CADTH Reimbursement Review

Tailored Review Sponsor Submission Template

Instructions for Sponsors

Background

A tailored review consists of CADTH conducting an appraisal of the clinical evidence and a pharmacoeconomic evaluation submitted by the sponsor using this template. Information from the sponsor’s submission will be validated and critically appraised by CADTH.

Please read the instructions below and consult the recommended documentation before completing the template. If you have any questions regarding the application process, please email requests@cadth.ca with the complete details of your question(s).

Roles and Responsibilities for Publication

All CADTH Reimbursement Review reports are posted on the CADTH website for anyone to access and review; although, in exceptional circumstances, embargo periods or redactions may be considered.

The sponsor is responsible for the quality, currency, propriety, and accuracy of the information provided to CADTH for publication via this tailored review submission template, and that the content complies with both [Canadian copyright law](https://laws-lois.justice.gc.ca/eng/acts/C-42/Index.html) and current Ontario accessibility guidelines for posting information online (see section on accessibility below).

Should the tailored review submission be accepted for review and publication, the sponsor will have the opportunity to review the final report for any inaccuracies or confidential information not in the public domain before final posting on cadth.ca as per current [Procedures for CADTH Reimbursement Reviews](https://cadth.ca/sites/default/files/Drug_Review_Process/CADTH_Drug_Reimbursement_Review_Procedures.pdf).

Accessibility for Ontarians

In keeping with the [*Accessibility for Ontarians with Disabilities Act*](https://www.ontario.ca/laws/statute/05a11) (AODA), all public documents must now be compliant with Ontario’s accessibility guidelines to ensure access for people who experience disabilities. MS Word (and other Microsoft software) provides an [Accessibility Checker](https://support.microsoft.com/en-us/office/rules-for-the-accessibility-checker-651e08f2-0fc3-4e10-aaca-74b4a67101c1) for identifying and repairing accessibility issues, which is located under the **Review** tab and **Check Accessibility** sub-tab.

When completing your submission:

* Reuse the existing AODA-compliant tables within this template if more tables are required. If using your own tables, ensure that all columns and rows have a header. Do not leave blank cells within tables.
* Suggest 1 to 2 lines of alternative text (alt-text) to describe any figures or images included within this document.
* When using figures and graphs, colour should not be used as the sole method for conveying content or distinguishing visual elements.

Before Completing Template

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

* [Procedures for CADTH Reimbursement Reviews](https://cadth.ca/sites/default/files/Drug_Review_Process/CADTH_Drug_Reimbursement_Review_Procedures.pdf)
* [CADTH Pharmaceutical Review Updates](https://www.cadth.ca/node/68411?keywords=&result_type%5B%5D=report&product_type%5B%5D=107782&sort=field_date%3Avalue-desc&amount_per_page=10&page=1) for any applicable information.

Completing Template

* Complete all sections of the template
* Use 9-point Arial font type
* Do not exceed the page limitations where note
* Delete all red font instructions once document is completed
* Save the completed template as a Word document

Completing References

Provide clear references to source documentation for all bioequivalence, efficacy, safety data, cost, or resource use provided in the template. In-text citations to sponsor references must be referenced alphabetically in order of appearance using superscript **letters**.

References must be provided at the end of the document in the References 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.

Submitting 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 CADTH.

Sponsor’s Summary of the Clinical Evidence

Pivotal Studies

Table 1: Details of Included Studies

| Characteristics | Study name | Study name | Study name |
| --- | --- | --- | --- |
| Designs and populations |
| **Study design** | DB RCT, OL RCT, etc. |  |  |
| **Locations** | List the number of centres and the countries involved |  |  |
| **Patient enrolment dates** |  |  |  |
| **Randomized (N)** | Provide the total number of randomized patients |  |  |
| **Inclusion criteria** | Provide a bulleted list of the key inclusion criteria for the study |  |  |
| **Exclusion criteria** | Provide a bulleted list of the key exclusion criteria for the study |  |  |
| Drugs |
| **Intervention** | Specify the drug, dose, route of administration, frequency of administration |  |  |
| **Comparator(s)** | Specify the drug, dose, route of administration, frequency of administration, for each comparator |  |  |
| Duration |
| **Phase** |  |  |  |
| Run-in | Specify the duration |  |  |
| Double-blind | Specify the duration |  |  |
| Follow-up | Specify the duration |  |  |
| Outcomes |
| **Primary end point** | Define the end point |  |  |
| **Secondary and exploratory end points** | Secondary end points:Provide a bulleted list of all secondary end pointsExploratory end points:Provide a bulleted list of all exploratory end points |  |  |
| Notes |
| **Publications** | Provide references for all publications related to this study.Provide the clinicaltrials.gov identification code |  |  |

List abbreviations in alphabetical order (e.g., RCT = randomized controlled trial).

