA-AMC:

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

The panel will aim to invite the applicant(s) to make a brief presentation within 30 business days of the conference date deadline, if an agreement cannot be reached during the conference period, to uncover as much information as possible about the alleged breach of process.

A maximum of 90 minutes will be allocated to present the issues that remain unresolved between the parties and to respond to questions from the panel. Where there are multiple eligible applicants, the maximum allowable time will not exceed 120 minutes and will be divided equally among the applicants in the joint proceeding meeting. Each requesting organization may bring up to 4 representatives knowledgeable about the issue at hand to the meeting. No legal representation is permitted at the meeting.

The meeting will be conducted via web/teleconference and will not be open to the public. The meeting will be recorded for internal use purposes. The panel may request additional information from the applicant and may also engage in additional internal fact-finding activities (e.g., interviews with the relevant director, other staff members, or other parties), as needed.

7. Making Decisions on Procedural Reviews and Targeted Timelines

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

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

A maximum of 1 procedural review per final recommendation will be undertaken (i.e., no additional procedural review requests may be filed against the same recommendation at issue).

8. Outcomes of Decision on Procedural Reviews

The panel may issue the following decision:

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

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

9. Communicating Decisions on Procedural Reviews and Posting on CDA-AMC Website

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

In cases where the panel finds that a deviation from process has occurred, the final recommendation at issue will be removed from the website and replaced with a notice indicating that additional work is underway and new targeted timelines due to the findings of the procedural review, until the matter can be appropriately remedied.

High-level details about the submitted procedural review request, including the name of the applicant(s), and the decision and reason for the decision, will be publicly posted on the CDA-AMC website.

Appendix 3: List of Templates

These templates are to be used whenever applicable (also available on CDA-AMC website).

Templates for Pre-submission Phase

- Pharmaceutical submission SharePoint access request form
- Submission eligibility form
- Resubmission eligibility form
- Pre-submission meeting request form
- Pre-submission meeting briefing paper template
- Advance notification form
- Proposed place in therapy template
- Tailored review application form
- Request for deviation from pharmacoeconomic requirements form

Templates for Requirements

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

Templates for Stakeholder Input

- Patient group input template
- Clinician group input template
- Drug program input template
- Industry input template (non-sponsored reimbursement reviews)
- Sponsor comments on draft reports template
- Stakeholder feedback on draft recommendation
- Reconsideration request template
- Identification of confidential information template
- Procedural review request template
- Stakeholder input on scope of a provisional funding algorithm
- Stakeholder feedback on a draft provisional funding algorithm
- Stakeholder input on implementation advice request
- Stakeholder feedback on draft implementation advice

Appendix 4: Suggested Reporting Format for Economics

Table 31: Disaggregated Clinical Outcomes and Costs for a Cost-Utility Analysis

Parameter	Drug under review	Comparator #1	Comparator #2 (add as required)
Discounted life-years			
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 or event			
Add others (as required)			

QALY = quality-adjusted life-years; LY = life-years.

Table 32: Presentation of Sequential Incremental Cost-Utility Ratio for a Cost-Utility Analysis

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

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

Table 33: Disaggregated Costs for a Cost-Minimization Analysis

Parameter	Drug under review	Comparator #1	Comparator #2 (add as required)
Discounted costs			
Total costs			
Drug			
Administration			
Other resource costs			
Health state or event			
Add others (as required)			

Appendix 5: Checklists for Preparing Applications

Sponsors may use the checklists provided in this appendix to help ensure that all required documents have been included in their application.

1. Clinical and Administrative Requirements
    - A. Submission for a standard review or complex review
    - B. Submission for a tailored review
    - C. Resubmission
    - D. Reassessment
2. Pharmacoeconomic requirements
3. Budget impact requirements

1A. Clinical and Administrative Requirements: Submission for a Standard or Complex Review

Requirement	Specific items and criteria	Included
General information		
Application overview	• Completed application overview template	☐
Signed cover letter	• Clear description of application being filed	☐
	• The indication(s) to be reviewed	☐
	• Requested reimbursement conditions, if applicable	☐
	• Names and contact information for primary and backup contacts	☐
Executive summary	• Completed executive summary template for a submission	☐
	• Maximum 5 pages for standard review or 6 pages for complex review (excluding references)	☐
	• Document is referenced	☐
Product monograph	**Submission filed on a pre-NOC basis:** • At the time of filing: A copy of the most recent draft product monograph • After NOC or NOC/c is issued: ▪ Draft product monograph with tracked changes up to time of Health Canada approval ▪ Clean and dated version of Health Canada–approved product monograph	☐ ☐ ☐
	Submission filed on a post-NOC basis: • A copy of the most current version of the Health Canada–approved product monograph	☐
Declaration letter	• Completed declaration letter template	☐
Regulatory and HTA Status	• At the time of filing: a completed template summarizing the status at selected regulatory and Health Technology Assessment agencies as a Microsoft Word document • At the time of fling comments on the draft reports: updated copy of the template as a Microsoft Word document	☐
Request for deviation	• Request for deviation response letter or statement that a deviation was not requested (applications received on or after November 1, 2023)	☐
Sponsor Clinical Evidence Template		
Submission template	• Complete sponsor summary of clinical evidence template	☐
RIS file with references	• RIS file with the references that have been cited in the sponsor summary of clinical evidence template	☐
Health Canada documentation		

