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

Proposed Consolidated Eligibility Inquiry Form

This form is used by Canada's Drug Agency (CDA-AMC) to determine if a product is eligible for review through our Reimbursement Review process, to assess the complexity of the pending submission. This form must be completed by sponsors before filing an application in the following situations:

- **General eligibility inquiry (section 2):** The sponsor is seeking direction regarding whether a product is eligible for review through the Reimbursement Review processes.
- **Complex review process (section 3):** The sponsor is seeking guidance on eligibility for review through the complex review process.
- **Tailored review process (section 4):** The sponsor has a pending application for a new combination product or a new formulation of an existing drug and is seeking to confirm if the pending application is eligible for review through the tailored review process.
- **Time-limited recommendations (section 5):** The sponsor is seeking direction regarding whether a product is eligible for consideration as a time-limited recommendation.
- **Resubmission or reassessment (section 6):** The sponsor is seeking a decision from CDA-AMC regarding a proposed resubmission or reassessment for a drug previously reviewed through the Reimbursement Review process.
- **Rolling submission pilot process (section 7):** The sponsor is seeking to file the application through the rolling submission pilot process.
- **Requests for deviation from pharmacoeconomic requirements (section 8):** The sponsor is proposing a deviation from the pharmacoeconomic requirements.
- **Testing procedure assessment (section 9):** The sponsor is seeking clarification if CDA-AMC will initiate a testing procedure assessment as part of the Reimbursement Review process.
- **Application splitting and/or multiple application fees (section 10):** The sponsor has a pending application that includes multiple treatment populations and/or treatment regimens and is seeking guidance regarding splitting the application into multiple projects and/or clarification regarding the number of application fees.

CDA-AMC will review the information in the form and seek advice from the drug programs (as needed). CDA-AMC will typically notify the sponsor regarding eligibility within 10 business days of receiving the form (in some cases, a longer duration may be required to consult with the drug programs). CDA-AMC may share this form with the federal, provincial, and territorial governments, including their agencies and departments, and the pan-Canadian Pharmaceutical Alliance (pCPA).

Section 1: Background Information

This section **must be completed** for all inquiries.

Confidentiality Guidelines

By filing this *Eligibility and Complexity Assessment Form* with Canada's Drug Agency (CDA-AMC), the sponsor accepts and agrees to the terms of the *Procedures for Reimbursement Reviews* and CDA-AMC's confidentiality guidelines, and consents to comply with the requirements of the confidentiality guidelines, which form an agreement between CDA-AMC and the sponsor. For clarity, the sponsor acknowledges that CDA-AMC may share certain information, including this document, with the authorized recipients.

Details	Sponsor's responses
Date form submitted	Day month, year
Sponsor name	Please provide the complete company name of the sponsor
Product name	Please state the brand name (if known)
Generic name	Please list the nonproprietary names of active substance(s) included in the drug of interest
Dosage forms and strengths	Please identify the dosage forms and strengths (if applicable)
Indication(s) for consideration by CDA-AMC	Please list the indications that are approved or undergoing review by Health Canada for the drug of interest
Health Canada approval status	☐ Pre-NOC ☐ Post-NOC Date of approval: Date or anticipated date of Health Canada approval
Contact information	Name: Title: Email:
Questions for CDA-AMC	Please state the specific questions that you have regarding the review processes:

CDA-AMC = Canada's Drug Agency; NOC = Notice of Compliance.

Section 2: General Eligibility Application for Reimbursement Reviews

Purpose

This section must be completed by sponsors who are seeking confirmation if a drug is eligible for review through the Reimbursement Review process.

Sponsor-Provided Information

Product characteristics	Sponsor's responses
What is the prescription status of the drug in question?	☐ Prescription drug ☐ Over the counter ☐ Ethical ☐ Other, please specify:
Which of the following best describes the product and indication(s) in question?	☐ New active substance ☐ New indication for existing drug ☐ New combination product ☐ New dosage form or strength of an existing drug ☐ Subsequent entry nonbiologic complex drug ☐ Other, please specify:
Which of the following best describes the drug in question?	☐ Chemically synthesized drug ☐ Biologic ☐ Radiopharmaceutical ☐ Gene therapy ☐ Cell therapy (e.g., chimeric antigen receptor T cells) ☐ Preventive vaccine ☐ Therapeutic vaccine ☐ Other, please specify:

