**Reimbursement Review**

**Product Variation Tailored Review Sponsor Submission Template**

**Instructions for Sponsors**

Background

A product variation tailored review consists of CDA-AMC 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 CDA-AMC.

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@cda-amc.ca with the complete details of your question(s).

Roles and Responsibilities for Publication

All Reimbursement Review reports are posted on the CDA-AMC website for anyone to access and review.

The sponsor is responsible for the quality, currency, propriety, and accuracy of the information provided to CDA-AMC 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 (refer to section on accessibility below).

Should the tailored review submission be accepted for review and publication, the sponsor will have the opportunity to review the report for any inaccuracies or confidential information not in the public domain before posting on the CDA-AMC website.

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.
* Include 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 the Template

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

* [Procedures for Reimbursement Reviews](https://www.cda-amc.ca/sites/default/files/Drug_Review_Process/Drug_Reimbursement_Review_Procedures.pdf)
* Pharmaceutical Review Updates for any applicable information.

Completing the Template

General Guidelines

Complete all sections of the template using 9-point Arial font type in text and 9-point Arial font in tables. Do not alter the page margin settings. 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. **The total length of the Sponsor’s Summary of the Clinical Evidence section (excluding the tables of contents, abbreviations list, appendices, and reference list), cannot exceed 15 pages.**

When the template is complete, delete this cover page with the instructions, the record of updates section, and all red font instructions throughout the template. Save the completed template as a Word document.

Completing References

Provide clear references to source documentation used (including citations and corresponding table and figure numbers from data sources) 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. An RIS file is a standardized bibliographic format that enables citation management programs to exchange documents. References must be provided at the end of the document in the References section.

**Background**

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. Appendix 1 accompanies this section and must be completed.

**Sponsor’s Summary of the Clinical Evidence**

In this section the sponsor is required to summarize the results from pivotal and key clinical studies. Appendices 2 to 5 accompany this section and must be completed.

**Pharmacoeconomic Evaluation**

This section is reserved for the CDA-AMC review of the sponsor’s submitted cost information. Appendix 6 accompanies this section and must be completed.

Record of Updates to Template

|  |  |  |
| --- | --- | --- |
| **Version** | **Date** | **Summary of revisions** |
| 1 | February 27, 2025 | Original version posted |

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* Please add a list of tables.

List of Figures

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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

Background

Sponsor’s Summary of Disease Background and Current Management

Application Summary

Table 1: Application Submitted for Review

| Item | Description |
| --- | --- |
| **Drug (product)** | Non-proprietary name (Brand Name), strength, dosage form(s), route of administration  |
| **Sponsor** |  |
| **Health Canada indication** | Health Canada indication as per product monograph (abbreviate if necessary); if pre-NOC submission state: Proposed: |
| **Sponsor’s reimbursement request** | Ensure this is consistent throughout all components of the application If same as indication, state “As per indication.”  |
| **Health Canada approval status** | NOC, NOC/c, Under review (pre-NOC) |
| **NOC date** | If NOC received, state: Month day, yearIf pre-NOC submission, state: anticipated Month day, year |

NOC = Notice of Compliance. Abbreviations must be listed under the table in alphabetical order.

Disease Background

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, and survival/mortality.

Diagnosis of the Condition

Briefly describe any 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 the name, analyte, and rationale for each diagnostic test. 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.

Current Management and Place in Therapy of the Drug Under Review

Current Treatment Options

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.

Key characteristics of [drug under review] are summarized with other treatments available for [condition under review] in Appendix 1.

Impact of the Drug Under Review on Treatment Options

Please briefly describe the potential impact of the introduction of the drug under review on currently reimbursed treatments for the indication, including which treatments are expected to be displaced.

Sponsor’s Summary of the Clinical Evidence

Pivotal Studies

Table 2: Details of Included Studies

| Characteristics | Study name | Study name | Study name |
| --- | --- | --- | --- |
| Study design and population |
| **Study design** | DB RCT, OL RCT, etc. |  |  |
| **Locations** | List the number of centres and the countries involved (include the number of sites in Canada) |  |  |
| **Patient enrolment dates** |  |  |  |
| **Randomized (N)** | State the total N and include the sample size in each treatment group. |  |  |
| **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 |
| **Screening phase** |  |  |  |
| **Run-in phase** | Specify the duration |  |  |
| **Treatment phase** | Specify the duration |  |  |
| **Follow-up phase** | Specify the duration |  |  |
| Outcomes |
| **Primary end point** | State the primary endpoint including the timeframe (e.g., through 24 weeks) |  |  |
| Publication status |
| **Publications** | State reference(s) to journal publications Author et al. Yearcitation |  |  |

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

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 also be presented:
* Study objectives
* Randomization, whether randomization was stratified
* Data cut-off dates
* If applicable, briefly describe 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, briefly describe its purpose.
* If appropriate, include a figure showing the duration and characteristics of the different phases of the study (e.g., run-in period, treatment period, follow-up).

