Canada's Drug Agency
L'Agence des médicaments du Canada
Drugs. Health Technologies and Systems. Médicaments, technologies de la santé et systèmes.

Non-Sponsored Reimbursement Review Procedures

August 2024

Record of Updates

Version	Date	Summary of revisions
3	August 29, 2024	• Updated with CDA-AMC branding • "Stakeholders" changed to "Partners" or specific group
2	June 8, 2023	• Revisions to note that recommendations will be issued by the CDA-AMC's Formulary Management Expert Committee (FMEC). • Clarification that selected resubmissions and reassessments may be managed through the non-sponsored review process.
1	June 20, 2022	• Original version posted.

1. Eligibility

This section provides general guidance regarding eligibility for the majority of non-sponsored applications. In some situations, our organization may consult with Federal, Provincial, and Territorial governments and their drug programs to make a decision on a case-by-case basis.

Public drug programs may request a non-sponsored reimbursement review in situations where a potentially eligible sponsor does not file an application (e.g., submission, resubmission, or reassessment) through our sponsored reimbursement review process. To warrant a non-sponsored review and recommendation from the CDA-AMC, sufficient interest across individual jurisdictions is required from the applicable CDA-AMC advisory committee (the Formulary Working Group [FWG] or the Provincial Advisory Group [PAG]). For a drug to be eligible for a non-sponsored reimbursement review and recommendation, publicly available evidence of expired or impending loss of exclusivity, as indicated by the Health Canada patent register and/or register of innovative drugs is required.

Before initiating a non-sponsored reimbursement review, we will confirm with the Drug Identification Number (DIN) holder of the branded product that they are declining to file an application with the CDA-AMC (in accordance with section 2.6 of the *Procedures for CDA-AMC Reimbursement Reviews*). However, if the drug is already generic or biosimilars have been approved, DIN holders will not be contacted.

We will consider reviewing a drug through the non-sponsored reimbursement review process when:

- public drug programs, through the CDA-AMC's advisory committees, request a review and recommendation from our Formulary Management Expert Committee (FMEC);
- sponsors of the branded drug have declined to file an application with the CDA-AMC on the basis that competition from generic and/or biosimilar products is imminent;
- the drug is later in its life cycle based on publicly available Health Canada resources (patent register and/or register of innovative drugs); or
- genericized or biosimilar drugs are available, and the reference drug did not have a previous CDA-AMC reimbursement review for the indication of interest and/or new evidence has emerged and the sponsor declines to file a resubmission or reassessment with us.

When sponsors of the branded drug have declined to file an application with the CDA-AMC , we will consider reviewing a drug through the non-sponsored reimbursement review process for clinical indications for which a pharmaceutical manufacturer has not applied for a Health Canada Notice of Compliance (i.e., off-label use) when there is evidence of use of the drug for the condition of interest in Canadian clinical practice (e.g., integration of the drug into clinical practice guidelines, consultations with clinical specialists). If requested from public drug programs, drugs will be eligible when at least 1 of the following circumstances apply:

- clinical data are available for the indication of interest, to permit the CDA-AMC and the expert committees to evaluate the effectiveness of the drug;
- approval for use of the drug for the indication of interest has been issued by other regulatory authorities (e.g., US FDA or the European Medicines Agency); or
- there are existing international health technology assessment recommendations in favour of reimbursement.

We will prioritize non-sponsored reimbursement reviews based on advisory committee priority, availability of evidence, and capacity.

2. Application Requirements

To initiate a non-sponsored reimbursement review, we must receive an official written request from the chair of the CDA-AMC advisory committee (i.e., FWG or PAG). When a non-sponsored reimbursement review is accepted for review, we will post notice publicly. The posting will contain a description of the drug under review and the indication(s) to be reviewed. The draft research protocol to be conducted by our organization will also be posted publicly.

As the review is initiated by public drug programs, no documentation will be required from an industry sponsor, although additional information provided from industry may be considered. For the non-sponsored reimbursement review process, industry refers to all current and future DIN holders (including manufacturers of generic or biosimilar drugs).