Requirement	Specific items and criteria	Included
Notice of Compliance	**Submissions filed on a pre-NOC basis:** • At the time of filing: A placeholder document indicating the anticipated NOC date for the indications(s) to be reviewed • After NOC or NOC/c is issued: ▪ Copy of NOC or NOC/c granted for the indication(s) under review ▪ Letter of Undertaking (only if NOC/c granted)	☐ ☐ ☐
	Submission filed on a post-NOC basis: • Copy of NOC or NOC/c granted for the indication(s) under review • Letter of Undertaking (only if NOC/c granted)	☐ ☐
Clarimails/Clarifaxes	**Submissions filed on a pre-NOC basis:** • At time of filing: Summary table of clinical Clarimails/Clarifaxes up to time of filing • Ongoing basis until issuance of NOC or NOC/c: Revised Clarimail/Clarifax summary table(s)	☐ ☐
	Submission filed on a post-NOC basis: • Summary table of any clinical Clarimails/Clarifaxes up to issuance of NOC or NOC/c	☐
Efficacy, effectiveness, and safety Information		
Common technical document	• Section 2.5	☐
	• Section 2.7.1	☐
	• Section 2.7.3	☐
	• Section 2.7.4	☐
	• Section 5.2	☐
	• Or a statement indicating which section(s) were not required by Health Canada	☐
Clinical studies and errata	• Reference list of key clinical studies (published and unpublished) and any errata	☐
	• Copies of studies addressing key clinical issues • Copies of any errata (or a document stating that none found)	☐ ☐
Clinical study reports	• Clinical study reports for pivotal studies and other studies that address key clinical issues	☐
Table of studies	• Completed table of studies template (Microsoft Word or PDF document)	☐
Editorials	• Reference list of editorial articles (or document stating none found) • Copies of editorial articles	☐
New data	• Reference list of new data (or statement that none are available) • Copies of new data available	☐ ☐
Validity of outcome measures	• Reference list (or statement that none are available) • Copies of validity of outcome measure references available	☐ ☐
Indirect comparison	• Copies of any indirect comparisons used in pharmacoeconomic evaluation	☐

Requirement	Specific items and criteria	Included
	• Technical report	☐
Epidemiologic information		
Disease prevalence and incidence	• Disease prevalence and incidence with specified breakdown (if available)	☐
	• Document is referenced	☐
Number of patients accessing a new drug	• Number of patients accessing the new drug up to within 20 business days of filing the submission (Note: this requirement is only for a new drug submission or a new combination product submission if one of the components is a new drug.) • Use the number of patients accessing new drug template	☐
Reimbursement status of comparators		
Reimbursement status of comparators	• A completed template summarizing the reimbursement status of all appropriate comparators as a Microsoft Word document	☐
Pricing and distribution information		
Price and distribution method	• Submitted unit pricing to four decimal places	☐
	• Method of distribution	☐
Implementation plan	• Completed implementation plan template (only for cell and gene therapies)	☐
Provisional algorithm for oncology drugs		
Provisional algorithm (only for oncology drugs)	• Place in therapy template	☐
	• A reference list (or statement that none are available)	☐
	• Copies of studies that address sequencing of therapies	☐
	• Copy of the search strategy for sequencing of therapies	☐
Companion diagnostic (if applicable)		
Companion diagnostics	• Reference list	☐
	• Copies of articles that highlight the clinical utility of the companion diagnostic(s)	☐
	• Disclosable price for the companion diagnostic(s)	☐
Additional letter for submissions filed on Pre-NOC basis		
Letter for sending NOC or NOC/c	**After NOC or NOC/c is issued:** A signed letter indicating whether any wording changes to the Health Canada–approved final product monograph result in revisions to the clinical or pharmacoeconomic information filed on a pre-NOC basis (used the provided letter template)	☐

1B. Clinical and Administrative Requirements: Submission for a Tailored Review

Requirement	Specific items and criteria	Included
General information		
Application overview	• Completed application overview template	☐
Signed cover letter	• Clear description of application being filed	☐

Requirement	Specific items and criteria	Included
	• The indication(s) to be reviewed	☐
	• Requested reimbursement conditions, if applicable	☐
	• Names and contact information for primary and backup contacts	☐
Executive summary	• Completed executive summary template for a submission	☐
	• Maximum 5 pages (excluding references)	☐
	• Document is referenced	☐
Product monograph	**Submission filed on a pre-NOC basis:** • At the time of filing: A copy of the most recent draft product monograph • After NOC or NOC/c is issued: ▪ Draft product monograph with tracked changes up to Health Canada approval ▪ Clean and dated version of Health Canada–approved product monograph	☐
	Submission filed on a post-NOC basis: • A copy of the most current version of the Health Canada–approved product monograph	☐
Declaration letter	• Completed declaration letter template	☐
Regulatory and HTA Status	• At the time of filing: a completed template summarizing the status at selected regulatory and Health Technology Assessment agencies as a Microsoft Word document • At the time of fling comments on the draft reports: updated copy of the template as a Microsoft Word document	☐
Sponsor Clinical and Economic Summary Template		
Tailored review template	• Completed tailored review template	☐
Health Canada documentation		
NOC	**Submissions filed on a pre-NOC basis:** • At the time of filing: A placeholder document indicating the anticipated NOC date for the indications(s) to be reviewed • After NOC or NOC/c is issued: ▪ Copy of NOC or NOC/c granted for the indication(s) under review ▪ Letter of Undertaking (only if NOC/c granted)	☐ ☐ ☐
	Submission filed on a post-NOC basis: • Copy of NOC or NOC/c granted for the indication(s) under review • Letter of Undertaking (only if NOC/c granted)	☐ ☐
Clarimails and Clarifaxes	**Submissions filed on a pre-NOC basis:** • At time of filing: Summary table of clinical Clarimails/Clarifaxes up to time of filing • Ongoing basis until issuance of NOC or NOC/c: Revised Clarimail/Clarifax summary table(s)	☐ ☐
	Submission filed on a post-NOC basis: • Summary table of any clinical Clarimails/Clarifaxes up to issuance of NOC or NOC/c	☐

Requirement	Specific items and criteria	Included
Bioequivalence, efficacy, and safety evidence		
Common technical document	• Section 2.5	☐
	• Section 2.7.1	☐
	• Section 2.7.3	☐
	• Section 2.7.4	☐
	• Section 5.2	☐
	• Or a statement indicating which section(s) were not required by Health Canada	☐
Clinical studies and errata	• Reference list	☐
	• Additional source documentation for data reported in the tailored review template	☐
Clinical study reports	• Complete clinical study reports for all pivotal studies as well as other studies that address key clinical issues	☐
Table of studies	• Completed table of studies template (Microsoft Word or PDF document)	☐
Epidemiologic information		
Disease prevalence and incidence	• Disease prevalence and incidence with specified breakdown (if available)	☐
	• Document is referenced	☐
Number of patients accessing a new drug	• Number of patients accessing the new drug up to within 20 business days of filing the submission (Note: this requirement is only for a new drug submission or a new combination product submission if one of the components is a new drug.) • Use the number of patients accessing new drug template	☐ ☐
Reimbursement status of comparators		
Reimbursement status of comparators	• A completed template summarizing the reimbursement status of all appropriate comparators as a Microsoft Word document	☐
Pricing and distribution information		
Price and distribution Method	• Submitted unit pricing to four decimal places	☐
	• Method of distribution	☐
Additional letter for submissions filed on Pre-NOC basis		
Letter for sending NOC or NOC/c	**After NOC or NOC/c is issued:** • A signed letter indicating whether any wording changes to the Health Canada–approved final product monograph result in revisions to the clinical or pharmacoeconomic information filed on a pre-NOC basis (use the provided letter template)	☐