Source: Indicate data source including citation.

Description of Studies

* Please provide a brief summary of the following key trial information: the study objective(s), a description of the study design, eligible patients, sample size, locations including the number of sites in Canada, study treatments, and randomization methodology (if applicable).
* If available, please include a figure showing the duration and characteristics of the different phases of the study (e.g., run-in period, treatment period, follow-up).
* CADTH does not typically report data for treatment groups that evaluated dosages that are not aligned with the recommendations in the product monograph. If relevant, please include a statement that data will not be presented for treatment groups that are not aligned with the Health Canada–approved dose.

[Start typing report details here]

Populations

Inclusion and Exclusion Criteria

* Please describe the key inclusion and exclusion criteria of the study.
* Clearly state if there any differences in the inclusion and exclusion criteria between the studies.

[Start typing report details here]

Baseline Characteristics

* Summarize major and/or relevant baseline demographic and clinical characteristics using a table (please keep this to a maximum of 1 page).
* Comment on the similarity and differences between treatment groups within each study.
* Please note any key differences in the demographic and clinical characteristics of the included populations across studies.
* CADTH typically only presents baseline characteristics for treatment groups that reflect the dosage(s) that will be recommended in the product monograph for the drug under review.
* Indicate in the table which analysis set the baseline characteristics have been summarized for (e.g., ITT set).

[Start typing report details here]

Table 2: Summary of Baseline Characteristics

| Characteristics | Treatment 1 | Treatment 2 |
| --- | --- | --- |
| <Table Body Copy> | <Table Body Copy> | <Table Body Copy> |
| <Table Body Copy> | <Table Body Copy> | <Table Body Copy> |
| <Table Body Copy> | <Table Body Copy> | <Table Body Copy> |
| <Table Body Copy> | <Table Body Copy> | <Table Body Copy> |
| <Table Body Copy> | <Table Body Copy> | <Table Body Copy> |
| <Table Body Copy> | <Table Body Copy> | <Table Body Copy> |

List abbreviations in alphabetical order (e.g., SD = standard deviation).

Source: Indicate data source including citation.

Interventions

* Briefly describe the interventions employed in the included trials, including dose, frequency, duration, and so on.
* If the trial is blinded, indicate the use of matched placebos and/or double-dummy controls, and provide a description of the placebo(s).
* Describe any concomitant medications or cointerventions required or permitted during the study.
* Include any criteria for rescue medication use where applicable, along with dosing schedules and the maximum doses permitted.
* Describe any stopping criteria for the intervention if relevant.
* 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.
* For drugs that require titration, please include a description of the titration schedule and the criteria used for determining the titration schedule (e.g., at the investigators discretion, a fixed schedule, or titration to target).

[Start typing report details here]

Outcomes

* Briefly describe the efficacy outcomes for the included studies in sufficient detail for the reader to be able to understand and interpret the outcome data (definitions and measurement). Please do not include aspects of the statistical analysis or results in this section).

[Start typing report details here]

* 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 1 single overall score or individual domain scores or both)
* range of scores
* direction of the scale (e.g., do higher scores indicate greater or lesser impairment)
* range of estimated minimal clinically important differences for the end point (if known) for the overall and individual domain scores.

[Start typing report details here]

Statistical Analysis

* Provide a brief description of the statistical analysis for each study that includes the items outlined below. Avoid repetition if possible. If methods for the secondary outcomes are similar to those for the primary outcome, simply state this and highlight any differences. The same applies if more than 1 secondary outcome is analyzed using similar methodology.
* Items may be summarized in a table where appropriate.