3. Partner Engagement

Partner engagement during the non-sponsored reimbursement review will occur in the same manner as sponsored reimbursement reviews, with some minor amendments as described in the following.

3.1 Industry Engagement

Industry will have 35 business days from the notice date issued in the CDA-AMC weekly email update to provide input on the non-sponsored application under review. Industry will also have 10 business days to review the draft recommendation and provide feedback in accordance with section 9.4.2 of the *Procedures for CDA-AMC Reimbursement Reviews*. All input must be submitted using the templates provided by the CDA-AMC and must not contain any confidential information (all information included in the template will be considered disclosable by our organization). As the reimbursement reviews are not sponsored, input from industry manufacturers is not required.

3.2 Patient Engagement

Open calls for patient input will be solicited, utilized, and posted in accordance with section 6.2 of the sponsored reimbursement review procedures. Patient groups will have 35 business days from the notice date issued in the CDA-AMC weekly email update to provide input. Patient groups and other partners will have 10 business days to review the draft recommendation and provide feedback in accordance with section 9.4.2 of the *Procedures for CDA-AMC Reimbursement Reviews*.

3.3 Clinician Engagement

Groups or associations of health care professionals will have 35 business days from the notice date issued in the CDA-AMC weekly email update for preparing and submitting their input. Clinician group input will be solicited, utilized, and posted in accordance with section 6.3 of the sponsored reimbursement review procedures. Groups or associations of health care professionals and other partners will have 10 business days to review the draft recommendation and provide feedback in accordance with section 9.4.2 of the *Procedures for CDA-AMC Reimbursement Reviews*.

3.4 Drug Program Engagement

When a non-sponsored reimbursement review is initiated, public drug programs will provide input on issues that may impact their ability to implement a recommendation. The summary of implementation issues will be presented to FMEC by a lead jurisdiction (or designate). The draft recommendation will be discussed with the applicable advisory group (FWG or PAG) to collate and finalize their feedback.

3.5 Clinician Experts

CDA-AMC review teams will include at least 1 clinical specialist with expertise in the diagnosis and management of the condition for which the drug is indicated. The

expert(s) will be involved in all phases of the review process in accordance with section 6.3.2 of the *Procedures for CDA-AMC Reimbursement Reviews*.

Table 1: Key Milestones for Partner Engagement

Milestones	Industry, patient group, clinician group	Drug programs	Clinical expert(s)
Request non-sponsored reimbursement review	NA	Public drug programs, with support of applicable CDA-AMC advisory committee (FWG or PAG).	NA
Review phase	Our partners will have 35 business days from the notice date issued in the CDA-AMC weekly email update to provide input.	We will provide a standardized template for completion by a lead jurisdiction; the initial draft will be discussed and finalized at a scheduled PAG or FWG meeting.	Provide guidance on the development of the review protocol. Assist in the critical appraisal of clinical evidence and guidance on the potential place in therapy. Advise on the assumptions used in the economic review. Advise on implementation issues raised by jurisdictions.
Commentary on recommendations	There will be 10 business days to review and comment on the draft recommendations during the partner feedback period.	Eligible to file a request for reconsideration.	If necessary, provide input on requests for reconsideration.
Implementation phase	NA	Drug programs may request an additional CDA-AMC product to facilitate the implementation of the recommendation.	As part of an implementation advice panel, experts may advise on outstanding implementation issues and further develop and refine reimbursement conditions. Advise on treatment sequencing within a particular indication for oncology drugs.

FWG = Formulary Working Group; NA = not applicable; PAG = Provincial Advisory Group.

4. Review Procedure

4.1 Clinical Review

At the initiation of the review, our organization develops a protocol to ensure that the review will reflect the most relevant clinical information. The protocol specifies the following aspects of the review:

- the populations, intervention, comparators, outcomes, and study designs that will be used to conduct a systematic literature review
- any supplemental information that will be included in the review to provide additional context (e.g., description, evidence of validity, and clinical importance of the outcome measures)
- any relevant evidence that will be included but not be captured in the systematic literature review (e.g., indirect comparisons, long-term extension studies, and studies of other designs that address important gaps in the clinical trial evidence).