[Start typing report details here]

Eligibility Criteria

* Delete this section if not needed.
* Identify any important differences in inclusion and exclusion criteria between the studies.
* If there are additional eligibility criteria that are important consider when interpreting the results (beyond those in Table 1), they may be reported in Appendix 2.

[Start typing report details here]

Interventions

* Briefly describe the interventions employed in the included trials that are not already in the Details of Included Studies table (delete this section if not needed). This may include:
* 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).
* CDA-AMC 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]

Outcomes

* Summarize in text or in the summary table below the end points being reported, including outcome measure, time point, and type (primary, key secondary, secondary, or exploratory).
* Refer the reader to Appendix 2 for more information on scale measures.

Table 3: Summary of Relevant Outcomes

| Outcome measure | Timepoint | Study 1 | Study 2 |
| --- | --- | --- | --- |
| List outcome 1 | Please be specific (e.g., at 24 weeks; through 24 weeks) | Please state as:* Primarya
* Key secondarya
* 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.

Include a footnote to identify endpoints where statistical testing was adjusted for multiple comparisons | Please state as:* Primarya
* Key secondarya
* 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.

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 |  |  |  |

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. Data should reflect the results reported in the clinical study report(s) whenever possible.

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

[Start typing report details here]

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.

[Start typing report details here]

Statistical Testing

* Refer readers to detailed descriptions of statistical analysis methods in Appendix 2.
* 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.
* State whether there was any method used to adjust for multiple testing/control of type I error rate and describe the method and alpha levels used.
* 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.
* If there were interim analyses, please state how these were accounted for in the statistical testing plan.

[Start typing report details here]

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. If there were no relevant subgroup analyses, include a statement to that effect.

[Start typing report details here]

Analysis Populations

Define analysis sets (e.g., FAS, PP, safety set) for each study using text or a summary table.

Table 4: 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.

[Start typing report details here]

Sponsor’s Summary of the Results

Baseline Characteristics

* Summarize major and/or relevant baseline demographic and clinical characteristics using a table (please keep this to a maximum of 1 page).
* CDA-AMC 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).
* More than one table can be created if all studies do not fit in a single table.
* Additional text is not necessary for this section.

Table 5: Summary of Baseline Characteristics

| Characteristic | Study 1 | Study 2 |
| --- | --- | --- |
| Treatment 1(N = ) | Treatment 2(N = ) | Treatment 1(N = ) | Treatment 2(N = )  |
| Study variable (units), measurement (% or variability of measurement)Example: Age (years), median (range) |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |

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

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 the disposition for each included study. Additional text is not needed in this section.

Table 6: 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** |  |  |  |  |  |  |
| **Reason for screening failure, n (%)** |  |  |  |  |  |  |
| State reason 1 |  |  |  |  |  |  |
| Add/modify rows as required |  |  |  |  |  |  |
| **Randomized, N** |  |  |  |  |  |  |
| **Discontinued, N (%)** |  |  |  |  |  |  |
| **Reason for discontinuation, n (%)** |  |  |  |  |  |  |
| Adverse events |  |  |  |  |  |  |
| Lost to follow-up |  |  |  |  |  |  |
| Add/modify rows as required |  |  |  |  |  |  |
| **ITT, N** |  |  |  |  |  |  |
| **FAS, N** |  |  |  |  |  |  |
| **PP, N** |  |  |  |  |  |  |
| **Safety, N** |  |  |  |  |  |  |
| **Add/remove rows as required** |  |  |  |  |  |  |

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

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 Study Treatments

Study Treatments

* Summarize exposure, using text or a table.
* Include information on adherence to the study treatments.

[Start typing report details here]

Concomitant Medications and Co-Interventions

* Summarize exposure to concomitant interventions (e.g., rescue therapy if relevant).
* Additional information (i.e., a summary table) can be included in Appendix 3.

[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.
* To keep the main section of the report succinct, figures (e.g., measurements over time) can be placed in Appendix 4 with key takeaways stated here.

[Start typing report details here]

Table 7: Sample Table for Outcomes

| Variable | Study 1Treatment 1N = | Study 1Treatment 2N = | Study 2Treatment 1N = | Study 2Treatment 2N = |
| --- | --- | --- | --- | --- |
| Outcome 1 (units) |
| Number of patients contributing to the analysis |  |  |  |  |
| Baseline, mean (SD) |  |  |  |  |
| Change from baseline, mean (95% CI or SE) |  |  |  |  |
| 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 |  |  |  |  |

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

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.