[Start typing report details here]

Primary Outcome(s) of the Studies

Power Calculation

* Assumptions regarding expected differences in treatment effect and variation (e.g., standard deviation), as well as the rationale for selecting the parameters used in the calculation should be reported.

[Start typing report details here]

Statistical Test or Model

* The rationale for selection of the statistical test or model should be reported.
* The covariates and/or baseline values that were included in the statistical models should be specified.
* For co-primary end points or composite end points, specify whether the analysis approach accounted for multiple testing with an appropriate control of the type I error rate.
* It should be stated if the analysis was based upon the intention-to-treat (ITT) or per-protocol (PP) population.

[Start typing report details here]

Data Imputation Methods

* Please report the methods used for handling missing data (e.g., last observation carried forward, mixed-effect model with repeated measures, non responder imputation).

[Start typing report details here]

Subgroup Analyses

* Key details of subgroup analyses should be reported, including whether they were pre-specified, whether the comparability of the treatment arms was checked, and whether the type I error rate was controlled for in multiple testing.

[Start typing report details here]

Sensitivity Analyses

* The main sensitivity analyses, if any, and the rationale for the analyses should be described.

[Start typing report details here]

Secondary Outcomes of the Studies

* The description of the statistical analysis for secondary outcomes should generally cover the same points described previously in the Statistical Test or Model Section, particularly when the main outcomes of interest for the CADTH review are secondary outcomes in the clinical trial.
* Details of the method of adjustment for multiple testing or control of type I error rate must be provided. The description must identify which tests or outcomes were included in the testing strategy and identify those outcomes that were not included.

[Start typing report details here]

Analysis Populations

* Define analysis sets (e.g., ITT, PP, safety set) for each study. Actual numbers in each analysis population should be presented in the Patient Disposition section.

[Start typing report details here]

Sponsor’s Summary of the Results

Patient Disposition

* Summarize the disposition for each included study.
* Comment on the common reasons for screening failures and for study discontinuation.
* Note any differential dropout rates or large percentage of screening failures.

[Start typing report details here]

Table 3: Sample Table for Patient Disposition

| Characteristics | Study A | Study B | Study C |
| --- | --- | --- | --- |
| Tx 1 | Tx 2 | Tx 1 | Tx 2 | Tx 1 | Tx 2 |
| **Screened, N** |  |  |  |  |  |  |
| **Randomized, N** |  |  |  |  |  |  |
| **Discontinued, N (%)** |  |  |  |  |  |  |
| **Reason for discontinuation, N (%)** |  |  |  |  |  |  |
| **Adverse events** |  |  |  |  |  |  |
| **Lost to follow-up** |  |  |  |  |  |  |
| **ITT, N** |  |  |  |  |  |  |
| **PP, N** |  |  |  |  |  |  |
| **Safety, N** |  |  |  |  |  |  |
| **Screened, N** |  |  |  |  |  |  |
| **Randomized, N** |  |  |  |  |  |  |

List abbreviations in alphabetical order (e.g., ITT = intention to treat).

Source: Indicate data source including citation.

Exposure to Study Treatments

Study Treatments

* Summarize exposure, focusing on any discrepancies among treatment group or across trials.
* Include information on adherence to the study treatments.

[Start typing report details here]

Concomitant Medications

* Summarize exposure to concomitant interventions (e.g., rescue therapy if relevant).
* Note any imbalances between the treatment groups.

[Start typing report details here]

Efficacy

* Include a separate subsection for each of the key outcomes that were included in the study.
* 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.
* Present the results in a manner that emphasizes the magnitude of the treatment effect and the precision of the estimate (i.e., confidence interval) rather than focusing only on statistical significance.
* Focus on key results within the text; it is not necessary to repeat all the data that are reported within tables.

[Start typing report details here]

Table 4: Sample Table for Outcomes

| Characteristics | Study 1Treatment 1N = | Study 1Treatment 2N = | Study 1Treatment 3N = |
| --- | --- | --- | --- |
| Example of continuous outcome (units)a |
| 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 valueb |  |  |  |
| Example of dichotomous outcome (units)a |
| n (%) |  |  |  |
| Risk difference (preferred if available), if not, use RR or (95% CI) |  |  |  |
| P valueb |  |  |  |

List abbreviations in alphabetical order (e.g., CI = confidence interval; SD = standard deviation; SE = standard error).

a Specify model, covariates, analysis population and time point for each outcome.

b Specify if outcome was within or outside of the statistical testing hierarchy.

