

Reimbursement Review Sponsor Summary Template

Instructions for Sponsors

Background

Please read the instructions below and consult the recommended documentation before completing the template. If you have any questions regarding the application process, please [contact us](#) with the complete details of your question(s). Please note that the completed document will not be posted on the CDA-AMC website. CDA-AMC will use this document as one of the considerations when preparing the review report.

Before Completing the Template

Please review the following documents to ensure an understanding of the procedures and submission guidelines:

- [Procedures for Reimbursement Reviews](#)
- Pharmaceutical Review Updates for any applicable information.

Completing the Template

General Guidelines

Complete all sections of the template using 10-point Arial font type in text and 9-point Arial font in tables. Include figure and table numbers and provide a list of figures and a list of tables after the table of contents. Data should reflect the results reported in the clinical study report(s) whenever possible. Do not exceed the page limitations where noted.

Provide clear references to source documentation (including citations and corresponding table and figure numbers from data sources) used when completing the template. In-text citations to sponsor references must be referenced numerically in order of appearance using superscript numbers. The sponsor must provide an 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.

When the template is complete, delete this cover page with the instructions CDA-AMC and the record of updates section, delete all red font instructions through the template. Please feel free to add company-specific elements such as a cover page, disclaimer, header, footer, etc. as required. Save and submit the completed template as a Word document.

Section 1

In this section 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.

Section 3

In this section the sponsor is required to summarize long-term extension studies. The sponsor should ensure that all source documentation, 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 (i.e., do not delete the section if there are no data available).

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 comparative efficacy or safety and/or the assumptions in the pharmacoeconomic model). In addition to this summary, the sponsor must provide the complete technical reports for the indirect comparisons as described in the [Procedures for Reimbursement Reviews](#). Any sponsors who 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 (i.e., do not delete the section if there are no data available).

Section 5 (for applications eligible for a complex review only)

This section allows the sponsor to summarize evidence from additional studies that address important gaps in the evidence presented in sections 2 and 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 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.

CDA-AMC will consider the information provided by the sponsor in Section 5 and make a case-by-case determination of which 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 a clear and relevant gap in the pivotal and RCT evidence
- the sponsor has provided the additional information in a format that allows CDA-AMC to complete a detailed review and appraisal of the data (e.g., in accordance with the CONSORT reporting guidelines or [Guidance for Reporting Real-World Evidence](#), as applicable).

When assessing eligibility of an application for a complex review under scenario 5, CDA-AMC will determine during the eligibility assessment whether additional evidence will be included in this section of the clinical report.

Section 6

In this section of the template the sponsor must summarize the key methods and results of the pharmacoeconomic submission. The information provided by the sponsor will be incorporated into the Supplemental Materials document that is prepared by CDA-AMC. The information is intended to be a summary and additional relevant details should be included in the economic evaluation technical report. **Note: All sponsors are encouraged to complete this section; however, it is only a requirement for applications that will target the December 2026 expert committee meetings or later.**

Submitting the Completed Template

Incorporate the completed sponsor submission into the package of required documents. Please consult the relevant procedural documentation for details on how to file the application with CDA-AMC.

Record of Updates to Template

Version	Date	Summary of revisions
5	January 29, 2026	• Addition of the summary of the sponsor's pharmacoeconomic submission. • Clarified how the proposed reimbursement conditions will be considered by the expert committee.
4	February 27, 2025	• Updated from CADTH to CDA-AMC • Added guidance throughout to include corresponding table and figure numbers from data sources when they are cited. • Added a new section for proposed reimbursement conditions • Updated section 5 instructions to reflect changes to complex review eligibility • Made minor revisions to Table 1 (submission type and mechanism of action of the drug under review added) • Clarified guidance for providing a reference list and copies of articles addressing the validity of outcome measures • Added guidance to summarize the clinical evidence underlying or justifying the use of a surrogate outcome as well as the evidence for the validation of the surrogate outcome. • Added guidance for reporting statistical testing details for noninferiority studies and for reporting how intercurrent events were handled. • Added guidance on describing the feasibility assessment for included indirect treatment comparisons • Clarified guidance for reporting assessment of homogeneity for indirect treatment comparisons • Clarified guidance for focussing on relevant comparators when reporting results of network meta-analyses • Added example tables for reporting results of network meta-analyses • Clarified guidance that absolute effects for efficacy results should be reported when possible
3	June 8, 2023	Updated instructions for reporting efficacy results in the systematic review section now specify types of data that should be reported, including absolute differences in effects. In the absence of this information, the CADTH review team may not be able to fully assess the clinical importance of the estimated effect for a given outcome.
2	April 20, 2023	Clarification to the template instructions that section 2 of the template must be completed by sponsors and that all indirect comparisons included in the application must be summarized in section 4.
1	March 31, 2022	Original version posted

Table of Contents

Please update the Table of Contents prior to submitting the application.

Record of Updates to Template.....	4
List of Tables.....	6
List of Figures.....	6
Abbreviations.....	7
Section 1. Introduction.....	8
Application Summary.....	8
Drug under Review.....	8
Disease Background.....	9
Place in Therapy and Comparators.....	11
Section 2. Systematic Review.....	16
Objectives and Methods.....	16
Literature Search and Study Selection.....	17
Included Studies.....	20
Patient Population.....	25
Results.....	27
Sponsor Summary and Conclusion.....	32
Sponsor Identified Gaps in the Evidence.....	32
Section 3. Long-Term Extension Studies.....	33
Description of Studies.....	33
Patient Population.....	33
Results.....	35
Sponsor Summary and Conclusion.....	36
Sponsor Identified Gaps in the Evidence.....	36
Section 4. Indirect Evidence.....	38
Description of Indirect Comparison(s).....	38
Results.....	40
Sponsor Summary and Conclusion.....	43
Section 5. Studies Addressing Gaps in the Pivotal and RCT Evidence.....	44
Summary of Gaps in the Evidence.....	44
Description of (add Study ID).....	44



Patient Population.....	45
Results.....	47
Sponsor Summary and Conclusion.....	49
Section 6. Summary of the Sponsor’s Pharmacoeconomic Submission.....	50
Appendix 1: Literature Search Strategy.....	54
Appendix 2: List of Excluded Studies.....	55
References.....	56

List of Tables

Please add a list of tables.

List of Figures

Please add a list of figures.



Abbreviations

Examples of commonly used abbreviations are provided below. Please add or remove from the list as needed.

AE	adverse event
CI	confidence interval
DB	double blind
EMA	European Medicines Agency
FAS	full analysis set
FDA	Food and Drug Administration
ITT	intention-to-treat population
PP	per-protocol
RCT	randomized controlled trial
RR	relative risk
SAE	serious adverse event
SD	standard deviation
WDAE	withdrawal due to adverse event
Additional abbreviations	

—

Section 1. Introduction

Application Summary

Table 1: Submitted for Review

Item	Description
Drug (product)	Non-proprietary name (Brand Name), strength, dosage form(s), route of administration
Sponsor	Novo Nordisk
Health Canada indication	Health Canada indication as per product monograph (abbreviate if necessary); if pre-NOC submission state: "Proposed:"
Health Canada approval status	NOC, NOC/c, Under review (pre-NOC)
Health Canada review pathway	Standard, priority review, advance consideration under NOC/c, other (please specify)
NOC date	If NOC received, state: Month day, year If pre-NOC submission, state: anticipated Month day, year
Mechanism of action	Clinical and nonclinical data indicate that the weight-reducing effect of semaglutide is mediated mainly by reduced energy intake. GLP-1 RAs reduce body weight by lowering energy intake via induced feelings of satiety and fullness and by lowering feelings of hunger. This is consistent with the normal physiological effect of native GLP-1; GLP-1 is a known physiological regulator of appetite, and GLP-1 receptors are present in several areas of the brain involved in appetite regulation.
Recommended dosage	In the NN9536-4373 (STEP 1) trial, subjects were started on a once-weekly dose of 0.25 mg and followed a fixed-dose escalation schedule. The dose was increased every 4 weeks to 0.5, 1.0, 1.7, and 2.4 mg per week, with the goal of reaching the 2.4 mg maintenance dose after 16 weeks. If a subject could not tolerate the 2.4 mg maintenance dose and would otherwise have to stop the trial product, they could remain on a lower dose of 1.7 mg once weekly if deemed safe. It was recommended that the subject attempt to re-escalate to the 2.4 mg dose at least once, at the investigator's discretion. If a single dose was missed, it was to be taken as soon as possible, as long as the next scheduled dose was at least 2 days (48 hours) away. If the next dose was less than 2 days (48 hours) away, the missed dose was to be skipped. If two or more consecutive doses were missed, treatment could be re-commenced at the investigator's discretion if it was considered safe and the subject did not meet discontinuation criteria. The scheduled dosing day of the week was not to be changed due to missed doses.
Submission type	Initial or Resubmission or Reassessment
Reimbursement request	Ensure this is consistent throughout all components of the application If same as indication, state "As per indication."

Rationale for Filing the Resubmission or Reassessment

Briefly state the rationale for filing the resubmission (i.e., how the new information addresses issues raised in the previous CDA-AMC review) or reassessment (i.e., how the new information supports the sponsor's request for revised reimbursement criteria).

Drug under Review

Indication and Reimbursement Request

State the indication that has been approved or is currently under review by Health Canada.
State the reimbursement request; please include the rationale if this differs from the approved/proposed Health Canada indication.

Dosing and Administration

In the NN9536-4373 (STEP 1) trial, both semaglutide and placebo were investigational medicinal products (IMPs) formulated as a solution for subcutaneous injection. Semaglutide was supplied at strengths of 1.0 mg/mL and 3.0 mg/mL in a 3 mL PDS290 pre-filled pen-injector. Dosing was administered once weekly, with dose escalation every fourth week to reach the maintenance dose. Injections were given on the same day of the week, if possible, and could be administered in the thigh, abdomen, or upper arm at any time of day, without regard to meals.

