

**pan-Canadian Oncology Drug Review
Stakeholder Feedback on a pCODR Expert
Review Committee Initial Recommendation
(Manufacturer)**

**Blinatumomab (Blincyto) for Philadelphia
chromosome positive Acute Lymphoblastic
Leukemia**

April 4, 2019

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s): Blinatumomab (BLINCYTO®) for Philadelphia chromosome positive (Ph+) B-Cell precursor lymphoblastic leukemia (BCP-ALL)

Eligible Stakeholder Role in Review (Submitter and/or Manufacturer, Patient Group, Clinical Group): Submitter and Manufacturer

Organization Providing Feedback: Amgen Canada Inc.

**The pCODR program may contact this person if comments require clarification. Contact information will not be included in any public posting of this document by pCODR.*

3.1 Comments on the Initial Recommendation

a) Please indicate if the eligible stakeholder agrees, agrees in part, or disagrees with the Initial Recommendation:

agrees agrees in part disagree

Please explain why the Stakeholder agrees, agrees in part or disagrees with the Initial Recommendation. If the Stakeholder agrees in part or disagrees with the Initial Recommendation, please provide specific text from the recommendation and rationale. Please also highlight the applicable pERC deliberative quadrants for each point of disagreement. The points are to be numbered in order of significance.

Amgen Canada Inc. agrees with the Committee’s decision that there is a net clinical benefit associated with BLINCYTO® for patients with Ph+ BCP-ALL, and that BLINCYTO® aligned with patient values.

Amgen agrees in part with pERC’s initial recommendation, as it does not include patients who are intolerant to second-generation or later TKIs and intolerant to imatinib. Although “pERC felt that patients who were intolerant to second-generation or later TKIs and intolerant to imatinib have alternative therapies available to them,” Amgen questions this statement. This very small patient population has extremely limited treatment options (e.g., clinical trials). Some patients may be contraindicated for these treatments and/or the potential adverse event risk may make them ineligible.

BLINCYTO® offers a new mechanism of action. In addition, this patient population was included in the ALCANTARA study (refer to inclusion criteria in Martinelli et al., 2017). Amgen requests that the initial recommendation to be modified to recommend blinatumomab for the treatment of adult patient with Ph+ BCP-ALL who have been treated with at least two prior TKIs and have R/R disease OR are intolerant to second-generation or later TKIs and intolerant to imatinib.

In addition, Amgen disagrees with pERC’s statement that “there will be considerable wastage with

blinatumomab, given the challenges associated with implementing blinatumomab protocols.” The vial size for blinatumomab is as small as possible given current vial pressurization technology. Since blinatumomab is infused continuously for 28 days each cycle using an infusion pump, and that multi-day bags (i.e., 24hr, 48hr, 72hr, 96hr, or 7-day) can be prepared and stored for up to 10 days, there are numerous opportunities to minimize wastage. Note that when a multi-day bag is prepared, multiple vials of blinatumomab are typically required however the required volume of stabilizer that is to be added to the bag remains the same (5.5mL per bag). Over time, centres will have vials of stabilizer leftover that can be used to further minimize wastage.

b) Please provide editorial feedback on the Initial Recommendation to aid in clarity. Is the Initial Recommendation or are the components of the recommendation (e.g., clinical and economic evidence) clearly worded? Is the intent clear? Are the reasons clear?

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
			No comments

3.2 Comments Related to Eligible Stakeholder Provided Information

Notwithstanding the feedback provided in part a) above, please indicate if the Stakeholder would support this Initial Recommendation proceeding to Final pERC Recommendation (“early conversion”), which would occur two (2) Business Days after the end of the feedback deadline date.

- | | |
|--|--|
| <input type="checkbox"/> Support conversion to Final Recommendation.
Recommendation does not require reconsideration by pERC. | <input checked="" type="checkbox"/> Do not support conversion to Final Recommendation.
Recommendation should be reconsidered by pERC. |
|--|--|

If the eligible stakeholder does not support conversion to a Final Recommendation, please provide feedback on any issues not adequately addressed in the Initial Recommendation based on any information provided by the Stakeholder in the submission or as additional information during the review.

Please note that new evidence will be not considered at this part of the review process, however, it may be eligible for a Resubmission. If you are unclear as to whether the information you are providing is eligible for a Resubmission, please contact the pCODR program.

Additionally, if the eligible stakeholder supports early conversion to a Final Recommendation; however, the stakeholder has included substantive comments that requires further interpretation of the evidence, the criteria for early conversion will be deemed to have not been met and the Initial Recommendation will be returned to pERC for further deliberation and reconsideration at the next possible pERC meeting.

Page Number	Section Title	Paragraph, Line Number	Comments related to Stakeholder Information

1 About Stakeholder Feedback

pCODR invites eligible stakeholders to provide feedback and comments on the Initial Recommendation made by the pCODR Expert Review Committee (pERC). (See www.cadth.ca/pcodr for information regarding review status and feedback deadlines.)