Source: Indicate data source including citation.

Harms

* This section must not exceed 5 pages of text in 9-point Arial font.
* The required information or evidence must be succinct and entered directly into the template.
* Whenever possible, focus on integrated safety data in this section.

[Start typing report details here]

Safety Evaluation Plan

* Provide a brief overview of the overall safety evaluation plan for the drug under review.
* Keep this description to a maximum of a half page.

[Start typing report details here]

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).

[Start typing report details here]

Table 5: Sample Table for Summarizing Harms Data

| Adverse events | Study 1Treatment 1N =  | Study 1Treatment 2N =  | Study 2Treatment 1N =  | Study 2Treatment 2N =  | Study 2Treatment 3N =  |
| --- | --- | --- | --- | --- | --- |
| Patients with at least 1 adverse event |
| n (%) |  |  |  |  |  |
| Most common events, n (%) |  |  |  |  |  |
|  |  |  |  |  |  |
| Patients with at least 1 serious adverse event |
| n (%) |  |  |  |  |  |
| Most common events, n (%) |  |  |  |  |  |
|  |  |  |  |  |  |
| Patients who stopped treatment due to adverse events |
| n (%) |  |  |  |  |  |
| Most common events, n (%) |  |  |  |  |  |
|  |  |  |  |  |  |
| Adverse events of special interest |
| [specify event], n (%) |  |  |  |  |  |
|  |  |  |  |  |  |

List abbreviations in alphabetical order (e.g., n = number of patients with event).

Source: Indicate data source including citation(s).

Adverse Events

* Focus on treatment-emergent adverse events.
* State findings overall (across studies).

[Start typing report details here]

Serious Adverse Events

* Summarize treatment-emergent serious adverse events in this section.
* Do not limit this section to treatment-related adverse events.

[Start typing report details here]

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.

[Start typing report details here]

Adverse Events of Special Interest

* Provide a brief summary of any adverse events of special interest.

[Start typing report details here]

Bioequivalence (If Applicable)

* This section can be used to summarize relevant bioequivalence trials that are considered to be pivotal or supportive for the regulatory submission for the drug under review.
* Information provided in this section must be succinct and not exceed 3 pages.
* References must be provided and included in a list of references at the end of the template.

[Start typing report details here]

Table 6: Sample Table for Bioequivalence Data

|  |  |  |  |
| --- | --- | --- | --- |
| Pharmacokinetics | Drug under review | Comparator | Comparison |
| **AUC** |  |  | Difference (CI); P value |
| **Cmax** |  |  |  |
| **Tmax (h)** |  |  |  |
| **T1/2 (h)** |  |  |  |
| **Bioavailability** |  |  |  |
| **Degradation** |  |  |  |

List abbreviations in alphabetical order (e.g., CI = confidence interval).

Source: Indicate data source including citation(s).

Pharmacoeconomic Evaluation

Sponsor-Submitted Cost Information

New Combination Products

* The required information must be succinct and entered directly into the template.
* The information should include a statement or paragraph on each of the following components:
* scope of the cost comparison
* methods and assumptions used
* summary results (both narrative and tabular).
* The cost comparison should include all relevant comparators. For new combination products, this includes the individual components of the new combination product.
* Sources of price information and the recommended dosage regimen must be provided and are to be included as footnotes below the tables.
* Provide the price of the drug under review (price for all strengths per smallest unit to 4 decimal places) and its daily (or weekly/monthly) cost compared with the price of all relevant comparators (see Table 7 for a sample table).
* For new combination products, please ensure that the prices of the individual components are reported in the summary table. Include the cost differences and potential cost savings of the drug under review compared with the individual components.
* Provide examples of calculations within the submitted materials (i.e., full methods), either narratively or within a table or as a footnote, and ensure any data or assumptions informing the calculations are provided or referenced.
* Quantify the price difference of the drug under review compared with each of the comparators listed in the table.