Mechanism of action

State mechanism of action of the drug under review.

Prescribing

Please identify any confirmed or anticipated statements in the Canadian product monograph regarding restricting the prescribing and/or administration of the drug to certain health care professionals. If applicable, please provide details of any statements related to limiting the prescribing and/or administration of the drug to certain health care professionals.

Disease Background

Overview of the Condition

Provide a brief description of the disease. Please ensure the following information is reported with references (as applicable): incidence and prevalence (in Canada, if available), signs and symptoms, natural history, disease staging, survival/mortality, and relevant prognostic factors.

Estimated Disease Prevalence

Provide a breakdown of prevalence by participating province and territory. If the drug under review is expected to fall within the coverage mandate of the Non-Insured Health Benefits program of the First Nations and Inuit Health Branch, please provide a separate estimate for the prevalence in the First Nations and Inuit populations (if available). Please ensure these estimates align with the information in the pharmacoeconomic submission.

Table Number: Sample table for presenting the estimated prevalence in each region

Region	Estimated Prevalence		
	Lower Estimate	Best Estimate	Upper Estimate
Pan-Canadian (excluding Quebec)			
Alberta			
British Columbia			
Manitoba			
New Brunswick			
Newfoundland and Labrador			

Northwest Territories			
Nova Scotia			
Nunavut			
Ontario			
Prince Edward Island			
Saskatchewan			
Yukon			
Non-Insured Health Benefits			

Diagnosis of the Condition

Diagnostic Testing Requirements

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

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

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

Availability of Diagnostic Testing

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

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

Health Care Resources

Pre-Treatment Phase

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

- Provide the following information for any drugs that are required to prepare the patient to receive the drug under review:
 - non-proprietary name, dosage, route of administration
 - timing relative to the receiving the drug under review

- setting to administer the pre-treatment drugs (e.g., home, physician's office, outpatient clinic, inpatient hospital setting).
- Provide the following information for any medical procedures that are required to prepare the patient to receive the drug under review:
 - name and rationale of the procedure
 - timing of the procedure relative to receiving the drug under review
 - setting for the procedure (e.g., physician's office, outpatient clinic, inpatient hospital setting)
 - anticipated duration and setting expected for recovery from the procedures (e.g., hospitalization for a particular time period) and factors that could influence recovery time.

Treatment Phase

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

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

Post-Treatment Phase

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

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

Place in Therapy and Comparators

Current Treatment Paradigm

Describe current therapeutic approaches (including pharmacological and non-pharmacological interventions) in Canada for the condition of interest.

- Cite clinical practice guidelines as appropriate.

- Describe the treatment goals (such as prolonging life, delaying disease progression, improving symptoms, minimizing side effects, improving quality of life, increasing the patient's ability to maintain employment, maintain independence, reducing burden on caregivers, etc.).
- Identify all drug therapies that are currently available for the target population. If some drugs are not listed on public formularies, please describe how they can be accessed by the patient.

Unmet Therapeutic Needs

Please describe the therapeutic needs that are not being met by currently available treatments. The following are common examples of unmet therapeutic needs:

- not all patients respond to available treatments
- patients become refractory to current treatment options
- no treatments are available to halt progression or reverse the course of disease
- no treatments are available to address the outcomes of greatest importance to patients
- treatments are needed that are better tolerated
- treatments are needed to improve adherence
- formulations are needed to improve convenience for patients

Impact of Drug on Treatment Paradigm

Proposed Place in Therapy

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

Potential Impact on Currently Reimbursed Treatments

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

Provisional Algorithm Diagram (oncology drugs)

Provide one or more figures illustrating the proposed place in therapy of the drug or regimen under review; the figures should demonstrate the potential impact (if any) on currently reimbursed treatments for the indication. If drug sequencing varies by patient subpopulations, the sponsor should consider providing multiple algorithms, with each appropriately labelled to indicate the patient category. – Briefly state which diagrams are provided here.



Comparators

The comparators in the systematic review should align with those included in the economic evaluation. All relevant comparators should be included unless the sponsor has discussed with CDA-AMC and received formal notification that one or more relevant comparators may be excluded. Relevant comparators include the following:

- treatments currently reimbursed by at least 1 participating drug plan for the indication under review,
- reimbursed treatments that are currently used off-label in Canadian practice, or
- treatments that have previously received a recommendation in favour of reimbursement from CDA-AMC for the indication under review).

Table Number: Key characteristics of Drug 1, Drug 2, etc.

Drug	Indication(s)	Route and Dose	Role in Application	
			Included in indirect comparison	Included in PE
Drug under review	State indication under review	State recommended regimen	NA	NA
Comparator 1	State relevant indication(s) approved by Health Canada. If used off-label, note “not approved for the indication under review”.	State dosage regimen recommended in the product monograph. If the indication has not been approved by Health Canada, please state the dosage regimen that is used in clinical practice and provide supporting referencing.	If no, explain rationale	If no, explain rationale
Comparator 2	As above	As above	As above	As above
Add rows as needed	Add rows as needed	Add rows as needed	Add rows as needed	Add rows as needed

Source: Indicate data sources (i.e., product monographs) including citation.

Proposed Reimbursement Conditions

State the detailed proposed initiation, renewal, discontinuation, and/or prescribing conditions for accompanying a recommendation to reimburse the drug under review. These conditions will be considered by the expert committee

along with the other inputs to their deliberation, and there will be no expectations that these conditions will be adopted by the expert committee when developing the reimbursement recommendation. For each proposed condition, include a reason to support the condition.

- State each reimbursement condition in a separate row, using a numbered list.
- Use the words “and” and “or” between components of a condition to clearly indicate whether all components must be met or at least one must be met. Alternatively, use a bulleted list of components, preceded by “all of the following” or “any of the following”.
- Refer to the Examples of Commonly Used Reimbursement Conditions table in the Recommendation Framework section in the [Procedures for Reimbursement Reviews](#).
- Use generic drug names throughout the table

Table Number: Proposed Reimbursement Conditions for the Drug Under Review

Proposed reimbursement condition	Reason
Initiation	
1. <State condition here or “The sponsor proposes that there be no initiation conditions”>	Provide a rationale for each condition
2. If recommending alignment with existing criteria for other drugs: Eligibility for [drug] should be based on the criteria used by each of the public drug programs for reimbursement of [relevant drug(s)] for [brief indication].	
Add or delete rows as needed	
Renewal	
3. <State condition here or “The sponsor proposes that there be no renewal conditions”>	Provide a rationale for each condition
4. If recommending alignment with existing criteria for other drugs: “[Drug] should be renewed in a similar manner to [relevant drug(s)] for [brief indication].” Use a similar condition for discontinuation if applicable.	
Add or delete rows as needed	
Discontinuation	
5. <State condition here or “The sponsor proposes that there be no discontinuation conditions”>	Provide a rationale for each condition
Add or delete rows as needed	
Prescribing	
6. <State condition here or “The sponsor proposes that there be no prescribing conditions”>	Provide a rationale for each condition
Add or delete rows as needed	

Abbreviations must be listed under the table in alphabetical order.

Section 2. Systematic Review

Objectives and Methods

To perform a systematic review of the beneficial and harmful effects of [state non-proprietary drug name] and strength(s) for [state the indication of interest] versus relevant comparators in clinical practice in Canada.

Review Protocol

Population

For initial submissions and resubmissions, the population will be defined as the full population identified in the approved/proposed Health Canada indication for which the sponsor is submitting (unless otherwise decided upon in consultation with CDA-AMC). While a sponsor's reimbursement request may be specific to a subgroup or subpopulation of patients within the Health Canada indication, the population defined in the systematic review protocol will typically not be limited according to the reimbursement request. Subpopulations identified in the sponsor's reimbursement request should be pre-specified in the protocol as a subgroup(s) of interest and results reported where available. Other relevant subgroups that are likely to be of interest to clinicians, drug plans, patients, and those included in the sponsor's pharmacoeconomic submission should also be included in the protocol. These should be based on clinically important prognostic factors or modifiers of treatment effects.

For a reassessment, the systematic literature review should focus on the population that is relevant to the sponsor's request for revised reimbursement criteria for the drug under review.

Intervention

The intervention will be specified as the drug, formulation, and route of administration under review, and within the Health Canada approved dosage range. For studies that include multiple intervention arms with differing dosages, only those arms with dosages within the Health Canada approved range should be included in the systematic review. For pre-NOC submissions, where there is uncertainty about which doses will be approved by Health Canada, all dosage arms may be included.

Comparator(s)

The comparator(s) in the systematic review should align with those included in the economic evaluation. All relevant comparators should be included unless the sponsor has discussed with CDA-AMC and received formal notification that one or more relevant comparators may be excluded. Relevant comparators include the following:

- treatments currently reimbursed by at least 1 participating drug plan for the indication under review,
- reimbursed treatments that are currently used off-label in Canadian practice, or
- treatments that have previously received a recommendation in favour of reimbursement from CDA-AMC for the indication under review.

The review will typically focus on drug comparators that are reimbursed by public drug plans. Though not typical, in some circumstances nondrug comparators (e.g., transfusion, plasmapheresis) may also be included as comparators. Comparators not approved by Health Canada for the indication under review may also be considered relevant if they are the standard of care and their use is reimbursed by drug programs for the indication of interest. Comparators available through Health Canada's Special Access Program for the indication under review may also be considered.