Product characteristics	Sponsor's responses
Please state the route of administration for the drug.	☐ Oral ☐ IV ☐ Intramuscular ☐ Inhalation ☐ Subcutaneous ☐ Sublingual ☐ Other, please specify:
What type of submission has been or will be filed with Health Canada?	☐ NDS ☐ S/NDS ☐ A/NDS or S/ANDS ☐ Other, please specify:
Is the drug in question used in the treatment of cancer?	☐ No ☐ Drug is used in the active treatment of cancer ☐ Drug is used as a supportive therapy for cancer patients
Is the drug in question a blood or a plasma-related product?	☐ No ☐ Drug is derived from human blood or plasma ☐ Drug is not derived from human blood or plasma, but has the potential to displace existing drugs that are derived from human blood or plasma ☐ Drug is not derived from human blood or plasma, but has the potential to impact the need for the transfusion of blood in Canada
Does the product in question fit within the reimbursement mandate of 1 or more of the following? (Check all that apply)	☐ Public drug plans and/or cancer agencies ☐ Canadian Blood Services ☐ Hospital formularies ☐ Public health agencies ☐ Uncertain ☐ Other, please specify:
Please identify the location of administration	☐ Home administration ☐ Outpatient clinic or infusion centre ☐ Hospital setting ☐ Physician's office

Product characteristics	Sponsor's responses
	☐ Other setting, please specify:
What diagnostic or other testing procedure[a] is associated with the proposed drug submission?	☐ Companion diagnostic test ☐ Complementary or other diagnostic, predictive, or prognostic test ☐ Medical imaging test ☐ Other test ☐ None (i.e., no associated testing) If there is any testing procedure associated with the proposed drug submission, please complete section 9.
Clinical development program and comparative efficacy	
Overview	Please provide a brief description of the clinical development program for the drug and indication.
Are comparative efficacy data available for the drug versus appropriate comparators?	☐ No ☐ Yes (direct comparison) ☐ Yes (indirect comparison)

A/NDS = abbreviated new drug submission; NDS = new drug submission; S/NDS = supplemental new drug submission.

[a]Testing is defined as: "An intervention(s) and/or procedure(s) that can detect a condition, establish a diagnosis, inform a prognosis, plan treatment, or monitor treatment and its effect on a condition across time." (Source: Medline Plus: Medical Tests. Published by the National Library of Medicine. Available from: https://medlineplus.gov/lab-tests/. Accessed 14 December 2023.) Interventions and procedures that can inform discontinuation of treatment are also in scope.

Section 3: Eligibility Application for a Complex Review

Purpose

This section must be completed by sponsors who are seeking guidance regarding eligibility for review through the complex review process.

Sponsor-Provided Information

Scenario 1: First Drug Approved in the Therapeutic Area

The drug under review must meet **all** of the following criteria:

- The sponsor is claiming added clinical benefit compared with the most appropriate comparator(s) or best supportive care.
- It is the first drug approved by Health Canada for use in the therapeutic area.
- There are no unapproved comparator drugs with well-established reimbursement criteria in the therapeutic area.

1. Sponsor's Clinical Claim

Is the sponsor claiming the drug under review offers added clinical benefit compared with appropriate comparators?

Response:

☐ Yes ☐ No

Please explain your response.

2. First Drug in the Therapeutic Area

Will the product be the first drug approved by Health Canada for use in the therapeutic area (i.e., there are no other products approved at the time the sponsor is filing the inquiry with CDA-AMC)?

Response:

☐ Yes ☐ No

Please explain your response.

3. Availability of Alternative Therapies

Are there unapproved comparator drugs that are currently used in clinical practice?

Response:

☐ Yes ☐ No

Please explain your response.

4. Reimbursement Status and Criteria for Alternative Therapies

If there are unapproved comparators being used in clinical practice, are there established criteria being used to inform reimbursement decisions by the participating drug programs (e.g., initiation, renewal, discontinuation criteria)?

Response:

☐ Yes ☐ No

Please explain your response.

Scenario 2: Priority Review Drugs With the Potential to Alter the Existing Treatment Paradigm

The drug under review must meet **all** of the following criteria:

- The sponsor is claiming added clinical benefit compared with the most appropriate comparator(s).
- It is not the first drug approved in the therapeutic area but has the potential to alter the treatment paradigm based on superior efficacy and/or safety.
- It has been granted priority review by Health Canada (e.g., applications for drugs indicated for the treatment of a serious, life-threatening, or severely debilitating disease or condition for which there is substantial evidence of clinical effectiveness that the drug provides a significant increase in efficacy and/or significant decrease in risk such that the overall risk-benefit profile is improved over existing therapies, preventives, or diagnostic agents for a disease or condition that is not adequately managed by a drug marketed in Canada).

1. Sponsor's Clinical Claim

Is the sponsor claiming the drug under review offers added clinical benefit compared with appropriate comparators?

Response:

☐ Yes ☐ No

Please explain your response.

2. Improvement in Efficacy and/or Safety

Does the sponsor believe the drug under review has the potential to alter the treatment paradigm based on superior efficacy and/or safety versus appropriate comparators?

Response:

☐ Yes ☐ No

Please explain your response.

3. Priority Review

Has the drug been granted priority review by Health Canada for the indication of interest?

Response:

☐ Yes ☐ No ☐ Under consideration

Please explain your response.

If noted as being under consideration by Health Canada, please describe any accelerated approval pathways granted by other regulatory authorities. Please state the date that a decision regarding priority review will be issued by Health Canada. If the sponsor has requested or is planning to request reconsideration of Health Canada's decision regarding priority review, please clearly state this.