As part of the pCODR review process, pERC makes an Initial Recommendation based on its review of the clinical benefit, patient values, economic evaluation and adoption feasibility for a drug. (See www.cadth.ca/pcodr for a description of the pCODR process.) The Initial Recommendation is then posted for feedback from eligible stakeholders. All eligible stakeholders have 10 (ten) business days within which to provide their feedback on the initial recommendation. It should be noted that the Initial Recommendation may or may not change following a review of the feedback from stakeholders.

pERC welcomes comments and feedback from all eligible stakeholders with the expectation that even the most critical feedback be delivered respectfully and with civility.

A. Application of Early Conversion

The Stakeholder Feedback document poses two key questions:

1. Does the stakeholder agree, agree in part, or disagree with the Initial Recommendation?

All eligible stakeholders are requested to indicate whether they agree, agree in part or disagrees with the Initial Recommendation, and to provide a rationale for their response.

Please note that if a stakeholder agrees, agrees in part or disagrees with the Initial Recommendation, the stakeholder can still support the recommendation proceeding to a Final Recommendation (i.e. early conversion).

2. Does the stakeholder support the recommendation proceeding to a Final Recommendation (“early conversion”)?

An efficient review process is one of pCODR’s key guiding principles. If all eligible stakeholders support the Initial Recommendation proceeding to a Final Recommendation and that the criteria for early conversion as set out in the *pCODR Procedures* are met, the Final Recommendation will be posted on the CADTH website two (2) Business Days after the end of the feedback deadline date. This is called an “early conversion” of an Initial Recommendation to a Final Recommendation.

For stakeholders who support early conversion, please note that if there are substantive comments on any of the key quadrants of the deliberative framework (e.g., differences in the interpretation of the evidence), the criteria for early conversion will be deemed to have not been met and the Initial Recommendation will be returned to pERC for further deliberation and reconsideration at the next possible pERC meeting. Please note that if any one of the eligible stakeholders does not support the Initial Recommendation proceeding to a Final pERC Recommendation, pERC will review all feedback and comments received at a subsequent pERC meeting and reconsider the Initial Recommendation.

B. Guidance on Scope of Feedback for Early Conversion

Information that is within scope of feedback for early conversion includes the identification of errors in the reporting or a lack of clarity in the information provided in the review documents.

Based on the feedback received, pERC will consider revising the recommendation document, as appropriate and to provide clarity.

If a lack of clarity is noted, please provide suggestions to improve the clarity of the information in the Initial Recommendation. If the feedback can be addressed editorially this will be done by the pCODR staff, in consultation with the pERC chair and pERC members, and may not require reconsideration at a subsequent pERC meeting.

The Final pERC Recommendation will be made available to the participating federal, provincial and territorial ministries of health and provincial cancer agencies for their use in guiding their funding decisions and will also be made publicly available once it has been finalized.

2 Instructions for Providing Feedback

- a) The following stakeholders are eligible to submit Feedback on the Initial Recommendation:
 - The Submitter making the pCODR Submission, or the Manufacturer of the drug under review;
 - Patient groups who have provided input on the drug submission;
 - Registered clinician(s) who have provided input on the drug submission; and
 - The Provincial Advisory Group (PAG)
- b) Feedback or comments must be based on the evidence that was considered by pERC in making the Initial Recommendation. No new evidence will be considered at this part of the review process, however, it may be eligible for a Resubmission.
- c) The template for providing *Stakeholder Feedback on pERC Initial Recommendation* can be downloaded from the pCODR section of the CADTH website. (See www.cadth.ca/pcodr for a description of the pCODR process and supporting materials and templates.)
- d) At this time, the template must be completed in English. The Stakeholder should complete those sections of the template where they have substantive comments and should not feel obligated to complete every section, if that section does not apply.
- e) Feedback on the pERC Initial Recommendation should not exceed three (3) pages in length, using a minimum 11 point font on 8 ½" by 11" paper. If comments submitted exceed three pages, only the first three pages of feedback will be provided to the pERC for their consideration.
- f) Feedback should be presented clearly and succinctly in point form, whenever possible. The issue(s) should be clearly stated and specific reference must be made to the section of the recommendation document under discussion (i.e., page number, section title, and paragraph). Opinions from experts and testimonials should not be provided. Comments should be restricted to the content of the Initial Recommendation.
- g) References to support comments may be provided separately; however, these cannot be related to new evidence. New evidence is not considered at this part of the review process, however, it may be eligible for a Resubmission. If you are unclear as to whether the information you are considering to provide is eligible for a Resubmission, please contact the pCODR program.
- h) The comments must be submitted via a Microsoft Word (not PDF) document to pCODR by the posted deadline date.

- i) If you have any questions about the feedback process, please e-mail pcodrsubmissions@cadth.ca

Note: CADTH is committed to providing an open and transparent cancer drug review process and to the need to be accountable for its recommendations to patients and the public. Submitted feedback will be posted on the CADTH website (www.cadth.ca/pcodr). The submitted information in the feedback template will be made fully disclosable.