Outcomes

Endpoints should reflect those studied in the clinical development program for the drug review. This includes, but is not limited to:

- all primary endpoints in the clinical studies
- all secondary endpoints in the clinical studies
- any endpoints included in the economic evaluation
- health-related quality of life endpoints (irrespective of classification within the hierarchy of endpoints in the trial protocol)

Study design

In addition to the clinical trials submitted as pivotal studies to Health Canada, other phase 3 or 4 randomized controlled studies should be included in the systematic review. Consideration may be given to including other study designs in the protocol-selected studies on a case-by-case basis (e.g., if the pivotal trials are not Phase 3 randomized controlled trials).

Table Number: Inclusion criteria for the systematic review

Criteria	Description
Population	Specify population(s) Subgroups: List all relevant subgroups
Intervention	Drug, dose and route of administration, as applicable
Comparator	List all appropriate comparators
Outcomes	Efficacy outcomes: Harms outcomes: AEs, SAEs, WDAEs, Mortality, add AESI
Study Designs	Pivotal trials, phase 3 or 4 RCTs

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Literature Search and Study Selection

Literature Search Methodology

Literature searches must be developed following internationally accepted standards for systematic reviews. Examples of search guidance documents include:

- European Network for Health Technology Assessment. Process of information retrieval for systematic reviews and health technology assessments on clinical effectiveness. Methodological Guidelines. Diemen (The Netherlands): EUnetHTA; 2019.
- Lefebvre C, Glanville J, Briscoe S, Littlewood A, Marshall C, Metzendorf M-I, Noel-Storr A, Rader T, Shokraneh F, Thomas J, Wieland LS. Chapter 4: Searching for and selecting studies. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021). Cochrane, 2021.

Searching bibliographic databases

MEDLINE and Embase must be searched as these are the major biomedical bibliographic databases that concern pharmaceuticals. Other databases may be included as relevant, for example: (Cochrane, CENTRAL, PsycINFO, CINAHL, Scopus, Web of Science). Use a sensitive database search strategy, employing:

- controlled vocabulary (e.g., MeSH, Emtree terms, etc.)
- text words (e.g., synonyms)
- registry numbers
- chemical drug names
- trade drug names
- generic drug names

Follow field codes and syntax correctly for each database (platform) searched, for example:

- Ovid MEDLINE: (trade drug name or generic drug name or developmental drug name).ti,ab,kf,ot,hw,rn,nm.
- Ovid Embase: Generic drug name/ or (trade drug name or generic drug name or developmental drug name).ti,ab,kf,ot,rn,dq.

In some instances, it may be necessary to apply a search concept for the indication/condition. Similar principles to search strategy design apply: controlled vocabulary (e.g., MeSH, Emtree terms, etc.); text words (e.g., synonyms). If applying study ; design filters to the search, consult available search filters as outlined by these resources:

- [CDA-AMC search filters database](#)
- Glanville J, Lefebvre C, Manson P, Robinson S and Shaw N, editors. ISSG Search Filter Resource. York (UK): The InterTASC Information Specialists' Sub-Group; 2006 [updated 9 Nov. 2021; cited 9 Nov. 2021].

Peer review is strongly recommended, using the [PRESS Peer Review of Electronic Search Strategies](#)

Searching clinical trial registries

Multiple trial registries should be searched and reported on in the literature search appendix section, including:

- ClinicalTrials.gov: Produced by the U.S. National Library of Medicine
- WHO ICTRP: International Clinical Trials Registry Platform, produced by the World Health Organization
- Health Canada's Clinical Trials Database
- EU Clinical Trials Register: European Union Clinical Trials Register, produced by the European Union

Reporting of the literature search

Systematic literature searches must be reproducible. The search strategy should be reported in the literature search appendix section. Elements presented should follow the [PRISMA-S extension checklist](#).

Example of Reporting Clinical Literature Search Methods

The literature search for clinical studies was performed by an information specialist using a peer-reviewed search strategy according to the [PRESS Peer Review of Electronic Search Strategies](#). Published literature was identified by searching the following bibliographic databases: MEDLINE All (1946–) via Ovid; Embase (1974–) via Ovid; Cochrane Central Register of Controlled Trials (CCTR) via Ovid; and Cumulative Index to Nursing and Allied Health Literature (CINAHL) via EBSCO. All Ovid searches were run simultaneously as a multi-file search. Duplicates were removed using Ovid deduplication for multi-file searches, followed by manual deduplication in Endnote. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were [intervention] and [indication/population]. Clinical trials registries

were searched: the US National Institutes of Health's clinicaltrials.gov, World Health Organization's International Clinical Trials Registry Platform (ICTRP) search portal, Health Canada's Clinical Trials Database, and the European Union Clinical Trials Register.

No filters were applied to limit the retrieval by study type. Retrieval was not limited by publication date or by language. See Appendix 1 for the detailed search strategies. The initial search was completed on **MONTH DAY, YEAR**.

Study Selection

Figure Number: PRISMA Flow Diagram

In this space the sponsor should provide a PRISMA diagram depicting the flow of information through the different phases of the systematic review. For additional information, including examples and templates for PRISMA diagrams, please see: <http://prisma-statement.org/prismastatement/flowdiagram.aspx>



Included Studies

Table Number: Details of Included Studies

	Study Name	Study Name
Designs & Populations		
Study Design	Briefly describe (e.g., phase 3, double-blind, placebo-controlled RCT)	Briefly describe (e.g., phase 3, double-blind, placebo-controlled RCT)
Locations	List number of sites and state the countries/regions where the trial was conducted	List number of sites and state the countries/regions where the trial was conducted
Patient Enrolment Dates:	Start date: State date End date: State date	Start date: State date End date: State date
Randomized (N)	State the total N and include the sample size in each treatment group.	State the total N and include the sample size in each treatment group.
Inclusion Criteria	Please list key criteria only	Please list key criteria only
Exclusion Criteria	Please list key criteria only	Please list key criteria only
Drugs		
Intervention	State the drug, dosage, frequency of	State the drug, dosage, frequency of

	Study Name	Study Name
	administration, route of administration, duration	administration, route of administration, duration
Comparator(s)	For each comparator: state the drug, dosage, frequency of administration, route of administration, duration of treatment	For each comparator: state the drug, dosage, frequency of administration, route of administration, duration of treatment
Study duration		
• Screening phase	Specify duration	Specify duration
• Run-in phase	Specify duration (delete if not applicable)	Specify duration (delete if not applicable)
• Treatment phase	Specify duration	Specify duration
• Follow-up phase	Specify duration (note if entry into LTE was an option)	Specify duration (note if entry into LTE was an option)
Outcomes		
Primary End Point	State the primary endpoint including the timeframe (e.g., through 24 weeks)	State the primary endpoint including the timeframe (e.g., through 24 weeks)
Secondary and Exploratory End Points	Secondary: List the pre-specified secondary endpoints including the timeframe Exploratory: List the exploratory endpoints including the timeframe	Secondary: List the pre-specified secondary endpoints including the timeframe Exploratory: List the exploratory endpoints including the timeframe
Publication status		
Publications	State reference(s) to publications State reference to clinicaltrials.gov entry	State reference(s) to publications State reference to clinicaltrials.gov entry

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Description of Studies

For each study the following information should be presented (in the same order for each study): the study objectives, a description of the design, patients, sample size (N), locations including number of sites in Canada, study treatments, randomization, whether randomization was stratified.

- Provide data cut-off dates.
- Add a summary/simple figure if useful to explain/contrast study design where there are multiple trials with different run-ins, follow-up duration, different design features such as re-randomization, etc.
- Provide descriptions of the studies in text that point out key design features (e.g., adaptive design, enrichment design, withdrawal design, cross-over design) and key points related to those features (e.g., duration of washout period between treatment periods in a cross-over study).
- For studies with a run-in/screening period, a description of its purpose should be included.

Eligibility Criteria

Comment on criteria of note; there is no need to repeat all criteria listed in the summary table(s) provided above.

- Emphasize any key inclusion/exclusion criteria that are of importance to the condition or may identify a niche patient population
- Identify any important differences in inclusion and exclusion criteria between the studies.
- Maximum 1 paragraph

Interventions

Briefly describe the interventions employed in the included trials, including dose, route of administration, frequency of administration, and duration of treatment. A description of the titration schedule should be included for both the intervention and comparator(s) where relevant. The criteria used for determining the titration schedule should be included (e.g., fixed schedule or titration to target). For non-oral medications or medications requiring a device for administration (e.g., insulin pen, auto-injector, inhalation device), details related to the device, training, and administration should be included, examples of which are provided below:

- For an injection, details may include whether the injection was self-administered or administered by study personnel at a study visit.
- For an infusion, please include the infusion duration and indicate in what setting the infusion will be administered (i.e., hospital or infusion center).
- If a device was used, please describe the training that was given initially and at each study visit. Please indicate if the device that was used is the same one that is or will be available in Canada.

If the trial is blinded, indicate the use of placebos, double-dummy controls, and provide a brief description of the placebo including any methods to match administration and avoid unblinding.

Include any criteria for rescue medication use where applicable, along with dosing schedules and maximum dosages permitted. Describe any stopping criteria for the intervention if relevant.

Outcomes

Describe each of the outcome measures reported in the systematic review and provide information on minimal important differences (MID). Ensure that a reference list and copies of articles addressing the validity of outcome measures (including surrogate outcomes) are provided in the application.

- Briefly describe the relevant efficacy outcomes for the included studies (i.e., all outcomes included in the protocol) in sufficient detail for the reader to be able to understand and interpret the outcome data (definitions and measurement).
- Descriptions of scale measures should include a brief overview of the scale including:
 - Construct(s) or domain(s) measured
 - Structure of the scale (i.e., is there one single overall score or individual domain scores or both)
 - Range of scores.
 - Direction of the scale (e.g., do higher scores indicate greater impairment? Better HRQoL?)
 - Whether or not an estimated MID was identified (for overall and individual domain scores). Please clearly state the source of the MID (e.g., reference to publication, regulatory opinion, clinical expert opinion) and the method used for estimation (e.g., anchor-based) and whether the MID refers to within-group or between group differences (or both). Identify the population in which the MID was estimated (e.g., patients with severe COPD; general population estimate). If multiple estimates of the MID are identified, the full range of MIDs should be reported. If no MID has been identified, this should be explicitly stated.