1C. Clinical and Administrative Requirements: Resubmission

Section	Specific Items and Criteria	Included
General information		
Application overview	• Completed application overview template	☐
Signed cover letter	• Clear description of application being filed	☐
	• The indication(s) to be reviewed	☐
	• Requested reimbursement conditions, if applicable	☐
	• Names and contact information for primary and backup contacts	☐
Executive summary	• Completed executive summary template for a resubmission	☐
	• Maximum 5 pages (excluding references)	☐
	• Document referenced with all supporting references	☐
Product monograph	• A copy of the most current version of the Health Canada–approved product monograph	☐
Declaration letter	• Completed declaration letter template	☐
Regulatory and HTA Status	• At the time of filing: a completed template summarizing the status at selected regulatory and Health Technology Assessment agencies as a Microsoft Word document • At the time of fling comments on the draft reports: updated copy of the template as a Microsoft Word document	☐
Request for deviation	• Request for deviation response letter or statement that a deviation was not requested (applications received on or after November 1, 2023)	☐
Sponsor Clinical Evidence Template		
Submission template	• Complete sponsor summary of clinical evidence template	☐
RIS file with references	• RIS file with the references that have been cited in the sponsor summary of clinical evidence template	☐
Efficacy, effectiveness, and safety information		
Common technical document	• Section 2.5	☐
	• Section 2.7.1	☐
	• Section 2.7.3	☐
	• Section 2.7.4	☐
	• Section 5.2	☐
	• Or a statement indicating any section(s) not required for the Health Canada submission	☐
Clinical studies and errata that were included in the initial submission	• Reference list of key clinical studies (published and unpublished) and any errata provided in the initial submission and any previous resubmissions	☐
	• Copies of studies addressing key clinical issues • Copies of any errata (or a document stating that none found)	☐
New clinical studies included in the resubmission	• Reference lists of all new clinical studies and errata (or a document stating none is available) included in the resubmission that were not provided in the initial submission, or a previous resubmission	☐

Section	Specific Items and Criteria	Included
	• Copies of all new clinical information and errata	☐
Clinical study reports	• Complete clinical study reports for all pivotal studies as well as other studies that address key clinical issues	☐
Editorials	• Reference list of editorial articles (or document stating none found)	☐
	• Copies of editorial articles	☐
Validity of outcome measures	• Reference list for validity of outcome measures (or document stating none found)	☐
	• Copies of validity of outcome measure references available	☐
Table of studies	• An updated tabulated list of all published and unpublished clinical studies using the provided table of studies template (Microsoft Word or PDF document)	☐
Indirect comparison	• Copies of any indirect comparisons used in the pharmacoeconomic evaluation	☐
	• Indirect comparison technical report	☐
Epidemiologic information		
Disease prevalence and incidence	• Disease prevalence and incidence data, with specified breakdown (if available)	☐
	• Document is referenced	☐
Reimbursement status of comparators		
Reimbursement status of comparators	• A completed template summarizing the reimbursement status of all appropriate comparators as a Microsoft Word document	☐
Pricing and distribution information		
Price and distribution method	• Submitted unit pricing to 4four decimal places	☐
	• Method of distribution	☐
Provisional algorithm for oncology drugs		
Provisional algorithm (only for oncology drugs)	• Place in therapy template	☐
	• A reference list (or statement that none are available)	☐
	• Copies of studies that address sequencing of therapies	☐
	• Copy of the search strategy for sequencing of therapies	☐
Companion diagnostic(s)		
Companion diagnostics	• Reference list and copies of articles that highlight the clinical utility of the companion diagnostic(s)	☐
	• Disclosable price for the companion diagnostic(s)	☐

1D. Clinical and Administrative Requirements: Reassessment

Section	Specific items and criteria	Included
General information		
Application overview	• Completed application overview template	☐
Signed cover letter	• Clear description of application being filed	☐
	• The indication(s) to be reviewed	☐
	• Requested reimbursement conditions, if applicable	☐
	• Names and contact information for primary and backup contacts	☐
Executive summary	• Completed executive summary template for a resubmission	☐
	• Maximum 5 pages (excluding references)	☐
	• Document referenced with all supporting references	☐
Product monograph	• A copy of the most current version of the Health Canada–approved product monograph	☐
Declaration letter	• Completed declaration letter template	☐
Regulatory and HTA Status	• At the time of filing: a completed template summarizing the status at selected regulatory and Health Technology Assessment agencies as a Microsoft Word document • At the time of fling comments on the draft reports: updated copy of the template as a Microsoft Word document	☐
Request for deviation	• Request for deviation response letter or statement that a deviation was not requested (applications received on or after November 1, 2023)	☐
Sponsor Clinical Summary Template		
Submission template	• Complete sponsor summary of clinical evidence template	☐
RIS file with references	• RIS file with the references that have been cited in the sponsor summary of clinical evidence template	☐
Efficacy, effectiveness, and safety Information		
New clinical studies	• Reference lists of all new clinical studies and errata (or a document stating none is available) included in the reassessment	☐
	• Copies of all new clinical information and errata	☐
Clinical study reports	• Complete clinical study reports for all new studies included in the reassessment	☐
Editorials	• Reference list of editorial articles (or document stating none found)	☐
	• Copies of editorial articles	☐
Validity of outcome measures	• Reference list for validity of outcome measures (or document stating none found)	☐
	• Copies of validity of outcome measure references available	☐
Table of studies	• An updated tabulated list of all published and unpublished clinical studies using the provided table of studies template (Microsoft Word or PDF document)	☐
Indirect comparison	• Copies of any indirect comparisons used in the pharmacoeconomic evaluation	☐
	• Indirect comparison technical report	☐