Scenario 3: Primary End Point is a Novel Surrogate Outcome

1. Novel Surrogate End Point

Does the sponsor's clinical data include the evaluation of novel surrogate end points as the primary outcome(s) of their clinical trials (e.g., end points not previously reviewed by CDA-AMC)?

Response:

☐ Yes ☐ No

Please explain your response.

2. Sponsor Has Reviewed Previous Recommendations

When stating that the end point is novel, has the sponsor reviewed previous applications in the therapeutic area that are available on the CDA-AMC website?

Response:

☐ Yes ☐ No

Please explain your response.

Scenario 4: Tumour-Agnostic or Histology-Independent Therapies

Is the application for a tumour-agnostic or histology-independent indication that will be considered a complex review by CDA-AMC?

Response:

☐ Yes ☐ No

Scenario 5: Additional Evidence for an Application That Does Not Meet Criteria in Scenarios 1 to 4

Does the sponsor have additional evidence to address gaps in the pivotal clinical trial, randomized controlled trial, and direct or indirect comparative effectiveness and/or safety evidence (e.g., real-world evidence in relevant patient populations that were not included in the clinical trials), but the application is not otherwise eligible for review through the complex process? This evidence may include:

- studies designed to demonstrate safety and effectiveness in relevant patient populations that were not included in 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.

Response:

☐ Yes ☐ No

Please explain your response by identifying the gaps in the evidence that will be addressed by the additional studies.

Section 4: Eligibility Application for a Tailored Review

Purpose

This section should be completed by sponsors who are interested in eligibility for submissions through the tailored review process. Please only complete the section that is applicable for the pending application and delete the sections that do not apply.

- Section A: Applications for a PACES Tailored Review
- Section B: Applications for a Product Variation Tailored Review (New Combination Product)
- Section C: Applications for a Product Variation Tailored Review (New Formulation of an Existing Drugs)

Sponsor-Provided Information

Section A: Application for a PACES Tailored Review

Sponsors may file a PACES tailored review when a pending application meets **all** of the following criteria:

1. Sponsor's Clinical Claim

Is the sponsor claiming the drug under review offers added clinical benefit compared with appropriate comparators?

Response:

☐ Yes ☐ No

Please explain your response.

2. Indicated Patient Population

Does the drug under review have the same or a similar indication as at least 1 other drug previously reviewed by CDA-AMC and recommended for reimbursement?

Response:

☐ Yes ☐ No

Please explain your response.

3. Sponsor's Requested Reimbursement Criteria

Is the sponsor requesting alignment with existing criteria that have been recommended by CDA-AMC and/or are currently used for the reimbursement of the most appropriate comparator(s)?

Response:

☐ Yes ☐ No

Please explain your response.

4. Intervention

Is the drug under review part of the same therapeutic class as at least 1 other drug previously reviewed by CDA-AMC and recommended for reimbursement?

Response:

☐ Yes ☐ No

Please explain your response.

5. Therapeutic Regimen

Have the new application and the previous application(s) for comparators evaluated the use of the drugs using the same regimen (e.g., as monotherapy or in combination with the same background therapies)?

Response:

☐ Yes ☐ No

Please explain your response.

6. Comparators

Has CDA-AMC previously reviewed the most appropriate comparator(s) for the indication under review and issued recommendations in favour of reimbursement (irrespective of a jurisdictional listing decision)?

Response:

☐ Yes ☐ No

Please explain your response.

7. Outcomes

Do the end points evaluated by the sponsor align with those previously reviewed by CDA-AMC for applications in the same therapeutic area (e.g., end points measured and timing of the assessments)?

Response:

☐ Yes ☐ No

Please explain your response.

8. Studies or Evidence

Does the sponsor have evidence supporting 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) in one of the following formats?

- Direct comparative evidence from a randomized controlled trial

- Indirect comparative evidence that is based on aggregate clinical trial data (i.e., adjusted indirect comparison [Bucher method] or a mixed treatment comparison network meta-analysis)

Response:

☐ Yes ☐ No

Please explain your response.

Section B: Tailored Review Eligibility for a Fixed-Dose Combination Product

Sponsors may file a product variation tailored review when a pending application meets **all** of the following criteria:

1. Sponsor's Clinical Claim

Is the sponsor claiming the drug under review offers added clinical benefit compared with appropriate comparators?

Response:

☐ Yes ☐ No

Please explain your response.

2. Population

Are the individual components of the new combination product currently indicated for use in combination therapy with one another (i.e., the new combination product does not represent a new indication for the combined use of the components)?

Response:

☐ Yes ☐ No

Please explain your response.

3. Intervention

Does the new combination product contain a new active substance?

Response:

☐ Yes ☐ No

Are the individual components currently marketed in Canada in the same dosage strength as the new combination product?

Response:

☐ Yes ☐ No

Please explain your response.

4. Comparators

Is the new combination product intended to replace the separate use of the individual components?

Response:

☐ Yes ☐ No

Please explain your response.