- For surrogate outcomes, summarize the clinical evidence underlying or justifying the use of a surrogate as well as the evidence for the validation of the surrogate.
- Describe how outcomes are adjudicated (centrally adjudicated, or investigator adjudicated, or both).
- Responder definitions, cut points and rationale for cut point selection should be described and referenced.
- Define key harms outcomes.

The summary table below is required for all applications. When identifying primary and secondary endpoints, include a “*” and footnote identifying which endpoints were adjusted for multiple comparisons in the statistical analyses.

Table Number: Summary of Outcomes Relevant to the Systematic Review

Outcome Measure	Timepoint	Study 1	Study 2
List outcome 1	Please be specific (e.g., at 24 weeks; through 24 weeks)	Please state as: • Primary* • Key secondary* • Secondary • Tertiary • Exploratory • If the outcome listed in the row was used in some studies, but not others state ‘not applicable’ for those that did not include the outcome. Use a “*” and include a footnote to identify endpoints where statistical testing was adjusted for multiple comparisons	Please state as: • Primary* • Key secondary* • Secondary • Tertiary • Exploratory • If the outcome listed in the row used in some studies, but not others state ‘not applicable’ for those that did not include the outcome. Use a “*” and include a footnote to identify endpoints where statistical testing was adjusted for multiple comparisons
List outcome 2	As above	As above	As above
Add rows as necessary			

* Statistical testing for these endpoints was adjusted for multiple comparisons (e.g., hierarchal testing)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Statistical analysis

Clinical Trial Endpoints

Provide a brief description of the statistical analysis for each outcome reported in the systematic review.

- The rationale for selection of the statistical test or model (e.g., non-parametric or parametric testing, ANCOVA for continuous outcome, logistic regression or survival analysis for binary outcome) should be reported.
- The covariates and/or baseline values that were included in the statistical models should be specified. It should be stated that the analysis was unadjusted if no covariates and/or baseline values were included in the analysis.
- If a historical control was used, the source of the data and method for statistical comparison to the active treatment arm should be reported.
- Data imputation and other missing data methods (e.g., LOCF, statistical models such as MMRM, non-responder imputation) and the associated assumptions should be reported.

- How intercurrent events were handled. Intercurrent events are events of interest that occur after a treatment has been initiated that may impact the interpretation of the end point (e.g., the event modified the treatment effect, such as in the use of rescue medications or other concomitant treatments, or has implications for adherence to the treatment regimen, including premature treatment discontinuation).
- The main sensitivity analyses, if any, and the rationale for the analysis (e.g., alternate analyses that use different imputation techniques) should be described.
- Repetition within the description and the information provided in the summary table(s) should be avoided where possible. If methods for the secondary outcomes are similar to those for the primary outcome, simply state this and highlight any differences.
- Items should be summarized in a table where appropriate (see example below).

Table Number: Statistical Analysis of Efficacy Endpoints

Endpoint	Statistical Model	Adjustment Factors	Handling of missing data	Sensitivity Analyses
Study 1				
List endpoint 1	e.g., MMRM	Please list the factors which were adjusted (e.g., baseline values, age, etc.)	Please state how missing data were addressed	Please list all sensitivity analyses (e.g., multiple imputation)
Add rows as required	As above	As above	As above	As above
Study 2				
As above	As above	As above		As above

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Sample Size and Power Calculation

Report assumptions regarding expected differences in treatment effect and variation (e.g., SD), as well as the rationale for selecting the parameters used in the calculation. Other potentially relevant information (e.g., whether loss to follow-up was accounted for, if there were power calculations for secondary endpoints) should be reported as applicable.

Statistical Testing

Please provide the rationale for selection of the statistical test or model (e.g., non-parametric or parametric testing, ANCOVA for continuous outcome, logistic regression or survival analysis for binary outcome). The covariates and/or baseline values that were included in the statistical models should be specified. It should be stated that the analysis was unadjusted if no covariates and/or baseline values were included in the analysis.

For noninferiority studies, state the methods used in the construction of the confidence interval, the noninferiority margin, and the justification for its selection, including clinical and statistical considerations. If a secondary analysis of superiority was performed, state if this was planned or performed post hoc.

For multiple primary endpoints or analysis of the individual components of the composite endpoints, it should be specified if the analysis approach accounted for multiple testing with an appropriate control of the Type I error rate. For multi-arm trials, describe which arms were compared and whether a statistical adjustment was made for multiple testing with an appropriate control of the Type I error rate.

State whether the analyses presented in the report are the final analyses or interim analyses. If there were interim analyses, please state how these were accounted for in the statistical testing plan. For complex statistical testing structures (e.g., multiple endpoints) please ensure that the alpha level used for the endpoints is clearly stated in this section (please use a table to summarize if appropriate).

Subgroup Analyses

Key details of subgroup analyses should be reported, including whether they are pre-specified, whether the comparability of the treatment arms was checked, and whether multiplicity was taken into account.

Analysis populations

Define analysis sets (e.g., FAS, PP, safety set) for each study included in the systematic review using a summary table.

Table Number: Analysis Populations of Study 1 and Study 2

Study	Population	Definition	Application
Study 1	e.g., Full analysis set	Add definition as per study protocol	State how the population was used in the analyses (e.g., all efficacy analyses)
	e.g., Safety analysis set	Add definition as per study protocol	State how the population was used in the analyses
	Add rows as required	Add rows as required	Add rows as required
Study 2	Add rows as required	Add rows as required	Add rows as required

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Patient Population

Baseline characteristics

Summarize relevant baseline demographic and clinical characteristics of the population for each study using a table (example table below). Indicate in the table which analysis set the baseline characteristics have been summarized for (e.g., FAS set)

- for discrete data please report as n (%)
- for continuous data please report the mean (SD); where continuous data are skewed also report the median (IQR or range)

More than one table can be created if all studies do not fit in a single table.

Table Number: Summary of Baseline Characteristics of Study 1 and Study 2

Characteristic	Study 1		Study 2	
	Treatment 1 (N =)	Treatment 2 (N =)	Treatment 1 (N =)	Treatment 2 (N =)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Patient Disposition

Please summarize the patient disposition for each included study using a table.

Table Number: Sample Table for Patient Disposition

Patient disposition	Study 1		Study 2	
	Treatment 1 (N =)	Treatment 2 (N =)	Treatment 1 (N =)	Treatment 2 (N =)
Screened, N				
Reason for screening failure, N (%)				
State reason 1				
State reason 2				
Add rows as required				
Randomized, N (%)				
Discontinued from study, N (%)				
Reason for discontinuation, N (%)				
Adverse events				
Lost to follow-up				
Add rows as required				
FAS, N				
PP, N				
Safety, N				

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Exposure to Interventions

Study treatments

Summarize exposure using a table (example provided below). Within the text, please describe any discrepancies between treatment groups. Include information on adherence to treatment where relevant.

Table Number: Sample Table for Patient Exposure

Exposure	Study 1		Study 2	
	Treatment 1 (N =)	Treatment 2 (N =)	Treatment 1 (N =)	Treatment 2 (N =)
Total, patient-weeks or patient-years				
Duration, mean (SD)				
Duration, median (IQR or range)				
Adherence, %				

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Concomitant medications and co-interventions

- Provide a table summarizing relevant concomitant medications used during the studies.

Within the text, describe any concomitant medications or co-interventions required or permitted during the study. If concomitant medication doses were lowered or treatment stopped, describe the schedule as applicable (e.g., tapering corticosteroids).

Subsequent treatment (if applicable)

Please describe any protocols for managing cross-over to other treatment groups (e.g., placebo to active treatment) or the provision of additional therapies or interventions during the treatment period or follow-up phase (e.g., additional anticancer medication or surgery upon documented disease progression). Consider adding a table to summarize the overall use of subsequent treatments and provide a breakdown of specific treatments and/or interventions.

Table Number: Sample Table for Subsequent Treatment

Exposure	Study 1		Study 2	
	Treatment 1 (N = Click here to enter text)	Treatment 2 (N = Click here to enter text)	Treatment 1 (N = Click here to enter text)	Treatment 2 (N =)Click here to enter text
Received subsequent therapy, n (%)				
State therapy, n (%)				
State therapy, n (%)				
Add rows as required				

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Results

Efficacy

A separate subsection for each outcome should be included. Each subsection should summarize the results of the outcome for each study in which it was measured.

Summary of efficacy outcomes

Provide a table similar to the example below summarizing key efficacy outcomes for the studies. For any included figures, indicate the data source including citation (and corresponding figure number in the clinical study report where applicable).

For time-to-event analyses overall frequency of events, number of patients censored, and time of follow-up (e.g., total days of follow-up, median or mean time of follow-up) for each stratum should be presented descriptively.

In addition to any relevant relative differences in effects (e.g., odds ratio, relative risk, hazard ratio), absolute differences in effects with confidence intervals should be presented in the data tables when possible, even if they are not part of the statistical analysis plan. These include mean difference for continuous outcomes, risk difference for dichotomous outcomes, and difference in survival probability at relevant time points for outcomes from time-to-event analyses. Absolute effects and their confidence intervals are essential for the review team's appraisal of the clinical importance of the reported effects.