Section	Specific items and criteria	Included
Epidemiologic information		
Disease prevalence and incidence	• Disease prevalence and incidence data, with specified breakdown (if available)	☐
	• Document is referenced	☐
Reimbursement status of comparators		
Reimbursement status of comparators	• A completed template summarizing the reimbursement status of all appropriate comparators as a Microsoft Word document	☐
Pricing and distribution information		
Price and distribution method	• Submitted unit pricing to 4 decimal places	☐
	• Method of distribution	☐
Provisional algorithm for oncology drugs		
Provisional algorithm (only for oncology drugs)	• Place in therapy template	☐
	• A reference list (or statement that none are available)	☐
	• Copies of studies that address sequencing of therapies	☐
	• Copy of the search strategy for sequencing of therapies	☐
Companion diagnostic(s)		
Companion diagnostics	• Reference list and copies of articles that highlight the clinical utility of the companion diagnostic(s)	☐
	• Disclosable price for the companion diagnostic(s)	☐

2. Pharmacoeconomic Requirements

Requirement	Specific items and criteria	Included
Checklist of economic requirements		
Checklist	Completed checklist of economic requirements	☐
Cost-Utility Analysis		
Pharmacoeconomic evaluation: technical report	**Submission or Resubmission:** • Pharmacoeconomic evaluation reflects the full population identified in the Health Canada indication(s) to be reviewed • Scenario analysis of the population identified in the reimbursement request (if different from the population in the full indication) • Other relevant scenario analyses presented **Reassessments:** • Pharmacoeconomic evaluation reflects the scope of the reassessment: ▪ Population covered under the proposed revised reimbursement criteria ▪ Population covered under the current reimbursement criteria ▪ Relevant scenario analyses	☐ ☐ ☐ ☐ ☐ ☐
	• All relevant comparators have been included	☐
	• Rationale provided if potentially relevant comparators excluded	☐

	• Base case reflects the public health care payer perspective	☐
	• 1.5% discount rate on costs and QALYs	☐
	• Treatment effect measures are based on composite end points	☐
	• Submitted price per smallest dispensable unit used	☐
	• All submitted forms and strengths included	☐
	• Base case is presented probabilistically	☐
	• Base-case results are presented deterministically	☐
	• All ICERs reported sequentially if more than one comparator is presented	☐
	• Results are presented in disaggregated format	☐
	• QALYs, life-years and costs are reported	☐
	• If relevant, companion diagnostic test information incorporated	☐
	• Alignment between the pharmacoeconomic evaluation technical report and the economic model	☐
Economic model	• Model is programmed in Excel	☐
	• Model is fully unlocked and executable, and all code is provided	☐
	• Model functions in a stand-alone environment and does not require access to a web-based platform	☐
	• Probabilistic analyses run without error	☐
	• CDA-AMC can easily vary any individual input and view calculation	☐
	• Results of the probabilistic analysis are stable (congruence test provided)	☐
	• If used, seeding must be easily disabled or modifiable	☐
	• The model runs treatments simultaneously and results of all comparators are presented	☐
	• If relevant, flexible to assess all parametric distributions tested by the sponsor; present graphically the Kaplan-Meier and parametric curves to allow visual inspection of fit concurrently, within one graph	☐
	• Markov or event-time trace is provided via formulas within the Excel worksheets	☐
	• Model run time is no more than 1 business day (8 hours)	☐
	• Does not require CDA-AMC to agree to terms and conditions or have a legal disclaimer	☐
Cost-Minimization Analysis		
Pharmacoeconomic evaluation: technical report	• Drug is a new treatment in an existing therapeutic class in which there are treatments already reimbursed	☐
	• Drug under review demonstrates similar clinical effects compared with the most appropriate comparator(s)	☐
	Submission or Resubmission:	☐

	• Pharmacoeconomic evaluation reflects the full population identified in the indication(s) to be reviewed • Scenario analysis of the population identified in the reimbursement request (if different from the population in the full indication) **Reassessments:** • Pharmacoeconomic evaluation reflects the scope of the reassessment: ▪ Population covered under the proposed revised reimbursement criteria ▪ Population covered under the current reimbursement criteria	☐ ☐ ☐
	• All relevant comparators have been included	☐
	• Rationale provided if potentially relevant comparators excluded	☐
	• Base case reflects the public health care payer perspective	☐
	• 1.5% discount rate on costs if time horizon greater than 1 year	☐
	• Submitted price per smallest dispensable unit used	☐
	• All submitted forms and strengths included	☐
	• All results are presented probabilistically unless rationale for absence of parameter uncertainty	☐
	• Results are presented in disaggregated format	☐
	• Alignment between the pharmacoeconomic evaluation technical report and the economic model	☐
Cost calculations	• Excel workbook provided	☐
	• Workbook is fully unlocked and all calculations provided	☐
	• Model functions in a stand-alone environment, does not require access to a web-based platform, and all code is provided.	☐
	• CDA-AMC can easily vary any individual input and trace inputs through the workbook	☐
	• If probabilistic, analyses run simultaneously for all comparators without error, and results are stable over multiple runs	☐
	• Model run time is no more than 1 business day (8 hours)	☐
	• Does not require CDA-AMC to agree to terms and conditions or have a legal disclaimer	☐
Supporting documentation for the Pharmacoeconomic Evaluation		
Supporting documentation	• Economic model user guide	☐
	• Unpublished studies or analyses used to inform the pharmacoeconomic evaluation, including technical report(s) of the indirect comparison(s), utility studies, etc., provided within 1 folder. Reference numbering aligns with the pharmacoeconomic evaluation report.	☐
	• All other supporting documentation (i.e., references) used and/or cited in the pharmacoeconomic evaluation provided within one folder. Reference numbering aligns with the pharmacoeconomic evaluation report.	☐

	• Document summarizing key sources of information for the companion diagnostic test	☐
	• RIS file with economic references	☐