When drafting the review protocol, we considers a variety of information, such as clinical practice guidelines, the availability of comparator drugs, clinical trial protocols, and partner input (i.e., information from patient groups, clinical experts, drug programs, and expert committee members). Any clinical end points that were identified by patient groups as being particularly relevant for those living with the condition will be added to the protocol document.

The CDA-AMC conducts 1 or more independent systematic literature searches according to the protocol. The search strategy used and the relevant literature that is identified are included in the clinical review. We summarize and critically appraise the relevant studies in the clinical report. Strengths and limitations with respect to both internal validity (i.e., how well the study was designed, conducted, and reported) and external validity (i.e., how well the results of the study could be applied to the target population in Canada) are documented.

Patient and clinician group input are included in the clinical report. When discussing the available evidence, our organization reflects on the input from patient and clinician groups, particularly any areas where there is an unmet therapeutic need for those living with the condition; known advantages and disadvantages of the treatments that are currently available; and any expectations regarding new therapies (including the drug under review).

CDA-AMC review teams typically include at least 1 clinical expert who provides guidance and interpretation throughout the review. We increase the number of clinical experts depending on the complexity of the drug under review. We may also establish a panel of clinical experts to provide insight into the drug's potential place in therapy. Commentary in the clinical report regarding the potential place in therapy of the drug under review is provided by 1 or more clinical experts with expertise in the diagnosis and management of the condition for which the drug is indicated.

To accommodate the absence of an industry sponsor:

- DIN holders will not have the opportunity to review and comment on the draft CDA-AMC clinical review report before the expert review committee.
- DIN holders will not have the opportunity to review and request the redaction of any information in the clinical report before it is posted on the CDA-AMC website.

4.2 Economic Review

In the absence of an application filed by a sponsor, our organization does not have access to an economic model for the drug under review. As a result, the economic review will include a comparison between the costs of the drug under review and those of appropriate comparators.

In the absence of a sponsor, DIN holders will not have the opportunity to review and comment on the draft CDA-AMC economic report before the expert review committee. If additional information from outside the public domain is provided by industry, we will not provide an opportunity to review and request redactions before posting on the CDA-AMC website.

5. Recommendation Procedure

The output from the non-sponsored reimbursement review process will be a recommendation from the CDA-AMC's FMEC. Our organization's recommendations from the non-sponsored reimbursement review process will be issued based on the active substance to accommodate scenarios where there are or will be multiple DIN holders.

5.1 Recommendation Framework

FMEC will apply the recommendation framework in accordance with section 9.3.1 of the *Procedures for CDA-AMC Reimbursement Reviews*.

Table 2: Description of Recommendations

Category	Description
Reimburse	The drug under review demonstrates comparable or added clinical benefit and acceptable cost relative to 1 or more appropriate comparators to recommend reimbursement in accordance with the defined patient population under review.
Reimburse with conditions	Scenarios that could be considered under this category include: • The drug under review demonstrates comparable or added clinical benefit and acceptable cost relative to 1 or more appropriate comparators in a subgroup of patients within the indication under review. In such cases, conditions are specified to identify the subgroup. • The drug under review demonstrates comparable clinical benefit and acceptable cost relative to 1 or more appropriate comparators. In such cases, a condition may include that the drug be listed in a similar manner to 1 or more appropriate comparators. • The drug under review demonstrates clinical benefit, with a greater degree of uncertainty and an acceptable balance between benefits and harms in a therapeutic area with significant unmet clinical need.
Do not reimburse	There is insufficient evidence identified to recommend reimbursement. Scenarios that typically fit this recommendation category include: • The drug under review does not demonstrate comparable clinical benefit relative to 1 or more appropriate comparators. • The drug under review demonstrates inferior clinical outcomes or significant clinical harm relative to 1 or more appropriate comparators.