5. Reimbursement Status

Have the individual components of the new combination product been recommended by CDA-AMC and/or are reimbursed by the participating drug plans for use in the same combination?

Response:

☐ Yes ☐ No

Please explain your response.

Section C: Tailored Review Eligibility for a New Formulation of an Existing Drug

Sponsors may file a product variation tailored review when a pending application meets **all** of the following criteria:

1. Sponsor's Clinical Claim

Is the sponsor claiming the drug under review offers added clinical benefit compared with appropriate comparators?

Response:

☐ Yes ☐ No

Please explain your response.

2. Population

Is the indication under review for the new formulation the same as the indication previously reviewed and/or currently reimbursed by the participating drug programs for the existing formulations of the drug?

Response:

☐ Yes ☐ No

Please explain your response.

3. Intervention

Does the new formulation meet the eligibility criteria outlined in the *Procedures for Reimbursement Reviews* (e.g., new formulations of existing drugs that have a different route of administration than formulation[s] previously reviewed through the Reimbursement Review process), or has CDA-AMC confirmed eligibility with the participating drug programs?

Response:

☐ Yes ☐ No

Please explain your response.

4. Comparators

Is the new formulation intended to replace an alternative formulation of the same drug (e.g., the sponsor has a new subcutaneous formulation that would replace an existing IV formulation)?

Response:

☐ Yes ☐ No

Please explain your response.

Section 5: Eligibility Application for a Time-Limited Recommendation

Purpose

This section must be completed by sponsors with products that may be eligible to receive a time-limited reimbursement recommendation. Prior to completing this section, the sponsor should review the eligibility criteria described in the Procedures for Reimbursement Reviews.

Sponsor-Provided Information

Screening Eligibility Based on Regulatory Status, Conduct of a Phase III Trial

Eligibility for time-limited recommendations	Response	
The drug has been issued an NOC/c by Health Canada or is undergoing review through the advance consideration under the NOC/c policy.	☐	Yes
	☐	No
A phase III clinical trial is being planned and/or conducted at the time of the submission to CDA-AMC.	☐	Yes
	☐	No
The phase III trial is being or will be conducted in a patient population that is reflective of the indication being reviewed by CDA-AMC.	☐	Yes
	☐	No
The phase III trial will be completed within a time frame that will not exceed 3 years from the target expert committee meeting date.	☐	Yes
	☐	No
	☐	NA[a]
Target expert committee meeting date[b]	Month day, year	

NA = not applicable; NOC/c = Notice of Compliance with Conditions.

[a]Please check NA if the sponsor does not have a relevant phase III trial planned or ongoing for the indication of interest to the CDA-AMC submission.

[b]Please refer to the Expert Committee Meeting Schedule.

Commitment to File for Reassessment

Choose only 1 of the following options. This section should only be completed if the sponsor answered “Yes” to the regulatory status and evidence questions in the previous section.

☐ Yes, the sponsor is willing to commit to file a reassessment application with CDA-AMC in accordance with the time frames specified in the procedures for time-limited recommendations.

☐ No, the sponsor will not commit to filing a reassessment application with CDA-AMC in accordance with the time frames specified in the procedures for time-limited recommendations. The sponsor acknowledges that the CDA-AMC expert committee will be informed of the sponsor’s decision and that a time-limited recommendation will not be an option for the drug under review.

Details of the Evidence Generation Plans

Clearly identify the gaps and/or limitations with the preliminary evidence that will be submitted to CDA-AMC and briefly state how the forthcoming phase III trial will address the issues. Note: This should only be completed if you answered “Yes” to the regulatory status and evidence questions in the previous section.

Confirmed or Anticipated Postmarket Study Requirements

Category	Sponsor Response
Population	Please state the populations where additional phase III evidence will be generated.
Intervention	Please state the intervention(s) that will be studied in the phase III trial, including all relevant background therapies, dosage strength(s), and frequency of administration.
Comparator(s)	Please identify the comparator(s) that will be used in the phase III trial, including dosage strength and frequency of administration.
Outcome(s)	Please identify the outcomes that may be included to address the confirmed or anticipated regulatory conditions (e.g., as stated within the qualifying notice issued by Health Canada). Please include additional primary, secondary, or exploratory end points that will be investigated in the pending phase III trial. CDA-AMC acknowledges that sponsors may not have all of this information at the time of completing this form, particularly for files that will be filed prior to regulatory approval by Health Canada. Please provide as much detail as possible to help inform initial discussions regarding eligibility for consideration to receive a time-limited recommendation.
Timing (required follow-up)	Please state requirements to address the conditional market authorization (please focus on the relevant phase III trial).
Study design	Please briefly state the design of the phase III trial.
Study protocol	If available, please provide a link to the study protocol (or indicate that it is not currently published). If a protocol is currently unavailable, please note this within this section.
Clinicaltrials.gov	Please provide the clinicaltrials.gov identification number (or indicate that it is not currently available).

CDA-AMC = Canada’s Drug Agency.