3. Budget Impact Analysis Requirements

Requirement	Specific items and criteria	Included
Budget impact analysis		
Budget impact analysis: technical report	• Base case reflects pan-Canadian (national) drug program perspective (excluding Quebec)	☐
	• For PPRP reviews, an analysis from the Canadian Blood Services perspective is provided.	☐
	• For cell and gene therapies, products administered partially or solely in hospital, or infusion therapies, a scenario that considers the Canadian health system perspective has been provided	☐
	• Population(s) assessed in the base case and scenarios align with the economic evaluation	☐
	• Base-case analysis uses a 1-year baseline period and 3-year forecast period	☐
	• All relevant comparators included (aligns with the economic evaluation)	☐
	• Submitted price per smallest dispensable unit used	☐
	• All submitted forms and strengths are included	☐
	• Results presented deterministically	☐
	• Results presented for each specified jurisdiction before being aggregated to pan-Canadian results	☐
	• Report includes at minimum decision problem, methods, assumptions and results	☐
	• Alignment between the technical report and the model	☐
Budget impact model	• Model is programmed in Excel	☐
	• Model is fully unlocked and executable, and all code is provided.	☐
	• Model functions in a stand-alone environment and does not require access to a web-based platform	☐
	• CDA-AMC must be able to vary individual parameters, view the calculations, and run the model to generate results	☐
	• Model is flexible and allows assessment of each specified individual drug program	☐
	• Input values specific to the individual drug program	☐
	• Breakdown of costs by perspective reported within the submitted model	☐
	• Does not require CDA-AMC to agree to terms and conditions or have a legal disclaimer	☐
Supporting documentation for the Budget Impact Analysis		
Supporting documentation	• Unpublished studies or analyses used to inform the BIA provided within one folder. Reference numbering aligns with the BIA report.	☐

Requirement	Specific items and criteria	Included
	• All other supporting documentation (i.e., references) used and/or cited in the BIA provided within one folder. Reference numbering aligns with the BIA report.	☐
	• RIS file with economic references	☐

Appendix 6: File Structure and Naming Format

Instructions for Sponsors

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

Filing Requirements

All materials must be submitted using the Pharmaceutical Submissions SharePoint site. Sponsors should review the Pharmaceutical Submissions SharePoint Site – Setup Guide for full instructions on how to setup a project folder for their submission and gain access to the site.

Sponsors must complete the steps outlined in the guide to request access to the site a minimum of **10 business days prior** to their submission of any document to CDA-AMC (this is typically the Pre-Submission Meeting Request Form or the Advanced Notification Form [if not requesting a pre-submission meeting]). ***In the event the sponsor has not requested or received access prior to their target date for providing advance notification of the pending application, please contact requests@cadth.ca immediately. CDA-AMC will work with the sponsor to ensure that the application is not delayed due to the time frame for setting up the platform to securely receive the required documents.***

Files should be submitted as zipped (.zip) files. If there are several .zip files, the number of files should be noted in the file name (e.g., 1of4). The root folder(s) should be clearly named with the brand or generic drug name.

An email notification will be sent to the sponsor when the file has been submitted successfully.

The entire decoded file path, including the file name, cannot contain more than 400 characters. The limit applies to the combination of the folder path and file name after decoding.

Documents must be provided in PDF or Microsoft Word format, unless otherwise indicated in the requirement descriptions. These files must be unlocked, searchable, and printable. Document users must be able to extract information or combine documents.

Documents must be organized and labelled according to the file structure and naming format provided in this appendix.

If any extra supporting documents that do not have a designated folder are being submitted at the sponsor's discretion (e.g., clinical study reports), these should be appropriately named and filed in a logical location in the file structure.

Providing Additional Information During the Review

If CDA-AMC requests additional information during the review, sponsors must provide the requested information using the Pharmaceutical Submissions SharePoint site in the "4. Additional Information" folder.

Files should be submitted as zipped (.zip) files. The documents within the .zip file must be provided in PDF or Microsoft Word format. These files must be unlocked, searchable, and printable. Document users must be able to extract information or combine documents.

Submission Requirements for a Standard Review

 Represents 1 folder

- Represents 1 file (unlocked, searchable, and printable)

 **Brand Name**

 **1_Brand Name_General Information**

- 1 - Application Overview
- 2 - Signed Cover Letter
- 3 - Executive Summary
- 4 - Product Monograph
- 5 - Declaration letter
- 6 - Regulatory-HTA Status
- 7 - Request for Deviation (applications received on or after November 1, 2023)

 **2_Brand Name_Sponsor Clinical Evidence**

- 1 - Brand Name Clinical Evidence
- 2 - Brand Name References (Note: this must a RIS file)

 **3_Brand Name_Health Canada Documentation**

- 1 - Health Canada NOC
- 2 - Letter of Undertaking (Note: only if applicable)
- 3 - Table of Clarimails

 **4_Brand Name_Clinical Information**

 4.1_Common Technical Document

- 1 - Section 2.5
- 2 - Section 2.7.1
- 3 - Section 2.7.3
- 4 - Section 2.7.4
- 5 - Section 5.2

 4.2_Clinical Studies and Errata

- _List of Studies and Errata
- 1 - Trial Name_Author_Year
- 2 - Trial Name_Author_Year Erratum

4.3_Clinical Study Reports

- 1 - Trial Name
- 2 - Trial Name

4.4_Table of Studies

- Table of Studies

4.5_Editorials

- _List of Editorials
- 1 - Author_Year

4.6_New Data

- _List of New Data
- 1 - Trial Name_Author_Year

4.7_Validity of Outcomes

- _List of References
- 1 - Author_Year

4.8_Indirect Comparison

- Indirect Comparison
- Technical report

5_Brand Name_Epidemiologic Information

- Disease Prevalence and Incidence
- Number Patients Accessing New Drug (Note: only if applicable)

6_Brand Name_Comparator Status

- Comparator Reimbursement Status

7_Brand Name_Economic

- Pharmacoeconomic evaluation
- Economic model
- Checklist for economic requirements
- RIS file with economic references
- Supporting documentation

- Published
- Unpublished

8_Brand Name_BIA

8.1_BIA Report

- pan-Canadian BIA Report

8.2_BIA Model

- pan-Canadian BIA Model

8.3_BIA Supporting Documentation

- Published
- Unpublished

9_Brand Name_Pricing and Distribution

- Pricing and Distribution

10_Brand Name_Provisional Algorithm

- Brand Name_Place In Therapy
- Brand Name_List of References
- 1 - Author_Year

11_Brand Name_Companion Diagnostic

11.1_Clinical Utility

- _List of References
- 1 – Author_Year

11.2_Price

- Companion Diagnostic Price

Submission Requirements for a Complex Review

Represents 1 folder

- Represents 1 file (unlocked, searchable, and printable)