5.2 Draft Recommendations

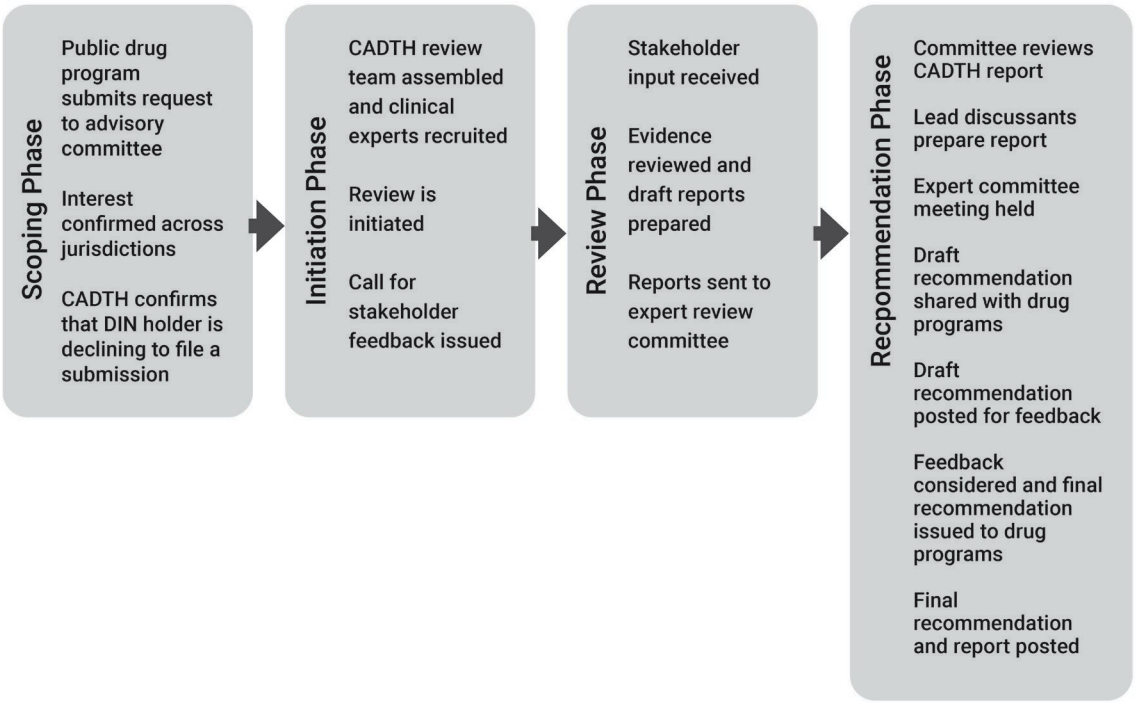
In accordance with the process described in the *Procedures for CDA-AMC Reimbursement Reviews*, draft recommendations will be posted for partner feedback for 10 business days. The drug programs, patient groups, clinician group(s), and DIN holders for the drug under review may provide feedback on the draft recommendation using the applicable CDA-AMC template.

5.3 Reconsideration

The participating drug programs may file a request for reconsideration of the draft recommendation. In the absence of a sponsor, DIN holders will not have the opportunity to request reconsideration of the draft recommendation; however, their feedback on the

draft recommendation may be considered if a reconsideration has been requested by the drug programs.

Figure 1: Overview of Non-Sponsored Reimbursement Review Process



DIN = Drug Identification Number.

6. Transparency

In accordance with our existing reimbursement processes, the following information will be posted on the CDA-AMC website for non-sponsored reimbursement reviews:

- calls for patient and clinician group input
- key dates of the non-sponsored reimbursement reviews
- CDA-AMC reports and recommendations
- partner feedback on the draft recommendation.

As previously stated, all information submitted by partners will be considered disclosable by our organization. DIN holders will not have the opportunity to review and request redactions of CDA-AMC reports or recommendations before they are posted on the CDA-AMC website.