[Start typing report details here]

New Formulations of Existing Drugs

* The required information must be succinct and entered directly into the template.
* The information should include a statement or paragraph on each following component:
* scope of the cost comparison
* methods and assumptions used
* summary results (both narrative and tabular).
* The cost comparison should include all relevant comparators. For new formulations of existing drugs, this includes the originator product(s) in addition to all relevant comparator treatments.
* Sources of price information and recommended dosage regimen must be provided and are to be included as footnotes below the tables.
* Provide the price of the drug under review (price for all strengths per smallest unit to 4 decimal places) and its daily (or weekly or monthly) cost compared with the price of all relevant comparators (see Table 7 as an example).
* Provide details if the drug under review is expected to result in any differences in health care resource use within the public payer perspective.
* State the assumptions for any differences in health care resource use and the justification for these assumptions (see Table 8 as an example).
* State the health care resources that will be used and the treatments to which these apply (see Table 9 as an example).
* Provide examples of calculations within the submitted materials (i.e., full methods), either narratively or within a table or as a footnote, and ensure any data or assumptions informing the calculations are provided or referenced.
* Quantify the difference in health care costs for the drug under review compared with each of the comparators (see Table 10 as an example).
* Present the aggregated differences in drug acquisition and health care costs in a summary table (see Table 11 as an example).

Table 7: Sample Table for Drug Acquisition Cost Comparison

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Generic name (brand name) | Strength | Dosage form | Price ($) | Recommendeddosage regimen | Annuala drug cost ($) | Difference in annuala cost |
| Drug under review  |  |  |  |  |  |  |
| Comparators |
| Comparator 1 |  |  |  |  |  |  |
| Comparator 2 |  |  |  |  |  |  |

List abbreviations in alphabetical order.

Note: Drug under review should be the reference cost for the incremental comparison.

a Annual cost should be reported unless the drug is used for a specified period, then a cost per course can be stated (revise the terminology in the table and provide clarity on the course duration in a footnote[s]).

Source: Indicate data source including citation(s).

Table 8: Sample Table for Assumptions

|  |  |
| --- | --- |
| Assumption | Justification |
| Assumption 1 | Provide references to support the justification where possible |
| Assumption 2 (add/remove as required) |  |
| Assumption 3 (add/remove as required) |  |

List abbreviations in alphabetical order.

Source: Indicate data source including citation(s).

Table 9: Sample Table for Health Resource Use

|  |  |  |  |
| --- | --- | --- | --- |
| Health care resource | Frequency (and duration if required) per yeara | Unit cost | Treatment(s) |
| State health care resource |  |  | State which treatments the resource is applicable to |
| If more than 1, state additional resources on each new row |  |  |  |
| Add/remove rows as required |  |  |  |

Note: Reference sources for frequency/duration and unit cost clearly within the table and/or via footnote(s).

a Information should be reported on an annual basis, unless the drug is used for a specified period, then information based on the course duration can be stated (revise the terminology in the table and provide clarity on the course duration in a footnote[s]).

Table 10: Sample Table for Associated Health Care Costs

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Generic name (Brand name) | [State health care cost/resource] | [State health care cost/ resource] (add/remove columns as required) | Aggregated health care costa per yearb | Difference in health care costs per yearb |
| Drug under review  |  |  |  |  |
| Comparators |
| Comparator 1 |  |  |  |  |
| Comparator 2 |  |  |  |  |

Note: Drug under review should be the reference cost for the incremental comparison.

a Based on health care components included in the table.

b Annual cost should be reported unless the drug is used for a specified period, then a cost per course can be stated (revise the terminology in the table and provide clarity on the course duration in a footnote[s]).

Table 11: Sample Table for Summary of Comparative Treatment Costs

|  |  |  |  |
| --- | --- | --- | --- |
| Generic name (Brand name) | Difference in drug acquisition costs per yeara | Difference in total health care costs per yeara | Difference in total costs per yeara |
| Drug under review  |  |  |  |
| Comparators |
| Comparator 1 |  |  |  |
| Comparator 2 |  |  |  |

Note: Drug under review should be the reference cost for the incremental comparison.

a Annual cost should be reported unless the drug is used for a specified period, then a cost per course can be stated (revise the terminology in the table and provide clarity on the course duration in a footnote[s]).

References

(See page 2 for instructions on adding references).

1. Xxxxxxx
2. Xxxxxxx
3. Xxxxxxx