Add footnotes (accompanied by superscript letters in the table) for the following:

* To specify (as applicable) model, adjustment factors, analysis population, and handling of missing data.
* To denote P values that have been adjusted for multiple testing.

Harms

* 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

* Refer readers to Appendix 5 for detailed results for harms
* Briefly summarize here (for treatment-emergent adverse events):
* Overall occurrence of AEs, SAEs, and deaths
* The most common AEs and SAEs
* If applicable, additional key takeaways

[Start typing report details here]

[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. Delete this section if not applicable.

[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.
* To keep the main section of the report succinct, figures (e.g., measurements over time) can be placed in Appendix 4 with key takeaways stated here.

[Start typing report details here]

Table 8: 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: 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.

Pharmacoeconomic Evaluation

* This section is reserved for the CDA-AMC review of the sponsor’s pharmacoeconomic evaluation and is to be left blank by the sponsor.

Appendix 1: Key Characteristics of Treatment Options

All relevant comparators should be included in the table. This table may be completed at the drug class level for some rows if there are multiple relevant comparators within the same drug class.

Relevant comparators are treatments that meet at least 1 of 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.

If relevant for the drug under review, include a brief paragraph on recommended dosage adjustments for notable subpopulations in the product monograph, as well as any confirmed or anticipated statements in the product monograph regarding restricting the prescribing and/or administration of the drug to certain health care professionals.

Table 9: Key Characteristics of Drug 1, Drug 2, etc.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Drug | Mechanism of action | Relevant indication(s) | Route of administration and dosage | Serious adverse effects or safety issues  |
| Drug under review | Briefly state the mechanism of action | State indication under review | State recommended regimen per the product monograph | State serious warnings and precautions and notable contraindications from the product monograph. |
| Comparator 1 | As above | 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. | As above |
| Comparator 2 | As above | As above | As above | As above |
| Add rows as needed |  |  |  |  |

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

Appendix 2: Methods of Included Studies

Additional Eligibility Criteria

* Delete this section if not applicable.

Description of Outcome Measures

Describe each of the outcome measures reported in the systematic review and provide information on minimal important differences (MID) using text or a summary table.

* + 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.
	+ 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.

Statistical Analysis

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

* + 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.
	+ 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 (refer to example below). Paragraph text is not needed if all details are in the table.

Table 10: Statistical Analysis of Efficacy End Points

| End point | 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.

Appendix 3: Exposure to Other Treatments for Included Studies

* If there is no relevant information to present in this appendix, include a statement to that effect.

Table 11: 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.

Appendix 4: Additional Efficacy and Bioequivalence Results

* This section may be used for efficacy and bioequivalence results that are presented in figures (e.g., measurements over time)
* If there is no relevant information to present in this appendix, include a statement to that effect.

Appendix 5: Detailed Harms Results for Included Studies

* 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., ≥ 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.

Table 12: Sample Table for Summarizing Harms Data

|  |  |  |
| --- | --- | --- |
| Adverse events | Study 1 | Study 2 |
| Treatment 1(N = ) | Treatment 2(N = ) | Treatment 1(N = ) | Treatment 2(N = ) |
| Patients with at least 1 adverse event, n (%)  |
| Most common events |  |  |  |  |
| State AE |  |  |  |  |
| Add rows as required |  |  |  |  |
|  |  |  |  |  |
| Patients with at least 1 serious adverse event, n (%) |
| Most common events |  |  |  |  |
| State SAE |  |  |  |  |
| Add rows as required |  |  |  |  |
|  |  |  |  |  |
| Patients who stopped treatment due to adverse events, n (%) |
| State AE |  |  |  |  |
| Add rows as required |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
| Deaths, n (%) |
| 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 |  |  |  |  |
| Add rows as required |  |  |  |  |

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

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.

Appendix 6: 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. Relevant comparators are treatments that meet at least 1 of 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.
* 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 (refer to Table 13 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 details if the drug under review is expected to result in any differences in health care resource use within the public payer perspective.
* State any assumptions regarding differences in health care resource use and the justification for these assumptions (refer to Table 14 as an example).
* State the health care resources that will be used and the treatments to which these assumptions apply (refer to Table 15 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 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. Relevant comparators are treatments that meet at least 1 of 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.
* 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 (refer to Table 13 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 any assumptions regarding differences in health care resource use and the justification for these assumptions (refer to Table 14 as an example).
* State the health care resources that will be used and the treatments to which these assumptions apply (refer to Table 15 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 (refer to Table 16 as an example).
* Present the aggregated differences in drug acquisition and health care costs in a summary table (refer to Table 17 as an example).

Table 13: 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 14: 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 15: Sample Table for Health Care 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 in a 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 Frequency of resource use 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 16: 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 17: 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

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.