Target Dates for Phase III Study

If dates are uncertain, please estimate to inform initial discussions regarding eligibility for consideration to receive a time-limited recommendation.

Category	Sponsor Response
Start[a]	Month day, year
Primary completion[b]	Month day, year
Study completion[c]	Month day, year
Clinical Study Report completion[d]	Month day, year
Filing SNDS-c (if known)	Month day, year (or state if unknown)

SNDS-c: Supplement to a New Drug Submission – Confirmatory

[a]Estimated date on which the clinical trial will be open for patient recruitment or the actual date on which the first patient was enrolled.

[b]Date the final study participant was examined or received an intervention for the purpose of the final collection of data for the primary outcome.

[c]Date the final study participant was examined or received an intervention for the purpose of the final collection of data for the primary and secondary outcome measures and adverse events.

[d]Estimate of the time required to finalize the Clinical Study Report after the study has been completed. (CDA-AMC appreciates that this information may not be known. Please provide an estimate based on prior experience.)

Section 6: Eligibility Application for a Resubmission or Reassessment

Purpose

This section must be completed by sponsors who are seeking a decision from CDA-AMC regarding a proposed resubmission or reassessment for a drug previously reviewed through the Reimbursement Review process.

Sponsor-Provided Information

Requested Reimbursement Criteria

Please state the reimbursement criteria that would be included in the proposed resubmission or reassessment. If the sponsor is only requesting reimbursement for a subpopulation of the overall indication approved by Health Canada, please clearly describe the rationale for the requested criteria.

Issues Addressed by the New Information

Descriptive Heading for Issue 1

Describe the issue in 1 to 2 sentences. Use a clear and descriptive subheading that highlights each issue that the resubmission or reassessment will focus on.

- **For a resubmission:** Focus on issues that were previously raised by the expert committee where the sponsor has new information that may address the concerns.
- **For a reassessment:** Identify each of the proposed revisions to the existing reimbursement criteria and provide an explanation about the new information supports the proposed revisions.

This section should not exceed 3 pages and should include citations to articles and/or supporting documentation provided by the sponsor.

Supporting evidence: Add a summary of the new evidence that supports the sponsor's perspective regarding the issue. Please provide a brief overview of new clinical studies, including a description of the study design, population, intervention, comparators, and outcomes.

Please repeat this approach for each of the issues being raised.

Summary of New Economic Information

This section should not exceed 3 pages and should include a description of any new economic information that was not available at the time of the last review. If the sponsor will not be submitting a revised or updated pharmacoeconomic evaluation, please clearly state this in this section and provide a rationale.

Section 7: Eligibility for Rolling Submission Pilot

Purpose

Sponsors who are seeking to file an application through the rolling submission pilot process must complete this section prior to filing their application.

Sponsor-Provided Information

Contact Information

Company name:

Name of primary contact:

Title:

Email:

Drug to Be Submitted to CDA-AMC

Please state the brand name (if known) and nonproprietary names of active substance(s) included in the drug of interest.

Indication(s) to Be Reviewed

Please list the indications that are approved or undergoing review by Health Canada for the drug of interest.

Health Canada Review Timelines

Please state the anticipated date of the Health Canada decision:

☐ Unknown

☐ Month day, year

Health Canada Review Pathway

Is the drug undergoing review by Health Canada through an expedited pathway?

☐ No (standard review pathway)

☐ Yes (priority review)

☐ Yes (Notice of Compliance with Conditions [NOC/c] filed at the outset)

☐ To be confirmed (requested or will be requested)

☐ Other expedited pathway, please specify:

Health Canada Information Sharing

☐ Yes, Health Canada will be or has been provided with a consent form.

☐ No, Health Canada will not be provided with a consent form.

Anticipated CDA-AMC Submission Timelines

Anticipated filing date without rolling submission: Month Day, Year

Anticipated filing date with rolling submission: Month Day, Year

Benefits of Rolling Submission From Sponsor's Perspective

Please provide a brief explanation about how the rolling submission process will be beneficial for the pending application. Please provide the rationale for any application requirements that must be filed sequentially (e.g., the sponsor is awaiting results from the clinical study to populate the economic model).

Proposed Sequential Filing of Application Requirements

Application requirement	Proposed filing date	Rationale for sequential filing
Pivotal clinical trial data	Month day, year	
Indirect comparison(s)	Month day, year	
Studies addressing gaps	Month day, year	
Economic model	Month day, year	
Economic report	Month day, year	
Budget impact model	Month day, year	
Budget impact report	Month day, year	

Sponsor Acceptance of Reduced Timelines for Comments on Draft Reports

The sponsor consents to a reduction in their timelines for review of the draft reports (from 7 business days to 4 business days). Please note: This reduction may not always be required but may help ensure placement on the agenda at the earliest possible expert committee meeting.