Table Number: Sample table for key efficacy outcomes

	Study 1 Treatment 1 N =	Study 1 Treatment 2 N =	Study 2 Treatment 1 N =	Study 2 Treatment 2 N =
Outcome 1				
Number of patients contributing to the analysis				
Baseline, mean (SD)				
Change from baseline, mean (95% CI preferred; SE if not available)				
Treatment group difference versus control (95% CI)				
P value				
Outcome 2				
n (%)				
OR/RR (95% CI)				
RD (95% CI)				
P value				
Outcome 3				
Events, n (%)				
Censored, n (%)				
Censoring reason 1 (add rows as needed), n (%)				
Overall survival (months), median (95% CI)				
HR (95% CI)				
P value				
Survival probability (%) at X months (95% CI)				
Difference in survival probability (%) (95% CI)				
Outcome 4				
As above				

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; FAS = full analysis set; RR = relative risk; OR = odds ratio.

*Specify if the P-value has been adjusted for multiple testing using a superscript 'a'

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Efficacy outcome 1

The text of the efficacy section should convey the main messages of the data that are presented in tables or graphs — please be concise and clear in the text.

Please avoid the following when presenting results:

- Interpreting the difference between two groups as being statistically significant based upon nonoverlapping confidence intervals for the individual within groups change (rather than a statistical test of the difference between groups).

- Interpreting the clinical relevance of statistically nonsignificant findings.
- Focusing on the clinical relevance of within groups changes rather than the clinical relevance of the difference in the between groups change when there is a comparison group or historical control.

For time-to-event analyses overall frequency of events, number of patients censored, and time of follow-up (e.g., total days of follow-up, median or mean time of follow-up) for each stratum should be presented descriptively.

In addition to any relevant relative differences in effects (e.g., odds ratio, relative risk, hazard ratio), absolute differences in effects with confidence intervals should be presented in the data tables when possible, even if they are not part of the statistical analysis plan. These include mean difference for continuous outcomes, risk difference for dichotomous outcomes, and difference in survival probability for outcomes from time-to-event analyses. Absolute effects are essential for the review team's appraisal of the clinical importance of the reported effects.

Report the results from key sensitivity analyses and subgroup analyses under each of the outcomes. Subgroup analyses should reflect those that are specified within the systematic review protocol.

If data within the report are derived from different cut-off dates, please ensure that the dates are clearly specified when reporting the results.

Efficacy endpoint 2

Please use a separate subheading for each endpoint.

Efficacy endpoint 3

Please use a separate subheading for each endpoint.

Table Number: Sample table for efficacy outcome

	Treatment 1 N = Click here to enter text	Treatment 2 N = Click here to enter text
Example of continuous outcome (units)		
Number of patients contributing to the analysis		
Baseline, mean (SD)		
End of treatment time point (specify), mean (SE)		
Change from baseline, mean (SE)		
Treatment group difference versus control (95% CI)		
P value		
Example of dichotomous outcome (units)		
n (%)		
OR/RR (95% CI)		
RD (95% CI)		
P value		
Example of outcome from time-to-event analysis		
Events, n (%)		
Overall survival (months), median (95% CI)		
HR (95% CI)		
P value		
Survival probability (%) at X months (95% CI)		

	Treatment 1 N = Click here to enter text	Treatment 2 N = Click here to enter text
Difference in survival probability (%) (95% CI)		

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Harms

In this space the sponsor must summarize key adverse event data for the drug under review. Whenever possible, focus on integrated safety data and only summarize individual trials if they are not included in the pooled safety analyses (e.g., relevant trials that conducted after the integrated analysis was completed). Do not report results of statistical analyses for safety outcomes.

Table Number: Sample table for key harms data

Adverse events	Treatment 1 (N = Click here to enter text)	Treatment 2 (N = Click here to enter text)
Most common adverse events, n (%)		
≥ 1 adverse event		
State adverse event		
State adverse event		
Add rows as required		
Serious adverse events, n (%)		
Patients with ≥ 1 SAE		
State SAE		
State SAE		
Add rows as required		
Patients who stopped treatment due to adverse events, n (%)		
Patients who stopped		
State adverse event		
State adverse event		
Add rows as required		
Deaths, n (%)		
Patients who died		
Add description of events or list of common causes of death		
Add rows as required		
Adverse events of special interest, n (%)		
Specify events based on those listed in the safety evaluation plan, n (%)		
Add rows as required		



Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Safety Evaluation Plan

Provide a brief overview of the overall safety evaluation plan for the drug under review and clearly identify the population that is summarized in this template. This will typically align with the safety population that is used in the product monograph. Keep this description to a maximum of a half page.

Overview of Safety

Summarize the key findings of the safety evaluation for the drug under review. Provide an overall summary table of key harms data (example shown below). Please note the following:

- Thresholds for common events may vary across development programs. Please ensure that the threshold for inclusion in the table is clearly reported (e.g., $\geq 5\%$ of patients). The threshold should generally align with what has been included in the draft or final product monograph.
- Please report individual events at the preferred term level.

Adverse Events

Report treatment-emergent adverse events (do not report treatment-related adverse events).

Serious Adverse Events

Summarize treatment-emergent serious adverse events (do not report treatment-related events).

Withdrawals Due to Adverse Events

Summarize withdrawals due to adverse events and adverse events that resulted in an interruption of the study treatment(s). Clearly identify if the adverse events resulted in discontinuation of the study treatment and/or complete discontinuation from the study.

Adverse Events of Special Interest

Provide a brief summary of any adverse events of special interest. If relevant, provide a summary of how these events were managed in the clinical trial.

Sponsor Summary and Conclusion

In this space the sponsor may provide a brief summary and their conclusions regarding the evidence included in the systemic review. **This section must not exceed 1 page.**

Sponsor Identified Gaps in the Evidence

Please clearly identify any important gaps in the evidence summarized in this section. If the sponsor is providing additional evidence in Section 5 to address important gaps in the evidence that has been presented within Section 2 of the template, the gaps must be identified in this space.

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.

Section 3. Long-Term Extension Studies

This section should provide a brief summary of long-term extension studies that are completed or have interim analyses at the time of filing the application with CDA-AMC.

- If there are multiple studies, please summarize each study separately.
- If any information in the sections below is the same as the parent study and described previously in the template, please state this, and refer the reader to the appropriate sections of the report. Do not repeat the information in this section.

Description of Studies

Study Design and Objectives

Briefly describe the study design and include any connection to studies included in the systematic review (if applicable). For example, “this study was a long-term extension of the [pivotal trial name]”.

Eligibility criteria

Briefly describe the inclusion and exclusion criteria. Any criteria for continuing from the pivotal trial into the extension trial should be specified.

Interventions

Briefly describe the interventions used in the study and use of concomitant medications and/or treatments.

Outcomes

Provide a brief summary of the efficacy and safety outcomes that will be included in this summary.

Statistical analysis

Provide a brief summary of the key components of any statistical analyses. For all analyses clearly define when the baseline assessments were performed (e.g., at the outset of the parent study or the beginning of the extension study).

Patient Population

Baseline characteristics

Summarize relevant baseline demographic and clinical characteristics using a table (example table below). Indicate in the table which analysis set the baseline characteristics have been summarized for (e.g., safety analysis set).

Table Number: Summary of Baseline Characteristics

Characteristic	Study 1		Study 2	
	Treatment 1 (N = Click here to enter text)	Treatment 2 (N = Click here to enter text)	Treatment 1 (N = Click here to enter text)	Treatment 2 (N =)Click here to enter text

Characteristic	Study 1		Study 2	
	Treatment 1 (N = Click here to enter text)	Treatment 2 (N = Click here to enter text)	Treatment 1 (N = Click here to enter text)	Treatment 2 (N =)Click here to enter text

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Patient Disposition

Summarize patient disposition for the study using a summary table.

Exposure to study treatments

Study treatments

Summarize exposure using a table (example provided below). Within the text, please describe any discrepancies between treatment groups. Include information on adherence to treatment where relevant.

Table Number: Sample Table for Patient Exposure

Exposure	Study 1		Study 2	
	Treatment 1 (N = Click here to enter text)	Treatment 2 (N = Click here to enter text)	Treatment 1 (N = Click here to enter text)	Treatment 2 (N =)Click here to enter text
Total, patient-weeks or patient-years				
Duration, mean (SD)				
Duration, median (IQR or range)				
Adherence, %				

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Concomitant medications and co-interventions

Provide a summary table summarize relevant concomitant medications used during the studies.

Within the text, describe any concomitant medications or cointerventions required or permitted during the study. If concomitant medication doses were lowered or treatment stopped, describe the schedule as applicable (e.g., tapering corticosteroids).

Subsequent treatment (if applicable)

Please describe any protocols for managing cross-over to other treatment groups (e.g., placebo to active treatment) or the provision of additional therapies or interventions during the treatment period or follow-up phase (e.g., additional anticancer medication or surgery upon documented disease progression). Consider adding a table to summarize the overall use of subsequent treatments and provide a breakdown of specific treatments and/or interventions.

Table Number: Sample Table for Subsequent Treatment

Exposure	Study 1		Study 2	
	Treatment 1 (N =)	Treatment 2 (N =)	Treatment 1 (N =)	Treatment 2 (N =)
Received subsequent therapy, n (%)				
State therapy, n (%)				
State therapy, n (%)				
Add rows as required				

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Results

Efficacy

Efficacy outcomes presented should be aligned with those reported for the studies included in the systematic review protocol. Present the efficacy outcomes in a table or figure, highlighting only key results in the text. For all analyses clearly define when the baseline assessments were performed (e.g., at the outset of the parent study or the beginning of the extension study).

Efficacy endpoint 1

Please use a separate subheading for each endpoint.

Efficacy endpoint 2

Please use a separate subheading for each endpoint.

Efficacy endpoint 3

Please use a separate subheading for each endpoint.

Harms

Present the safety outcomes in a table and summarize key findings in the text. Include AEs, SAEs, WDAEs, deaths, and adverse events of special interest. Make sure to use data from treatment-emergent adverse events.