Brand Name

1_Brand Name_General Information

- 1 - Application Overview
- 2 - Signed Cover Letter
- 3 - Executive Summary
- 4 - Product Monograph
- 5 - Declaration letter
- 6 - Regulatory-HTA Status
- 7 - Request for Deviation (applications received on or after November 1, 2023)

2_Brand Name_Sponsor Clinical Evidence

- 1 - Brand Name Clinical Evidence
- 2 - Brand Name References (Note: this must a RIS file)

3_Brand Name_Health Canada Documentation

- 1 - Health Canada NOC
- 2 - Letter of Undertaking (Note: only if applicable)
- 3 - Table of Clarimails

4_Brand Name_Clinical Information

4.1_Common Technical Document

- 1 - Section 2.5
- 2 - Section 2.7.1
- 3 - Section 2.7.3
- 4 - Section 2.7.4
- 5 - Section 5.2

4.2_Clinical Studies and Errata

- _List of Studies and Errata
- 1 - Trial Name_Author_Year
- 2 - Trial Name_Author_Year Erratum

4.3_Clinical Study Reports

- 1 - Trial Name

- 2 - Trial Name

4.4_Table of Studies
- Table of Studies

4.5_Editorials
- _List of Editorials
- 1 - Author_Year

4.6_New Data
- _List of New Data
- 1 - Trial Name_Author_Year

4.7_Validity of Outcomes
- _List of References
- 1 - Author_Year

4.8_Indirect Comparison
- Indirect Comparison
- Technical report

5_Brand Name_Epidemiologic Information
- Disease Prevalence and Incidence
- Number Patients Accessing New Drug (Note: only if applicable)

6_Brand Name_Comparator Status
- Comparator Reimbursement Status

7_Brand Name_Economic
- Pharmacoeconomic evaluation
- Economic model
- Checklist for economic requirements
- RIS file with economic references
- Supporting documentation
  - Published
  - Unpublished

8_Brand Name_BIA

8.1_BIA Report
- pan-Canadian BIA Report

- 8.2_BIA Model
  - pan-Canadian BIA Model
- 8.3_BIA Supporting Documentation
  - Published
  - Unpublished

9_Brand Name_Pricing and Distribution

- Pricing and Distribution

10_Brand Name_Implementation Plan *(for cell and therapies only)*

- Implementation Plan

11_Brand Name_Provisional Algorithm *(for oncology drugs only)*

- Brand Name_Place In Therapy
- Brand Name_List of References
- 1 - Author_Year

12_Companion Diagnostic

- 12.1_Clinical Utility
  - _List of References
  - 1 - Author_Year
- 12.2_Price
  - Companion Diagnostic Price

Submission Requirements for a Plasma Protein and Related Product Review

Represents 1 folder

- Represents 1 file (unlocked, searchable, and printable)

Brand Name

1_Brand Name_General Information

- 1 - Application Overview
- 2 - Signed Cover Letter
- 3 - Executive Summary
- 4 - Product Monograph
- 5 - Declaration letter
- 6 - Regulatory-HTA Status
- 7 - Request for Deviation (applications received on or after November 1, 2023)

2_Brand Name_Sponsor Clinical Evidence

- 1 - Brand Name Clinical Evidence
- 2 - Brand Name References (Note: this must a RIS file)

3_Brand Name_Health Canada Documentation

- 1 - Health Canada NOC
- 2 - Letter of Undertaking (Note: only if applicable)
- 3 - Table of Clarimails

4_Brand Name_Clinical Information

4.1_Common Technical Document

- 1 - Section 2.5
- 2 - Section 2.7.1
- 3 - Section 2.7.3
- 4 - Section 2.7.4
- 5 - Section 5.2

4.2_Clinical Studies and Errata

- _List of Studies and Errata
- 1 - Trial Name_Author_Year
- 2 - Trial Name_Author_Year Erratum

4.3_Clinical Study Reports

- 1 - Trial Name

- 2 - Trial Name

4.4_Table of Studies
- Table of Studies

4.5_Editorials
- _List of Editorials
- 1 - Author_Year

4.6_New Data
- _List of New Data
- 1 - Trial Name_Author_Year

4.7_Validity of Outcomes
- _List of References
- 1 - Author_Year

4.8_Indirect Comparison
- Indirect Comparison
- Technical report

5_Brand Name_Epidemiologic Information
- Disease Prevalence and Incidence
- Number Patients Accessing New Drug (Note: only if applicable)

6_Brand Name_Comparator Status
- Comparator Reimbursement Status

7_Brand Name_Economic
- Pharmacoeconomic evaluation
- Economic model
- Checklist for economic requirements
- RIS file with economic references
- Supporting documentation
  - Published
  - Unpublished

8_Brand Name_BIA

8.1_BIA Report
- pan-Canadian BIA Report

- 8.2_BIA Model
  - pan-Canadian BIA Model
- 8.3_BIA Supporting Documentation
  - Published
  - Unpublished

9_Brand Name_Pricing and Distribution

- Pricing and Distribution

10_Companion Diagnostic

- 10.1_Clinical Utility
  - _List of References
  - 1 - Author_Year
- 10.2_Price
  - Companion Diagnostic Price

Submission Requirements for a Tailored Review

Represents 1 folder

- Represents 1 file (unlocked, searchable, and printable)

Brand Name

1_Brand Name_General Information

- 1 - Application Overview
- 2 - Signed Cover Letter
- 3 - Executive Summary
- 4 - Product Monograph
- 5 - Declaration Letter
- 6 - Regulatory-HTA Status

2_Brand Name_Health Canada Documentation

- 1 - Health Canada NOC
- 2 - Letter of Undertaking (Note: only if applicable; adjust following file numbers if necessary)
- 3 - Table of Clarimails

3_Brand Name_Submission Template

- 1 – Tailored Review Submission Template

4_Brand Name_Clinical Information

4.1_Common Technical Document

- 1 - Section 2.5
- 2 - Section 2.7.1
- 3 - Section 2.7.3
- 4 - Section 2.7.4
- 5 - Section 5.2