☐ Yes ☐ No

Performance Metric

The sponsor agrees to waive the 180–calendar day performance metric. Please note: CDA-AMC will strive to deliver the draft recommendation in accordance with the performance metrics outlined in the Fee Schedule for Pharmaceutical Reviews (i.e., ≤ 180 calendar days from the date the file is accepted for review by CDA-AMC to the date the draft recommendation is issued to the sponsor and drug programs). However, as the application materials will be filed sequentially for a rolling submission, the sponsor will be required to waive the performance metric for any application filed through the rolling submission process. This is required as extensions to the review timelines may be required for reasons outside the control of CDA-AMC.

☐ Yes ☐ No

Section 8: Request for Deviation From Pharmacoeconomic Requirements

Purpose

Sponsors seeking to provide 1 or more economic requirements that deviate from the Reimbursement Review procedures must complete this section prior to filing their application.

CDA-AMC will assess the information and determine if deviation from the requirements will be acceptable. The decision to accept a deviation from the requirements will be made by CDA-AMC on a case-by-case basis, consulting with the participating drug programs as required.

CDA-AMC will notify the sponsor as to whether their request to deviate from the requirements is acceptable. Prior to filing the application form, the sponsor must consult the scenarios outlined in the following table, which provides general guidance on the situations where deviations may be acceptable.

Sponsor's Request for Deviation From Pharmacoeconomic Requirements

Requirement(s)	Rationale for request for deviation
State the pharmacoeconomic requirement(s) where deviation is being proposed by the sponsor.	Provide a clear rationale for the requested deviation. Please indicate which of the scenarios listed in the framework apply to the sponsor's request. If the request is not addressed in the framework, please clearly state this when completing the application.
Add rows as required	
Add rows as required	

Guidance on Acceptability for Requests for Deviation

Rationale	Implication for pharmacoeconomic evaluation	Implication for budget impact analysis	Scope of Clinical Review and recommendation
Acceptable deviations based on patient populations			
1. Discrepancy between trial population and indication (i.e., no clinical data for some relevant patients): The sponsor has noted that there is a discrepancy between the patient population that was studied in the clinical development program and the full patient population that is specified in the indication that has been approved or is undergoing review by Health Canada. The sponsor indicates that there are no clinical data to inform the economic model for the	Narrowed to focus on the trial population	The **base case** must model the full indicated population. A **scenario analysis** must model the subpopulation identified within the deviation request.	Will consider the full indicated population unless the sponsor specifically requests that the scope is restricted to reflect the trial population.

Rationale	Implication for pharmacoeconomic evaluation	Implication for budget impact analysis	Scope of Clinical Review and recommendation
patients who were excluded from the development program.			
2. **The sponsor believes that the indication filed with Health Canada is likely to change:** The sponsor is filing a submission on a pre-NOC basis and anticipates that the indication that is likely to be approved by Health Canada will reflect a narrower population than the proposed indication that is has been or will filed for review with Health Canada.	Narrowed to focus on reimbursement request	Narrowed to focus on reimbursement request	Narrowed to focus on reimbursement request
3. **The sponsor is seeking alignment of criteria with reimbursed comparators:** The sponsor is requesting that the reimbursement criteria for the drug under review be aligned with the reimbursement criteria that are currently used or have been recommended for the most relevant comparator(s).	Narrowed to focus on reimbursement request	Narrowed to focus on reimbursement request	Narrowed to focus on reimbursement request
4. **The sponsor is only seeking reimbursement for 1 indicated population within a broader overall indication:** The sponsor has a broader indication that covers multiple distinct populations (e.g., populations addressed in separate development programs or clinical trials) but is only seeking reimbursement for a subset of the total population. In these cases, CDA-AMC may accept the different population as a distinct indication.	Narrowed to focus on reimbursement request	Narrowed to focus on reimbursement request	Narrowed to focus on reimbursement request
5. **The sponsor is filing a submission for a new indication that expands the age group who may be eligible for treatment:** The sponsor is seeking to expand reimbursement to a new age group of patients where the clinical management and/or comparators are sufficiently different than the existing broader population within the approved indication (e.g., approved indication is for patients aged 6 years and older and the sponsor is only seeking reimbursement for those aged 6 to 11 years).	Narrowed to focus on the revised reimbursement request	Narrowed to focus on the revised reimbursement request	Case-by-case decision on new recommendation superseding older recommendation or new focused recommendation
6. **The sponsor is filing reassessment to**	Narrowed to focus	Narrowed to	Narrowed to