Table Number: Summary of Harms

Adverse events	Treatment 1 (N = Click here to enter text)	Treatment 2 (N = Click here to enter text)
Most common adverse events, n (%)		
≥ 1 adverse event		
State adverse event		
State adverse event		
Add rows as required		
Serious adverse events, n (%)		

Patients with ≥ 1 SAE		
State SAE		
State SAE		
Add rows as required		
Patients who stopped treatment due to adverse events, n (%)		
Patients who stopped		
State adverse event		
State adverse event		
Add rows as required		
Deaths, n (%)		
Patients who died		
Add description of events or list of common causes of death		
Add rows as required		
Adverse events of special interest, n (%)		
Specify events based on those listed in the safety evaluation plan, n (%)		
Add rows as required		

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Sponsor Summary and Conclusion

In this section the sponsor may provide a brief summary and their conclusions regarding the evidence from the long-term extension studies. **This must not exceed 1 page.**

Sponsor Identified Gaps in the Evidence

Please clearly identify any important gaps in the evidence summarized in this section. If the sponsor is providing additional evidence in Section 5 to address important gaps in the evidence that has been presented within Section 3 of the template, please clearly identify the gaps in this space.

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.

Section 4. Indirect Evidence

In this section of the template the sponsor must summarize all indirect comparisons that have been included in the application (i.e., to support comparative efficacy or safety and/or the assumptions in the pharmacoeconomic model).

If no indirect comparisons are included in the application, please provide the following:

- Rationale for why no indirect comparisons have been included in the application.
- If a feasibility assessment was performed and the sponsor concluded that an indirect comparison was not possible based on the available information, please clearly describe the assessment and the barriers that precluded the indirect comparison.

Description of Indirect Comparison(s)

In this section the sponsor should summarize the methods and results of all indirect comparisons included in the application.

Objectives

Provide the objective of the indirect comparison focusing on the evidence gap it is aiming to address (e.g., absence of direct evidence for relevant comparators).

Study Selection Methods

Summarize each included ITC in tabular format using one or more tables similar to the one below. Do not repeat information in the text that is presented in the tables.

- Describe the methods used to conduct the systematic review and to select studies for inclusion in the indirect comparison.
- Describe the methods used to extract data (e.g., duplicate extraction, or single reviewer extraction with check).
- Describe how the authors assessed study quality, and how this information was used (e.g., to exclude certain studies).

Table Number: Study Selection Criteria and Methods for Indirect Comparisons

Characteristics	Indirect Comparison
Population	Click here to enter textBriefly state the population(s) of interest for the indirect comparison
Intervention	Click here to enter textList intervention including dosing information
Comparator	Click here to enter textList comparators including dosing information
Outcome	Click here to enter textList outcomes including time points
Study designs	Click here to enter textBriefly describe the study designs included in the indirect comparison
Publication characteristics	Click here to enter textSpecify inclusion of published and/or unpublished studies
Exclusion criteria	Click here to enter textBriefly describe the exclusion criteria used for selecting studies
Databases searched	Click here to enter textBriefly list databases included in the literature search
Selection process	Click here to enter textBriefly describe the review methods (e.g., articles screened independently by 2 researchers)
Data extraction process	Click here to enter textBriefly describe the review methods
Quality assessment	Click here to enter textBriefly describe the methods used to assess the quality of studies (e.g., appraisal tools)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation.

Indirect comparison analysis methods

- Describe the statistical model and the justification in the selection of the methods.
- Describe the feasibility assessment and how well the underlying assumptions of the methods were supported.
- Describe how model fit was assessed. If multiple models were run, describe how the model selected as the primary analysis was chosen. If only 1 model was used, please provide the reason(s).
- Please note the following for Bayesian models:
 - o Describe prior distributions for modeling parameters.
 - o Describe justification for use of informative priors, and whether sensitivity analyses were done to assess the impact of the priors selected.
 - o Convergence diagnostics, burn-in period, number of iterations and number of chains should also be described.
- Matching-adjusting indirect comparison (MAIC):
 - o Describe the justification conducting a MAIC and for the comparator chosen.
 - o Specify whether an anchored or unanchored MAIC was conducted
 - o Describe sources of heterogeneity that were identified between trials in the comparison. Specify whether any methods were used to account for heterogeneity prior to the weighting process including whether any patients were excluded from the trial.
 - o Describe any processes used to identify baseline characteristics that are potential effect modifiers and, for unanchored comparisons, prognostic factors.
 - o Describe what characteristics were identified in the variable selection process, and which of these variables were ultimately adjusted for in the weighting process. Specify the justification for excluding any variable identified in the variable selection process.
 - o Describe the method used to calculate the weight of individual patient data.
 - o Describe the approach used to estimate the parameters of the model.
 - o Describe if effective sample size measures and any other weight assessments were reported.
- Describe how homogeneity was assessed. Please ensure to address clinical, methodological, and statistical heterogeneity.
- Discuss any steps taken to address potential sources of heterogeneity (e.g., excluding studies, doses, or timepoints from the analysis) or meta-regression analyses.
- Provide rationale for sensitivity analysis with description of methods used.
- Provide rationale for subgroup analysis with description of methods used.
- Describe how consistency between direct and indirect comparisons were evaluated if relevant (e.g., inconsistency modelling, simple direct versus indirect, or if it was not possible to assess consistency due to the lack of a closed loops)
- Describe methods used to conduct standard pairwise meta-analysis (if conducted).
- For Network Meta-Analyses, describe how nodes in the network were constructed, how different doses, different routes of administration, different drugs within the same class, and comparators were handled (separate nodes or pooled analysis).

- Describe (where appropriate) methods used for rescaling or conversion of results to a common scale, in cases where studies reported different scales or measures. Discuss appropriateness of any methods for reconstructing individual patient data from summary data.
- Describe (where appropriate) which set of analysis results have been used where studies have conducted multiple analyses of a given endpoint (e.g., multiple approaches to dealing with missing data).
- List which outcomes were analyzed and the rationale for excluding any of those that were pre-planned for analyses.
- The table below provides an example of how the key data element may be described using a table format. The sample table is focussed on describing Bayesian NMA methods and likely needs modification for other approaches. Add or delete rows as appropriate. As methods may vary for different types of outcomes (continuous, dichotomous) or by network or population, additional columns may be added as needed.

Table Number: Indirect Comparison Analysis Methods

Methods	Description
Analysis methods	Click here to enter text Briefly describe the methods
Priors	Click here to enter text As above
Assessment of Model fit	Click here to enter text As above
Assessment of Consistency	Click here to enter text As above
Assessment of Convergence	Click here to enter text As above
Outcomes	Click here to enter text As above
Follow-up timepoints	Click here to enter text As above
Construction of nodes	Click here to enter text As above
Sensitivity analyses	Click here to enter text As above
Subgroup analysis	Click here to enter text As above
Methods for pairwise meta-analysis	Click here to enter text As above

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation.

Results

Summary of included studies

The table below is an example of what may be used to provide a description of important differences across trials for key characteristics. The list of characteristics are examples; please add rows as appropriate (and delete a row only if the characteristic is irrelevant). No evidence of effect modification may be added as a comment, if appropriate.

Describe the trials included in the systematic review, and the indirect comparison analysis (including number of trials and patients), highlighting any potential sources of heterogeneity (e.g., in the patients, interventions, outcomes, study design or follow up time). Please ensure that features that could lead to differences in treatment effect modifiers are addressed (e.g., patients recruited to studies of A versus B have less advanced disease than those in A versus C).

Consider: Dosage, treatment duration, route of administration, supportive care as well as information on treatment titration, induction or maintenance treatment. Highlight the differences between trials, if any.

Table Number: Sample Table for Assessment of Homogeneity

Characteristics	Description and handling of potential effect modifiers
Disease severity	Click here to enter textComment on similarities and differences across studies and note if there were any relevant adjustments or sensitivity analyses. Indicate when the information required to compare across studies is missing (i.e., not reported).
Treatment history	Click here to enter textAs above
Trial eligibility criteria	Click here to enter textAs above
Dosing of comparators	Click here to enter textAs above
Placebo response	Click here to enter textAs above
Definitions of endpoints	Click here to enter textAs above
Timing of endpoint evaluation	Click here to enter textAs above
Withdrawal frequency	Click here to enter textAs above
Clinical trial setting	Click here to enter textAs above
Study design	Click here to enter textAs above

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation.

Evidence Networks

Provide a graphical depiction of the evidence network for each outcome of interest, if available. If a graphical description is not available, briefly describe the network, including the overall number of studies and number of studies contributing to the direct and indirect estimates for important comparisons. For any included figures, indicate the corresponding figure number in the technical report.

Efficacy

Provide a summary of the indirect comparison results for efficacy outcomes, including point estimates and 95% confidence intervals and/or credible intervals (as appropriate for the method of analysis) for pairwise comparisons of interest to the review. The focus should be on comparisons with relevant comparators, particularly those not assessed in the systematic review evidence. If appropriate, present a tabular summary of the results that contains only the results for the most relevant interventions and outcomes). The tables below provide example formats that may be used to summarize results.

- Describe the results relating to how well the selected model(s) fits the data
- Describe the results of any assessments that were conducted such as assessments of heterogeneity, consistency, and, for MAICs, an assessment of weights. An assessment of weights for a MAIC should at minimum include reporting the effective sample size, both overall and as a percentage of the original sample size of the trial after exclusions.
- Provide a brief summary of the results of subgroup analyses and/or meta-regression, if relevant. Only if relevant/necessary, present the results of one or more sensitivity analyses. It is often sufficient to state that the results of all sensitivity analysis were consistent with the base case (if the methods used for the sensitivity analyses are appropriate and described adequately).