4.2_Source Documentation

- _List of Documentation
- 1 - Name_Year
- 2 - Name_Year

4.3_Clinical Study Reports

- 1 - Trial Name
- 2 - Trial Name

- 4.4_Table of Studies
  - Table of Studies

5_Brand Name_Epidemiologic Information

- Disease Prevalence and Incidence

6_Brand Name_Comparator Status

- Comparator Reimbursement Status

7_Brand Name_Pricing and Distribution

- Pricing and Distribution

8_Brand Name_BIA

- 8.1_BIA Report
  - pan-Canadian BIA Report
- 8.2_BIA Model
  - pan-Canadian BIA Model
- 8.3_BIA Supporting Documentation
  - Published
  - Unpublished

9_Companion Diagnostic

- 9.1_Clinical Utility
  - _List of References
  - 1 - Author_Year
- 9.2_Price
  - Companion Diagnostic Price

Resubmission Requirements

Represents 1 folder

- Represents 1 file (unlocked, searchable, and printable)

Brand Name

1_Brand Name_General Information

- 1 - Application Overview
- 2 - Signed Cover Letter
- 3 - Executive Summary
- 4 - Product Monograph
- 5 - Declaration letter
- 6 - Regulatory-HTA Status
- 7 - Request for Deviation (applications received on or after November 1, 2023)

2_Brand Name_Sponsor Clinical Evidence

- 1 - Brand Name Clinical Evidence
- 2 - Brand Name References (Note: this must a RIS file)

3_Brand Name_Clinical Information

3.1_Common Technical Document

- 1 - Section 2.5
- 2 - Section 2.7.1
- 3 - Section 2.7.3
- 4 - Section 2.7.4
- 5 - Section 5.2

3.2_Clinical Studies and Errata

- _List of Studies and Errata
- 1 - Trial Name_Author_Year
- 2 - Trial Name_Author_Year Erratum

3.3_New Clinical Studies

- _List of New Clinical Studies
- 1 - Trial Name_Author_Year
- 2 - Trial Name_Author_Year

3.4_Clinical Study Reports

- 1 - Trial Name
- 2 - Trial Name

3.5_ New Editorials and Errata

- _List of Editorials and Errata
- _No Editorials or No Errata (*Note: placeholder document, only if applicable)*

- 1 - Author_Year_Editorial
- 2 - Trial Name_Author_Year_Erratum

3.6_Validity of Outcomes
- List of References
- 1 - Author_Year

3.7_Updated Table of Studies
- Table of Studies

3.8_Indirect Comparison
- Indirect Comparison
- Technical report

4_Brand Name_Epidemiologic Information
- Disease Prevalence and Incidence

5_Brand Name_Comparator Status
- Comparator Reimbursement Status

6_Brand Name_Economic
- Pharmacoeconomic evaluation
- Economic model
- Checklist for economic requirements
- RIS file with economic references

Supporting documentation
- Published
- Unpublished

7_Brand Name_BIA

7.1_BIA Report
- pan-Canadian BIA Report

7.2_BIA Model
- pan-Canadian BIA Model

7.3_BIA Supporting Documentation
- Published
- Unpublished

8_Brand Name_Pricing and Distribution
- Pricing and Distribution

9_Brand Name_Provisional Algorithm
- Brand Name_Place In Therapy

- Brand Name_List of References
- 1 - Author_Year

10_Companion Diagnostic

10.1_Clinical Utility

- _List of References
- 1 - Author_Year

10.2_Price

- Companion Diagnostic Price

Standard Reassessment Requirements

Represents 1 folder

- Represents 1 file (unlocked, searchable, and printable)

Brand Name

1_Brand Name_General Information

- 1 - Application Overview
- 2 - Signed Cover Letter
- 3 - Executive Summary
- 4 - Product Monograph
- 5 - Declaration letter
- 6 - Regulatory-HTA Status
- 7 - Request for Deviation (applications received on or after November 1, 2023)

2_Brand Name_Sponsor Clinical Evidence

- 1 - Brand Name Clinical Evidence
- 2 - Brand Name References (Note: this must a RIS file)

3_Brand Name_Clinical Information

3.1_Clinical Studies and Errata

- _List of Clinical Studies and Errata
- 1 - Trial Name_Author_Year
- 2 - Trial Name_Author_Year

3.2_Clinical Study Reports

- 1 - Trial Name
- 2 - Trial Name

3.3_Editorials

- _List of Editorials
- _No Editorials (*Note: placeholder document, only if applicable)*
- 1 - Author_Year

3.4_Validity of Outcomes

- List of References
- 1 - Author_Year

3.5_Updated Table of Studies

- Table of Studies

3.6_Indirect Comparison

- Indirect Comparison
- Technical report

- **4_Brand Name_Epidemiologic Information**
  - Disease Prevalence and Incidence
- **5_Brand Name_Comparator Status**
  - Comparator Reimbursement Status
- **6_Brand Name_Economic**
  - Pharmacoeconomic evaluation
  - Economic model
  - Checklist for economic requirements
  - RIS file with economic references
  - Supporting documentation
    - Published
    - Unpublished
- **7_Brand Name_BIA**
  - 7.1_BIA Report
    - pan-Canadian BIA Report
  - 7.2_BIA Model
    - pan-Canadian BIA Model
  - 7.3_BIA Supporting Documentation
    - Published
    - Unpublished
- **8_Brand Name_Pricing and Distribution**
  - Pricing and Distribution
- **9_Brand Name_Provisional Algorithm**
  - Brand Name_Place In Therapy
  - Brand Name_List of References
  - 1 - Author_Year
- **10_Companion Diagnostic**
  - 10.1_Clinical Utility
    - _List of References
    - 1 - Author_Year
  - 10.2_Price
    - Companion Diagnostic Price

Appendix 7: Key Definitions

The following are high-level definitions for key terms used in this document. Readers should consult the appropriate sections of the document for more detailed context as it relates to some terms.

Active substance: A therapeutic substance that has pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease (refer to new active substance).

Additional information: Additional information includes any information that is additional to the documents that are required for an application to be accepted for review. This information is requested from the sponsor to complete the review or to clarify information.

Application: Written documentation filed by a sponsor to have a drug reviewed through the reimbursement review process.

Appropriate comparator: Typically, a drug listed by one or more drug programs for the indication under review. However, the choice of appropriate comparator(s) in reviews is made on a case-by-case basis.

