CADTH and Canadian Blood Services Interim Plasma-Protein Product (PPP) Review Process

1. Background on Interim Process

CADTH and Canadian Blood Services are pleased to announce the establishment of a new interim process for the review of plasma-protein products. The interim process builds upon the strengths of both agencies to provide stakeholders with an objective, transparent, evidence-informed review process for plasma-protein products. The interim process will be in place while provincial and territorial governments (except Québec) complete a review of PPP and drug formulary processes in collaboration with Canadian Blood Services, CADTH, as well as other key stakeholders.

The objectives of the interim process for the review of plasma-protein products are as follows:

- Promote efficiency within Canadian health technology assessment processes by seeking alignment of procedures, guidelines, and timelines.
- Facilitate greater transparency, collaboration and information sharing between CADTH, Canadian Blood Services, and stakeholders.

This document provides a brief overview of the new interim process.

2. Eligibility under the Interim Process

Submission from manufacturers, also known as “sponsors”, for new categories to the Canadian Blood Services formulary will be assessed by Canadian Blood Services and CADTH using the current Canadian Blood Services Plasma Protein Product Selection eligibility criteria, subject to approval by the Provincial/Territorial Governments (excluding Quebec) for a new category on the Canadian Blood Services formulary. The current eligibility criteria are that the product:

- is a biological drug manufactured from human plasma or a biological drug whose active ingredient(s) are functional equivalents of the foregoing, used in the practice of Transfusion Medicine; AND
- is not carried in the health system already;
Canadian Blood Services and CADTH will initiate a review after confirmation by the Provincial and Territorial Blood Liaison Committee (PTBLC) on whether:

- the product meets the eligibility requirements for consideration as a new category on the Canadian Blood Services formulary; or,
- whether the product would be reviewed by Canadian Blood Services as a new brand within an already approved category on the Canadian Blood Services formulary.

Manufacturers making product submissions with questions regarding whether or not a product is eligible for review through the interim process are asked to complete an eligibility request form and submit it to requests@cadth.ca. CADTH will forward the information to Canadian Blood Services for discussion with the PTBLC. Eligibility should be determined prior to requesting a pre-submission meeting or providing advance notification. If it has been determined that the product does not meet the eligibility criteria the manufacturer can consider filing a submission through the CADTH Common Drug Review (CDR) process.

3. Interim Pre-submission Procedure

Pre-submission activities for the interim PPP process will be similar to the processes that are used in the CADTH’s Common Drug Review (CDR) process. This includes the opportunity for a pre-submission meeting with CADTH and Canadian Blood Services anytime within 12 months of the anticipated date of filing the submission. To request a pre-submission meeting, sponsors are required to complete a pre-submission meeting request form and submit it to CADTH (meetingrequests@cadth.ca).

In accordance with CADTH’s advance notification processes, sponsors for plasma-related drugs are required to provide CADTH with a minimum of 30 business days of advance notice for anticipated submissions. To fulfill the advance notification requirement, manufacturers must complete the advance notification template in its entirety and submit it to CADTH (requests@cadth.ca). CADTH will subsequently inform Canadian Blood Services and provide them with the completed advance notification template.

4. Stakeholder Engagement

In accordance with CADTH’s existing pharmaceutical review processes, the interim PPP process will include engagement with patient groups, clinical specialists, Canadian Blood Services, and public payers. These processes will occur in a similar manner to CADTH’s existing CDR process; however, CADTH and Canadian Blood Services will continue to discuss the specific requirements related to review of plasma-related products, and work together to jointly identify input needs from relevant patient groups and specialists with expertise in the diagnosis and management of condition for which the plasma-related products is indicated. In
addition, the stakeholder input from the public payers will be provided through the PTBLC, along with relevant information from Canadian Blood Services as the formulary manager.

5. Interim Submission Requirements

The clinical, economic, and administrative submission requirements for the interim PPP process are similar to those used in CADTH’s CDR process, with the exception of the following additional requirements:

• a budget impact report that provides an overall aggregate budget impact analysis (BIA) for plasma-product under review (i.e., a pan-Canadian analysis)

• a copy of the model used to produce the aggregate pan-Canadian BIA

• a reference list and copies of all supporting documentation used and/or cited in the BIA

6. Interim Application and Screening Procedure

The application filing and screening procedures for plasma-protein drugs will be identical to those currently used in the CDR process. Sponsors must be registered with CADTH Collaborative Workspaces Registration before filing a submission or resubmission. CADTH will provide a copy of the submission requirements to Canadian Blood Services to ensure that they have this information prior to the expert committee meeting.

All submissions filed by manufacturers of plasma-protein products are subject to an application fee according to the fee scheduled that is applied for the CDR process (for details please consult Fee Schedule for CADTH Reviews).

In accordance with CADTH’s processes, the status and key dates for the review of plasma-protein drugs will be posted on the CADTH website.

7. Interim Review Procedure

Table 1 indicates the targeted time frames for key tasks within the interim PPP process. The clinical and economic review processes will be completed in accordance with CADTH’s standard review procedure (see the Procedure and Submission Guidelines for the CADTH Common Drug Review). As with CADTH’s existing process, the sponsor will have the opportunity to review and comment on the draft reports prior to the expert review committee meeting.