Rationale	Implication for pharmacoeconomic evaluation	Implication for budget impact analysis	Scope of Clinical Review and recommendation
expand reimbursement to a broader population: The sponsor is requesting that the existing reimbursement criteria for the drug under review be expanded to address a broader patient population.	on reimbursement request	focus on reimbursement request	focus on reimbursement request
7. **The sponsor is filing resubmission and CDA-AMC has already evaluated the full population in the initial submission:** The sponsor is requesting reimbursement criteria that are narrower than the approved indication and CDA-AMC has already reviewed an economic evaluation from the sponsor for the full population in the review of the initial submission.	Narrowed to focus on reimbursement request	Narrowed to focus on reimbursement request	Case-by-case decision depending on the data the sponsor plans to include in the resubmission
Acceptable deviations for exclusion of relevant comparator(s)			
8. **Challenges with indirect comparison:** The sponsor is seeking to exclude 1 or more comparator(s) from the economic evaluation due to challenges in conducting an indirect comparison (e.g., substantial heterogeneity precludes meaningful comparison).	Comparator may be excluded, but it may be noted as an important limitation of the application	Comparator must be included in the budget impact analysis	Comparator may be considered relevant for the clinical evaluation and the lack of indirect comparison may be noted as an important limitation of the application
9. **Patients are ineligible for comparator:** The sponsor is seeking to exclude 1 or more comparator(s) from the economic evaluation on the basis that patients eligible for the drug under review will have already received or been considered ineligible for the comparator of interest. These requests will generally only be accepted when the request aligns with 1 or more of the following: the request reflects the populations studied in the clinical trials; the request aligns with previous recommendations from CDA-AMC and/or existing reimbursement criteria used by the public drug programs; or the sponsor notes that Health Canada is likely to restrict the indication based on initial feedback and/or	Comparator may be excluded, but it may be noted as an important limitation of the application	Comparator may be excluded, but it may be noted as an important limitation of the application. The sponsor may be required to ensure that the budget impact analysis model provides flexibility for CDA-AMC to include these	Comparator may be considered relevant for the clinical evaluation and the lack of indirect comparison may be noted as an important limitation of the application

Rationale	Implication for pharmacoeconomic evaluation	Implication for budget impact analysis	Scope of Clinical Review and recommendation
previous examples for similar drugs.		comparators (if appropriate).	
Acceptable scenario for submission of pairwise comparison(s)			
10. Efficacy for the economic model is derived from multiple MAICs, because the sponsor has deemed an NMA to not be feasible.	Pairwise comparisons are acceptable when the sponsor cannot conduct an NMA, and MAICs are required to derive estimates of comparative efficacy	Not applicable	Not applicable
Requests for deviation that will not be accepted			
11. The sponsor is requesting to file for only a subgroup: The sponsor is only interested in requesting reimbursement for a subset of patients where the clinical data are most favourable or where the sponsor has suggested a preferred place in therapy (e.g., positioning the drug as a later line of therapy).	**CDA-AMC rationale:** Interested parties (including the public drug programs and patients) expect CDA-AMC to consider the full indication in these situations. The sponsor may specify the subgroup analysis within their reimbursement request and provide scenario analyses within their economic evaluation.		
12. The sponsor is requesting to file multiple economic models: The sponsor states that the full indication under review includes distinct patient populations that require separate economic evaluations to model. In accordance with CDA-AMC procedures, this will only be accepted if the submissions are reviewed as separate distinct indications.	**CDA-AMC rationale:** Only 1 economic evaluation can be included in an application for the review of a single indication. For example, the following will not be accepted: including more than 1 economic model for the review of a single indication; or submitting both a cost-minimization analysis and cost-utility analysis for the review of a single indication.		

CDA-AMC = Canada's Drug Agency; MAICs = matching-adjusted indirect comparisons; NMA = network meta-analysis; NOC = Notice of Compliance.

Section 9: Eligibility Application for a Testing Procedure Assessment

Purpose

This section must be completed by sponsors who are seeking clarification if CDA-AMC will initiate a testing procedure assessment of the companion diagnostic or other testing associated with the drug as part of the Reimbursement Review process. If there are multiple testing procedures, please complete the following table for each testing procedure. CDA-AMC will assess the information and determine if a testing procedure assessment is warranted, and if yes, whether a full assessment (in the form of a separate section of the main report) or a brief summary of the testing procedure considerations (as part of the introduction) is appropriate. Please refer to Issue 47 of CDA-AMC's Pharmaceutical Reviews Update for our announcement.

Questions and required information	Sponsor's responses
Provide a brief description of the testing procedure[a] associated with the drug and any testing platforms available.	
Is any aspect of the testing procedure (e.g., biomarker, testing platform) new to Canada or for the indication under review (e.g., first application to the disease or condition)?	☐ Yes ☐ No Please explain your answer:
Provide an overview of the current testing pathway for the indication and where in that pathway the testing procedure best fits (e.g., reflex during diagnosis, upon disease progression, monitoring during treatment).	
Has another drug associated with the same testing procedure already been evaluated by CDA-AMC?	☐ Yes ☐ No If yes, please specify:
What is the estimated number of individuals in Canada who would be expected to require the testing procedure (e.g., per year)?	
What is the availability and reimbursement status of the testing procedure in each of the jurisdictions across Canada?	
Is the testing procedure currently performed as part of routine care for the indication under review?	☐ Yes ☐ No If yes, please describe the current process (e.g., at what disease stage, using what sample) and highlight any differences between the jurisdictions across Canada.
Is it anticipated that the testing procedure will be repeated more than once before, during, or after the	☐ Yes