Table Number: ITC Sample Data Table for Continuous Outcomes (e.g., Summary of NMA Results for Efficacy Results, [Treatment] Versus Comparators)

Comparator	Outcome 1 (units) at time point, mean difference (95% CrI)	Outcome 2 (units) at time point, mean difference (95% CrI)
[Comparator 1]		
[Comparator 2]		
[Comparator 3]		

Abbreviations must be listed under the table in alphabetical order. For example, CrI =, credible interval; OR = odds ratio; NA = not applicable; NMA = network meta-analysis.

Source: Indicate data source including citation (and corresponding table number[s] in the technical report where applicable).

Table Number: ITC Sample Data Table for Dichotomous Outcomes (e.g., Summary of NMA Results for Efficacy Results, [Treatment] Versus Comparators)

Comparator	Outcome 1 (units) at time point, OR (95% CrI)	Outcome 2 (units) at time point, OR (95% CrI)
[Comparator 1]		
[Comparator 2]		
[Comparator 3]		

Abbreviations must be listed under the table in alphabetical order. For example, CrI =, credible interval; OR = odds ratio; NA = not applicable; NMA = network meta-analysis.

Source: Indicate data source including citation (and corresponding table number[s] in the technical report where applicable).

Efficacy endpoint 1

Please use a separate subheading for each endpoint.

Efficacy endpoint 2

Please use a separate subheading for each endpoint.

Efficacy endpoint 3

Please use a separate subheading for each endpoint.

Harms

Provide a summary of the indirect comparison results for harms outcomes using the guidance provided above. If no harms endpoints were evaluated in the indirect comparison, please state this within this section (i.e., do not delete the section heading in the absence of comparative harms data).

Sponsor Summary and Conclusion

In this section the sponsor may provide a brief summary and their conclusions regarding the evidence from the indirect comparisons. **This section must not exceed 1 page.**

Section 5. Studies Addressing Gaps in the Pivotal and RCT Evidence

In this section the sponsor may 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. Justification for the inclusion of real-world evidence must be provided; this should cover, as relevant, the reasons for the absence of randomized evidence, the limitations of existing trials, and the ability to produce meaningful real-world evidence for the specific research question.

If no additional evidence is provided, this section can be deleted.

Summary of Gaps in the Evidence

The summary table below is required for all applications where the sponsor chooses to include additional evidence.

Table Number: Summary of Gaps in the Evidence

Gap in Pivotal and RCT Evidence	Studies that Address Gaps	
	Study Description	Summary of Key Results
Click here to enter text. e.g. Describe the populations and/outcomes that were not studied in the pivotal studies or other RCTs	Click here to enter text. Briefly describe (e.g., 52-week, prospective observational study)	Click here to enter text. Briefly describe the key results focusing on how the evidence addresses the important gap in the evidence
Add rows as required	As above	As above

If multiple studies are included, report the format below for each study under the appropriate subsection (either Clinical Trials or Studies of Other Designs). The Clinical Trials section may include trials that did not meet the inclusion criteria of the systematic review protocol but are included in Section 5 to fill a gap in the evidence and should be placed under a separate subsection from Studies of Other Designs (e.g., observational designs including real-world evidence studies). The Clinical Trials subsection may be further subdivided based on study design (e.g., Phase II RCTs, single-arm trials, RWE). Clinical trials of similar design may be summarized together with a subsection. Please delete the Clinical Trials or Studies of Other Designs subsection if no evidence is included in that subsection.

Description of (add Study ID)

If multiple studies are included, report the format below for each study.

Study Design and Objectives

Provide a brief overview of the study including study description (name, type, design).

For clinical trials included in Section 5, provide a brief overview of the study including a study description (e.g., study name, key design features, patient type, sample size (N), locations including number of sites in Canada, intervention, and comparator).

Eligibility criteria

For clinical trials included in Section 5, briefly describe the inclusion and exclusion criteria. Emphasize any key inclusion/exclusion criteria that are of importance to the condition or may identify a niche patient population.

Interventions

For clinical trials included in Section 5, briefly describe the interventions and comparators (if relevant) used in each study and use of concomitant medications and/or treatments.

Outcomes

Provide a brief summary of the efficacy and safety outcomes that will be included in this summary, with a focus on those outcomes that fill gaps in pivotal and phase 3 clinical trial evidence.

Statistical analysis

Provide a brief summary of the key components of any statistical analyses.

Patient Population

Baseline characteristics

Summarize relevant baseline demographic and clinical characteristics of each study using a table (example below). Where multiple clinical trials of the same design have been included in a subsection, this information can be summarized in a single table. Indicate in the table which analysis set the baseline characteristics have been summarized for (e.g., FAS set).

- for discrete data please report as n (%)
- for continuous data please report the mean (SD); where continuous data are skewed also report the median (IQR or range)

More than one table can be created if all studies do not fit in a single table.

Table Number: Summary of Baseline Characteristics of Study 1 and Study 2

Characteristic	Study 1		Study 2	
	Treatment 1 (N = Click here to enter text)	Treatment 2 (N = Click here to enter text)	Treatment 1 (N = Click here to enter text)	Treatment 2 (N =)Click here to enter text

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Patient disposition

Summarize patient disposition for each additional study using a summary table (if appropriate). Where multiple clinical trials of the same design have been included in a subsection, this information can be summarized in a single table.

Exposure to Interventions

Study treatments

Summarize exposure using a table (example provided below). Within the text, please describe any discrepancies between treatment groups. Include information on adherence to treatment where relevant. Where multiple clinical trials of the same design have been included in a subsection, this information can be summarized in a single table.

Table Number: Sample Table for Patient Exposure

Exposure	Study 1		Study 2	
	Treatment 1 (N = Click here to enter text)	Treatment 2 (N = Click here to enter text)	Treatment 1 (N = Click here to enter text)	Treatment 2 (N =)Click here to enter text
Total, patient-weeks or patient-years				
Duration, mean (SD)				
Duration, median (IQR or range)				
Adherence, %				

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Concomitant medications and co-interventions

Provide a table summarizing relevant concomitant medications used during the studies.

Within the text, describe any concomitant medications or cointerventions required or permitted during the study. If concomitant medication doses were lowered or treatment stopped, describe the schedule as applicable (e.g., tapering corticosteroids).

Subsequent treatment (if applicable)

Please describe any protocols for managing cross-over to other treatment groups (e.g., placebo to active treatment) or the provision of additional therapies or interventions during the treatment period or follow-up phase (e.g., additional anticancer medication or surgery upon documented disease progression). Consider adding a table to summarize the overall use of subsequent treatments and provide a breakdown of specific treatments and/or interventions.

Table Number: Sample Table for Subsequent Treatment

Exposure	Study 1		Study 2	
	Treatment 1 (N = Click here to enter text)	Treatment 2 (N = Click here to enter text)	Treatment 1 (N = Click here to enter text)	Treatment 2 (N =)Click here to enter text
Received subsequent therapy, n (%)				
State therapy, n (%)				
State therapy, n (%)				
Add rows as required				

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Results

Efficacy

Present the efficacy outcomes in a table or figure, highlighting only key results in the text. For all analyses clearly define when the baseline assessments were performed (e.g., at the outset of the parent study or the beginning of the extension study).

Efficacy endpoint 1

Please use a separate subheading for each endpoint.

Efficacy endpoint 2

Please use a separate subheading for each endpoint.

Efficacy endpoint 3

Please use a separate subheading for each endpoint.

Harms

Present the safety outcomes in a table and summarize key findings in the text. Include AEs, SAEs, WDAEs, deaths, and adverse events of special interest. Make sure to use data from treatment-emergent adverse events.

Studies of Other Design

If multiple studies of other designs are included in Section 5, report the format below for each study sequentially. Modify the heading as appropriate (e.g., Real-World Evidence).

Description of (add Study ID)

Study Design and Objectives

For studies of other designs included in Section 5 (e.g., observational designs including real-world evidence studies) briefly describe the specific objectives, any prespecified hypotheses, and key elements of study design. Key elements of study design may include setting, locations, and relevant study dates, including periods of recruitment, exposure, follow-up, and data collection. The data source should be specified, including linkages between datasets if relevant. For prospective studies, methods of follow-up should be described.

Eligibility criteria

Report the eligibility criteria for participant selection, taking into consideration the specific study design. Provide the sources and methods for selection of participants or case ascertainment (as relevant according to the specific study design). Diagnostic criteria or algorithms used to identify or classify participants or cases should be described. When matching is a design feature, criteria for matching (for example, selecting controls to match to cases) should be described.

Interventions and Exposures

Include clear definitions of exposures to treatment and to potential confounders. Clear descriptions of the assumptions and algorithms used to classify exposures to the intervention, comparator, any concomitant treatments (where relevant) and potential confounders should be provided. The time window during which an individual is considered exposed to an intervention should be described, as well as the approach used to handle individuals with more than one

relevant drug exposure during the study period. Where multiple data sources have been combined, the comparability across data sets or groups should be described.

Outcomes

Clearly define all relevant efficacy and safety outcomes with a focus on those that are reported to fill gaps in pivotal and phase 3 clinical trial evidence. Include clear descriptions of the assumptions and algorithms used to define outcome variables where applicable. If data are obtained from more than one source, the comparability across data sets or groups should be described.

Statistical analysis

For studies of other designs included in Section 5 (e.g., observational designs including real-world evidence studies), the description of the statistical analysis will be specific to the study design but generally should include a description or explanation of the following (where relevant):

- How the sample size was determined
- The statistical models and tests including all covariates or confounders adjusted for.
- Methods to control for confounding
- Handling of quantitative variables in the analysis
- Methods for matching
- Handling of missing data and data imputation
- How loss to follow-up was addressed for cohort studies
- Methods used to control for multiple comparisons
- Sensitivity analysis
- Subgroup analysis

Patient Population

Participant Characteristics

Summarize the characteristics of the eligible participants (e.g., demographic, clinical, social) and provide information on exposures and potential confounders. A table adapted to fit the specific study design should be included. Indicate the number of participants with missing data for each variable of interest. For cohort studies, the follow-up time (e.g., average and total amount) should also be reported.