CADTH will post the clinical and economic report(s) for all submissions reviewed through the process. The sponsor will be responsible for identifying any confidential information included in the reports.
Table 1: Targeted Timelines for the Interim Plasma-Protein Product Review Process

<table>
<thead>
<tr>
<th>Phase of Review</th>
<th>Key Milestone</th>
<th>Business Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening and administration</td>
<td>Submission requirements received by CADTH</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Submission requirements screened for acceptance</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Review initiated</td>
<td>1 to 10</td>
</tr>
<tr>
<td>Review of submission or resubmission</td>
<td>Draft review report(s) prepared and sent to sponsor for comments</td>
<td>45</td>
</tr>
<tr>
<td>Deliberation and recommendation</td>
<td>Sponsor receives draft review report(s) and provides comments</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>CADTH’s responds to comments(^a) and final review report(s) prepared</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Expert committee brief completed and distributed</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Review of meeting materials and preparation of discussant reports</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Expert committee meeting</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Embargoed recommendation sent to the sponsor, Canadian Blood Services, PTBLC, and the drug plans</td>
<td>8 to 10</td>
</tr>
<tr>
<td>Embargo period and options</td>
<td>Embargo period</td>
<td>10 to 30(^b)</td>
</tr>
<tr>
<td></td>
<td>Request for clarification or request for reconsideration</td>
<td>Variable(^c)</td>
</tr>
<tr>
<td>Finalizing and posting</td>
<td>Final recommendation issued to the sponsor, Canadian Blood Services, PTBLC, and the drug plans</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Final recommendation and review report(s) posted</td>
<td>2</td>
</tr>
</tbody>
</table>

\(^a\) Sponsors will be sent CADTH’s responses eight business days prior to the expert committee meeting.

\(^b\) An extension of up to 20 business days may be requested to prepare a request for reconsideration (i.e., a total of 30 business days).

\(^c\) The time frame required to address a request for clarification, or request for reconsideration, depends on the amount of work needed to address the request, as well as the available dates for expert committee meetings.

8. Interim Recommendation Procedure

The output from the process will be a recommendation from a subcommittee of the Canadian Drug Expert Committee (CDEC), which will be enhanced with two additional members with expertise in plasma-protein products. This subcommittee will serve as an advisory body to CADTH that will issue recommendations and advice to inform reimbursement decisions for plasma-protein products that are reviewed through the interim PPP process. The CDEC subcommittee, with two additional members with expertise in plasma-protein products, will be referred to during this interim basis as the Canadian Plasma-Protein Product Expert Committee (CPEC).

The recommendation options available in the interim process for the review of plasma-protein products will be the same as those that are currently used in CADTH’s pharmaceutical review processes: that a drug be reimbursed; that a drug be reimbursed with conditions; or that a drug not be reimbursed. A confidential embargoed recommendation will be sent to the sponsor, Canadian Blood Services, and the PTBLC, and to the public drug plans for information. The procedures for the embargo period and options for filing a request for reconsideration and/or clarification will be identical to those that are currently used in the CDR process.
9. Interim Implementation of Recommendations

Recommendations for products that would require a new category to the Canadian Blood Services formulary would be submitted to Canadian Blood Services and shared with PTBLC. As formulary manager, Canadian Blood Services will supplement recommendations with additional information and submit to the PTBLC for review and decision by the Conference of Deputy Ministers. After the final recommendation has been issued, CADTH may provide implementation support for the PTBLC and Canadian Blood Services as required. This support is distinct from the interim PPP process and is offered for the purposes of assisting Canadian Blood Services and the PTBLC in operationalizing recommendations from CADTH and/or making reimbursement policy decisions. Examples of implementation support activities are described in section 14 of the Procedure and Submission Guidelines for the CADTH Common Drug Review.

10. Other Administrative Items

9.1 Temporary Suspension and Withdrawal

Procedures for temporary suspension and withdrawal from the interim PPP process are similar to those used in CADTH’s existing CDR process and are described in the Procedure and Submission Guidelines for the CADTH Common Drug Review.

9.2 Confidentiality and Document Management

Confidential information obtained by CADTH for the purposes of the interim PPP process will be protected and handled in accordance with CADTH’s Confidentiality Guidelines for the CADTH Common Drug Review. These guidelines are available in the Procedure and Submission Guidelines for the CADTH Common Drug Review.
Figure 1: Overview of the Interim Plasma-Protein Products Review Process

1. PTBLC confirms that product is eligible for review through the interim plasma-protein process
2. Advance notification received by CADTH
3. CADTH and CBS issue call for patient group input
4. Submission screened and accepted for review
5. CADTH review report(s) prepared by the review team
6. CADTH review reports sent to sponsor for comments
7. Sponsor’s comments sent to CADTH
8. Finalized reviews, comments, responses, and patient input sent to the expert committee, CBS, PTBLC, and the drug plans
9. Deliberation
10. Embargoed recommendation issued to sponsor, CBS, PTBLC, and the drug plans
11. Embargo period
12. Request for reconsideration by the sponsor and/or request for clarification by CBS, PTBLC, and/or drug plans
13. Deliberation
14. Recommendation substantially revised
15. Recommendation upheld or minor revisions
16. Sponsor completes redaction requests and CADTH redacts confidential information
17. Final recommendation posted and CADTH review report(s) posted
18. CBS reviews and provides implementation support
19. Public payers make reimbursement decision

CBS = Canadian Blood Services; PTBLC = Provincial/Territorial Blood Liaison Committee