Questions and required information	Sponsor's responses
course of treatment (e.g., for diagnosis, to ascertain treatment eligibility, treatment response, and/or disease progression)?	☐ No Please explain your answer:
What are the anticipated impacts on human and other health care resources (e.g., training or infrastructure requirements) by provision of the testing procedure for the indication under review?	
Is the testing procedure broadly accessible to patients across Canada?	☐ Yes ☐ No If yes, please identify which patient groups might not have access to testing and why.
What is the current or expected turnaround time for the testing procedure?	
Does the testing procedure impose a burden on patients, families, or caregivers?	☐ Yes ☐ No Please explain your answer:
Provide a brief description of the clinical utility and diagnostic accuracy of the testing procedure under consideration.	
What are the potential risks of harm associated with the testing procedure?	
What is the projected cost of the testing procedure, including the cost of the test as well as pathologist and radiologist time for training and interpretation of results? Is the projected cost of the testing procedure expected to have impacts on health systems?	

[a]Testing is defined as: "An intervention(s) and/or procedure(s) that can detect a condition, establish a diagnosis, inform a prognosis, plan treatment, or monitor treatment and its effect on a condition across time." (Source: Medline Plus: Medical Tests. Published by the National Library of Medicine. Available from: https://medlineplus.gov/lab-tests/. Accessed 14 December 2023.)

Section 10: Inquiries Regarding Application Splitting and/or Multiple Application Fees

Purpose

In situations where there are multiple target populations and/or treatment regimens addressed in the indication that would be reviewed, CDA-AMC makes a case-by-case decision regarding splitting the application into multiple projects and invoicing for multiple application fees. Any sponsors with questions concerning these issues are encouraged to complete this section of the template and contact CDA-AMC early in the presubmission phase to seek guidance. CDA-AMC will assess the information provided and issue a decision on each of the following:

- **Number of application packages:** CDA-AMC will advise the sponsor if a single application package with all relevant information may be filed or if the application must be separated into more than 1 filing based on the different patient population. In the case of a single application, CDA-AMC may subsequently split the application into 2 projects to reflect the different patient populations and/or treatment regimens.
- **Number of clinical and economic reports:** CDA-AMC will advise the sponsor if a combined clinical and economic report will be prepared reflecting the different patient populations and/or treatment regimens (e.g., 1 clinical report addressing all populations within the indication).
- **Number of recommendations:** CDA-AMC will advise the sponsor if a single recommendation or multiple recommendations will be issued for the drug under review. Alignment of reimbursement criteria is a key consideration for CDA-AMC (e.g., multiple recommendations will typically be the preferred option if recommended reimbursement criteria may be different across the different patient populations).
- **Number of application fees:** CDA-AMC will advise the sponsor if multiple application fees will be invoiced. This would typically be a decision to charge 2 schedule A application fees to reflect the separation of the projects. As noted in the *Fee Schedule for Pharmaceutical Reviews*, this is a case-by-case decision made by CDA-AMC.

Sponsor-Provided Information

1. **Populations:** Does the indication under review include different patient populations (e.g., populations that are identified by different biomarkers)?

   Please briefly explain the sponsor's assessment.

2. **Proposed place in therapy:** Is the expected place in therapy of the drug under review different for the subpopulations addressed within the indication under review?

   Please briefly explain the sponsor's assessment.

3. **Intervention:** Is the intervention different depending on the characteristics of the patient population (e.g., a different combination regimen is used depending on a patient's biomarker status)?

   Please briefly explain the sponsor's assessment.

4. **Comparators:** Are the relevant comparators different across the patient populations included in the indication under review (e.g., comparators are only relevant for a subset of the population)?

   Please briefly explain the sponsor's assessment.

5. **Clinical trial data:** Are the clinical data supporting use of the drug under review generated in different clinical trials or from predefined subgroup analyses (e.g., situations where CDA-AMC may need to evaluate each subgroup separately)?

   Please briefly explain the sponsor's assessment.

6. **Indirect comparison:** Are the indirect data supporting the comparative efficacy of the drug under review generated in different clinical trials or from predefined subgroup analyses (e.g., situations where CDA-AMC may need to evaluate each subgroup separately)?

   Please briefly explain the sponsor's assessment.

7. **Prescribers:** Are the patient populations sufficiently different to require consultation with different clinical specialists and/or would input from patient and clinician groups potentially differ across the patient populations?

   Please briefly explain the sponsor's assessment.

8. **Separate pharmacoeconomic evaluations:** Is the sponsor planning to include separate base cases and/or separate economic models for each of the patient populations?

   Please briefly explain the sponsor's assessment.

9. **Budget impact evaluations:** Is the sponsor planning to include separate budget impact analyses for each of the patient populations (e.g., results presented separately)?

   Please briefly explain the sponsor's assessment.

10. **Recommendations:** Is the sponsor anticipating a single expert committee recommendation for the indication under review, or would multiple recommendations be more appropriate (e.g., would reimbursement differ across the patient populations)?

    Please briefly explain the sponsor's assessment.