Participant eligibility

Report the numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. The reasons for non-participation at each stage should be reported. Consider use of a flow diagram for reporting.

Exposure to Interventions

Exposures

For studies of other design that are included in Section 5 (e.g., observational designs including real-world evidence studies), the exposure(s) should be summarized in a table designed to fit the specific study design.



Concomitant medications, co-interventions, confounding treatments

Please summarize any concomitant or subsequent treatments.

Results

Efficacy

Present the efficacy outcomes in a table or figure, highlighting only key results in the text. Provide both unadjusted estimates and, if applicable, confounder-adjusted or covariate-adjusted estimates and their precision (e.g., 95% confidence interval). Report the results of key sensitivity analyses and subgroup analyses if relevant.

Efficacy endpoint 1

Please use a separate subheading for each endpoint.

Efficacy endpoint 2

Please use a separate subheading for each endpoint.

Efficacy endpoint 3

Please use a separate subheading for each endpoint.

Harms

Report the available or relevant adverse events which may include AEs, SAEs, deaths, and adverse events of special interest. Availability of harms data may be related to the specific design and may be reported as percent of population who experience one or more event, frequency of adverse events, or as rate (e.g., per patient-year)

Sponsor Summary and Conclusion

In this section the sponsor may provide a brief summary and their conclusions regarding the evidence from additional studies. **This must not exceed 1 page.**

Section 6. Summary of the Sponsor's Pharmacoeconomic Submission

Note: All sponsors are encouraged to complete this section; however, it is only a requirement for applications that will target the December 2026 expert committee meetings or later.

In this section of the template the sponsor must summarize the key methods and results of the pharmacoeconomic submission. The information is intended to be a summary and additional relevant details should be included in the economic evaluation technical report.

- The total length of this template cannot exceed 6 pages.
- Provide all references to source documentation.
- A RIS file containing all references used in this template must be submitted.

Key Components of the Sponsor's Economic Evaluation

Component	Description
Treatment information	
Drug under review (DUR)	• Click here to enter textState the generic name (Brand) of DUR, dosage form, and all strengths/concentrations as relevant. • Note if DUR is to be used in addition to other treatment(s), if relevant • Summarize the recommended dosage of DUR per the product monograph.
Submitted price of drug under review	• Click here to enter textState the price per lowest dispensable unit (e.g., per tablet, vial, prefilled syringe) to 2 decimal places for all submitted strengths/forms. • Prices must be aligned with those on the Pricing and Distribution form
Regimen	• Click here to enter textDescribe the dosage regimen used in the model for DUR • If this differs from the dosage regimen in the product monograph, state any differences and provide source/rationale for alternate dosing regimen. • Note if DUR is used in addition to other treatments (e.g., standard of care) or as part of a regimen (e.g., oncology regimens). Clearly state all components and dosages.
Annual cost, per-cycle cost, or one-time cost of drug under review	• Click here to enter textState the acquisition cost used in the model for DUR. For oncology submissions, this will typically be per 28-day treatment cycle. For non-oncology submissions, this will typically be annual treatment cost. If something different, clearly state the duration. • Note any modifying assumptions that were made in the calculation of drug costs (e.g., weight, if weight-based dose; relative dose intensity; different costs in first course vs. subsequent course) • If DUR is used in addition to standard of care (or another treatment), clearly state the acquisition cost of DUR and the other components
Model information	
Type of economic evaluation	• Click here to enter textCost-utility analysis • State the model type: Markov model, PSM, decision tree etc.

Component	Description
Treatment	Click here to enter textState the DUR or regimen under review
Included comparator(s)	- Click here to enter textState the generic name of each comparator - Note if each comparator is used in addition to other treatment(s). - If best supportive care, standard of care, etc. is included as a comparator, clearly define the components. - If multiple comparators, use an alphabetized, bulleted list. - If relevant, note if comparators differ across subgroup analyses
Perspective	- Click here to enter textPublicly funded health care payer perspective - If this is a Complex Review (Scenario 1), add: Societal perspective
Time horizon	Click here to enter textState the model time horizon. If lifetime, state: Lifetime (# years), else state # years
Cycle length	Click here to enter textState the model cycle length. If not applicable (e.g., for decision tree), state Not applicable.
Modelled population(s)	- Click here to enter textBriefly describe the modelled population - If relevant, describe any submitted subgroups - Describe any meaningful differences between the modelled population and the Health Canada indication (draft or approved).
Characteristics of modelled population	- Click here to enter textState the mean starting age of patients in the population, along with any other relevant characteristics (e.g., sex, weight, BMI, BSA). - Specify data for subgroups if relevant.
Model health states	- Click here to enter textState the model health states. - Detailed information about the health states should be provided in the Model Structure section below.
Duration of treatment	- Click here to enter textDescribe the duration of treatment in the model for DUR and comparators (if different). - Describe any differences between duration of treatment in the economic model versus any proposed reimbursement criteria as well as any differences versus any duration/discontinuation criteria specified in the product monograph.
Data sources	
Comparative efficacy	- Click here to enter textDescribe the sources, inputs, and assumptions made that inform the comparative efficacy of the drug under review relative to the included comparators. - Provide references where appropriate
Natural history and/or clinical pathway	- Click here to enter textBriefly describe the sources, inputs, and assumptions made that inform other aspects of the operation and output of the model. This could include: - disease natural history, population demographics, epidemiological parameters - health state transitions

Component	Description
	• <i>Provide references where appropriate</i>
Health-related utilities and disutilities	• <i>Click here to enter text</i>Briefly describe the sources, inputs, and assumptions pertaining to the derivation and application of health state utilities and disutilities • <i>Provide references where appropriate</i>
Costs	• <i>Click here to enter text</i>Briefly describe the sources, inputs, and assumptions for costs included in the model) • <i>Provide references where appropriate</i>
Summary of the submitted results	
Base case results	• <i>Click here to enter text</i>If 1 comparator, state: ICER = \$[to nearest dollar] per QALY gained versus [comparator] (incremental costs = \$X; incremental QALYs = X) • <i>If multiple comparators, indicate the ICER for DUR compared to the next drug on the frontier. Include incremental costs and incremental QALYs for the comparator used to calculate the ICER. Do not include comparators not on the frontier</i> • <i>If relevant, provide the results by subgroup.</i> • <i>If this is a Complex Review (Scenario 1), additionally present the results from the societal perspective</i>
Scenario analysis results	• <i>Click here to enter text</i>Provide the ICERs for all submitted scenario analyses

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-years; *[add as required]*.

Model Structure

- *If a PSM has been submitted, this section may be omitted. For all other model structures, provide a narrative description of the submitted model*
- *This section should provide a high-level summary of the submitted model structure including the components of the submitted model structure (e.g., health states, events)*
- *Describe how patients move through the model (e.g., cycling, progress and/or improve, tunnel states, time dependencies).*

Figure 1: Model Structure

Alt text: *Provide alt-text describing the figure.*

Abbreviations, *add as required (all abbreviations in the figure must be described here).*

Appendix 1: Literature Search Strategy

Example of Literature Search Strategy Reporting

Databases

- Ovid – MEDLINE All (1946-present)
- Ovid – Embase (1974-present)
- Ovid – Cochrane Central Register of Controlled Trials (CCTR)
- EBSCO – CINAHL
- Scopus
- Web of Science

Note: Subject headings and search fields have been customized for each database. Duplicates between databases were removed in Ovid. Other duplicates were removed using bibliographic management software.

Date of searches: [Provide search date. If dates vary, provide search date for each database]

Search filters applied: Systematic reviews; meta-analyses; network meta-analyses; health technology assessments; guidelines; overview of reviews; randomized controlled trials; controlled clinical trials; qualitative studies; observational studies; economic evaluations; costs and cost analysis studies, and quality of life studies.

Limits

- Publication date limit: none
- Language limit: none
- Humans

Database Search Strategies

Provide search strategies

Clinical Trials Registries

ClinicalTrials.gov

Produced by the U.S. National Library of Medicine. Targeted search used to capture registered clinical trials. [Search terms – List search terms]

WHO ICTRP

International Clinical Trials Registry Platform, produced by the World Health Organization. Targeted search used to capture registered clinical trials. [Search terms – List search terms]

Health Canada's Clinical Trials Database

Produced by Health Canada. Targeted search used to capture registered clinical trials. [Search terms – List search terms]

EU Clinical Trials Register

European Union Clinical Trials Register, produced by the European Union. Targeted search used to capture registered clinical trials. [Search terms – List search terms]

Appendix 2: List of Excluded Studies

Table Number: Excluded Studies

Reference	Reason for Exclusion
Click here to enter textAdd reference	Click here to enter textWhen identifying the reason for exclusion, please use a similar format as the following examples: • Study design • Intervention (if the intervention in the study does not meet that identified in the systematic review protocol, for example, different dose, formulation, etc.) • Comparator • Study population • Duplicate study
As above	As above
Add rows as necessary	

References

References must be provided in this section and should adhere to standard citation practices for publication, as per the following examples:

1. Murray CJL. Maximizing antiretroviral therapy in developing countries: the dual challenge of efficiency and quality [published online December 1, 2014]. *JAMA*. doi:10.1001/jama.2014.16376
2. Centers for Medicare & Medicaid Services. CMS proposals to implement certain disclosure provisions of the Affordable Care Act. <http://www.cms.gov/apps/media/press/factsheet.asp?Counter=4221>. Accessed January 30, 2012.
3. McPhee SJ, Winker MA, Rabow MW, Pantilat SZ, Markowitz AJ, eds. *Care at the Close of Life: Evidence and Experience*. New York, NY: McGraw Hill Medical; 2011.