Biosimilar: A biosimilar is a biologic drug (i.e., a drug derived from living sources versus a chemically synthesized drug) that demonstrates a high degree of similarity to an already authorized biologic drug (i.e., a "reference product" that has been authorized in Canada, or in some circumstances can be an authorized non-Canadian biologic from a jurisdiction that has an established relationship with Health Canada).

Business day: Any day (other than a Saturday, Sunday, statutory holiday, or company holiday) on which the CDA-AMC office in Ottawa (Ontario, Canada) is open for business during regular business hours. Please refer to the Holiday Schedule.

Business hours: Any weekday (excluding statutory and company holidays) from 8:00 a.m. to 4:00 p.m. Eastern time.

Review team: A team assembled to undertake a reimbursement review. The review team may include CDA-AMC staff, contracted reviewers, and external experts with appropriate qualifications and expertise.

Cancelled review: The cessation of the review before all steps of the review process are completed.

Committee brief: A compilation of the materials regarding a drug under review, prepared by CDA-AMC staff for the members of the expert committee.

Companion diagnostic test: A medical device that provides information that is essential for the safe and effective use of corresponding drugs or biological products. They can identify patients who are likely to benefit or experience harms from particular therapeutic products or monitor clinical response to optimally guide treatment adjustments. Companion diagnostics detect specific biomarkers that predict more favourable responses to particular therapeutic products.

Date of acceptance for review: The date on which CDA-AMC has confirmed with the sponsor that the key requirements for initiating the review process have been met.

Date of filing: The date on which an application is received.

Date of initiation: The date on which the assigned CDA-AMC review team begins work on a review.

Drug: An active substance considered to be a drug under the Canadian Food and Drugs Act and Food and Drug Regulations that has been granted by Health Canada (or will be granted in the case of a submission filed on a pre-Notice of Compliance basis) a Notice of Compliance or Notice of Compliance with conditions and is approved for human use.

Drug programs: The federal, provincial, and territorial drug programs participating in the CDA-AMC Reimbursement Review processes.

Final recommendation: A document that provides guidance to the drug programs participating in the reimbursement review processes to make a reimbursement decision for the drug under review. Final recommendations are non-binding to the drug programs.

Formulary Working Group: A working group of the Pharmaceutical Advisory Committee. Formulary Working Group provides advice to CDA-AMC on pharmaceutical issues and helps with the effective jurisdictional sharing of pharmaceutical information.

Generic drugs: Copies of Canadian reference products (i.e., Health Canada–approved brand name drugs) that demonstrate bioequivalence on the basis of pharmaceutical equivalence (i.e., they contain identical amounts of the identical active medicinal ingredients as the reference product, in comparable dosage forms, but do not necessarily contain the same non-medicinal ingredients as the Canadian reference product, and the conditions of use fall with those of the Canadian reference product) and bioavailability characteristics, where applicable, with the Canadian reference product. Generic drugs are not typically reviewed through the reimbursement review processes.

New active substance: A therapeutic substance that has never been approved for marketing in Canada in any form. It may be:

- a chemical or biological substance not previously approved for sale in Canada as a drug
- an isomer, derivative, or salt of a chemical substance previously approved for sale as a drug in Canada but differing in properties regarding safety and efficacy.

New combination product: Consists of 2 or more drugs that have not been previously marketed in Canada in that combination. It may consist of either 2 or more new drugs, 2 or more previously marketed drugs, or a combination of new drug(s) and previously marketed drug(s).

New drug: A therapeutic substance that has never been approved for marketing in any form, regardless of when the Notice of Compliance or Notice of Compliance with conditions was issued. It may be: a chemical

or biological substance not previously approved for sale in Canada as a drug; or an isomer, derivative, or salt of a chemical substance previously approved for sale as a drug in Canada but differing in properties regarding safety and efficacy.

New indication: A disease condition for which the use of a particular drug has not previously been approved by Health Canada.

New information: New clinical information and/or new cost information that was not part of an originally filed application.

Notice of Compliance: Authorization issued by Health Canada to market a drug in Canada when regulatory requirements for the safety, efficacy, and quality are met.

Notice of Compliance with conditions: Authorization issued by Health Canada to market a drug under the Notice of Compliance with conditions policy. This indicates that the sponsor has agreed to undertake additional studies to confirm the clinical benefit of the product.

Patient group: An organized group of patients or caregivers in Canada.

Post-Notice of Compliance: The timing of filing a submission after Health Canada has granted a Notice of Compliance or Notice of Compliance with conditions for the indication(s) to be reviewed.

Pre-Notice of Compliance: The timing of filing a submission before Health Canada has granted a Notice of Compliance or Notice of Compliance with conditions for the indication(s) to be reviewed, and for which the anticipated date of Notice of Compliance or Notice of Compliance with conditions is within 180 calendar days of the submission being filed.

Provincial Advisory Group: A working group of the Pharmaceutical Advisory Committee. The Provincial Advisory Group provides advice to CDA-AMC on pharmaceutical issues and helps with the effective jurisdictional sharing of pharmaceutical information.

Queuing: A delay in the initiation of a review.

Reasons for recommendation: These represent the key considerations and rationale used by the expert committee in formulating the recommendation.

Request for reconsideration: A written request from a sponsor or the drug programs for a draft recommendation to be reconsidered by the expert committee.

Sponsor: A person, corporation, or entity eligible to file an application for a reimbursement review. The sponsor could be a manufacturer, a supplier, a corporation, or entity recruited by the manufacturer or the supplier.

Submitted price: The submitted price is the price per smallest dispensable unit that is submitted to CDA-AMC and that must not be exceeded for any of the drug programs following completion of the review. The submitted price will be disclosed in all applicable CDA-AMC reports.

Suspended review: The temporary cessation of a reimbursement review. This occurs if questions or issues arise outside of the regular review process or if the review team is unable to perform a thorough assessment of the application due to incomplete or non-transparent information. Once the issue is resolved, the review proceeds from the point at which it was suspended.

Therapeutic review: An evidence-based review of publicly available sources regarding a therapeutic category of drugs (e.g., antihypertensive drugs) or a class of drugs (e.g., angiotensin-converting enzyme inhibitors) to support drug reimbursement and policy decisions and encourage the optimization of drug therapy. The scope and depth of the review are determined by jurisdictional needs.