pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

Provincial Advisory Group (PAG) Feedback on a pCODR Expert Review Committee Initial Recommendation

Blinatumomab (Blincyto) for Acute Lymphoblastic Leukemia

April 1, 2016

3 Feedback on pERC Initial Recommendation

Name of the drug indication(s): Blinatumomab (Blincyto) for Acute Lymphoblastic Leukemia

Endorsed by: Provincial Advisory Group Chair

Feedback was provided by all nine provinces (Ministries of Health and/or provincial cancer agencies) participating in pCODR.

3.1 Comments on the Initial Recommendation

a) Please indicate if the PAG (either as individual PAG members and/or as a group) agrees or disagrees with the initial recommendation:

_____ Agrees __x__ Agrees in part ____ Disagree

Some members providing feedback agree with the pERC initial recommendation. Some members agrees in part with the recommendation.

PAG agrees with the recommendation for the treatment of adult patients with Philadelphia chromosome-negative (Ph-) relapsed or refractory B precursor acute lymphoblastic leukemia (ALL) and who have had only one prior systemic chemotherapy.

PAG agrees in part with the recommendation for patients who had at least two prior lines of systemic therapy as pERC concluded there "may be a benefit" but PAG feels that the feasibility and high costs associated with implementation were under-estimated.

b) Notwithstanding the feedback provided in part a) above, please indicate if the PAG would support this initial recommendation proceeding to final pERC recommendation ("early conversion"), which would occur within 2(two) business days of the end of the consultation period.

_____ Support conversion to final recommendation.
Recommendation does not require reconsideration by pERC.

__x___ Do not support conversion to final recommendation.
Recommendation should be reconsidered by pERC.

Most PAG members providing feedback support conversion of the initial recommendation. Some members request pERC reconsider the recommendation to fund for patients with Ph- ALL who have had at least two prior lines of systemic therapy. Given that the evidence does not clearly demonstrate benefit, the lack of comparative and long term outcome data, the absence of quality of life data, and the toxicity pattern, it is difficult to justify the funding a high cost and resource intensive treatment, even with an improvement in cost-effectiveness. PAG is seeking reconsideration to ensure resources, both human and capital, and the feasibility issues are adequately addressed in the recommendation to fund in this setting.

c) Please provide feedback on the initial recommendation. 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
1	pERC Recommendation	Paragraph 2	This treatment is exceptionally resource-intensive, which further hinders its cost effectiveness. The fact that there is no alternative for patients who had two prior therapies should not be sufficient reasoning to recommend funding when the strength of evidence to support this is low, the magnitude of benefits unclear, and the cost of therapy in terms of drug cost and other resources is so high.
1	pERC Recommendation		PAG noted that the trials included in the review enrolled patients with ECOG performance status of 2 or less. PAG is seeking clarification on whether the performance status of 2 or less applies to this recommendation, as in other recommendations.
2	Potential Next Steps for Stakeholders	Paragraph 5	PAG feels that it should not be the jurisdictions' responsibility to advocate for the availability of a smaller vial size after agreeing to list the product. It is not acceptable to discard almost 10% of the vial each day given the regimen uses fixed-dosing. The manufacturer should be responsible to consider vial sizes that would minimize drug wastage.

3.2 Comments related to PAG input

Please provide feedback on any issues not adequately addressed in the initial recommendation based on the PAG input provided at the outset of the review on potential impacts and feasibility issues of adopting the drug within the health system.

Page Number	Section Title	Paragraph, Line Number	Comments related to initial PAG input
			This treatment is exceptionally resource-intensive, as identified in the PAG input. PAG would like the pERC

			recommendation to emphasize the difficulty of adopting the treatment into the health system, particularly the costs to the health system. In the provinces where a few patients are being treated with blinatumomab through the manufacturer's compassionate supply program, PAG identified the following: • Incremental costs to purchase the specified smart infusion pumps required to deliver the infusion • Training of pharmacy and nursing staff on the preparation and use of the smart infusion pumps is required. In centers where there may be only one or two patients per year, re-training would be required. • The coordination of outpatient and hospital resources is required for each 28-day cycle. • Resources to monitor and treat adverse effects. • Additionally, the carrying costs of an expensive antidote (tociluzumab) to treat patients who experience life-threatening cytokine release syndrome associated with blinatumomab (Teachey et al. Blood 2013: 121(26) http://www.bloodjournal.org/content/121/26/5154)

3.3 Additional comments about the initial recommendation document

Please provide any additional comments:

Page Number	Section Title	Paragraph, Line Number	Additional Comments
			According to one provincial hematology disease group: - If elderly (no transplant), will likely not use blinatumomab since it is toxic - If a young patient who is potentially curative (transplant eventually), would use this drug - If patient is palliative (not transplant eligible), would not use this drug.
			Although blinatumomab infusion bags are stable for 96 hours, PAG noted that the batteries in the infusion pumps may not last for 96 hours. Thus, in practice, the infusions bags would need to be prepared and changed every 48 hours to ensure continuous infusion. In addition, there is a change in dose in cycle 1 on day 8, at which point the infusion bags must be changed to accommodate the dose change.

About Completing This Template

pCODR invites the Provincial Advisory Group (PAG) to provide feedback and comments on the initial recommendation made by the pCODR Expert Review Committee. (See www.cadth.ca/pcodr for information regarding review status and feedback deadlines.)

As part of the pCODR re view process, the pCODR Expert Review Committee makes an initial recommendation based on its review of the clinical, economic and patient evidence for a drug. (See www.cadth.ca/pcodr for a description of the pCODR process.) The pERC initial recommendation is then posted for feedback and comments from various stakeholders. The pCODR Expert Review Committee welcomes comments and feedback that will help the members understand why the PAG, either as individual PAG members and/or as a group, agrees or disagrees with the pERC initial recommendation. In addition, the members of pERC would like to know if there is any lack of clarity in the document and if so, what could be done to improve the clarity of the information in the pERC initial recommendation. Other comments are welcome as well.

All stakeholders have 10 (ten) business days within which to provide their feedback on the initial recommendation and rationale. If all invited stakeholders agree with the recommended clinical population described in the initial recommendation, it will proceed to a pERC final recommendation by 2 (two) business days after the end of the consultation (feedback) period. This is called an "early conversion" of an initial recommendation to a final recommendation.

If any one of the invited stakeholders does not support the initial recommendation proceeding to a pERC final recommendation, pERC will review all feedback and comments received at the next possible pERC meeting. Based on the feedback received, pERC will consider revising the recommendation document as appropriate. It should be noted that the initial recommendation and rationale for it may or may not change following consultation with stakeholders.

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

Instructions for Providing Feedback

a) Only members of the PAG can provide feedback on the pERC initial recommendation; delegates must work through the PAG representative to whom they report.
    a. Please note that only one submission is permitted for the PAG. Thus, the feedback should include both individual PAG members and/or group feedback.

b) Feedback or comments must be based on the evidence that was considered by pERC in making the pERC 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 *Provincial Advisory Group (PAG) Feedback on a pERC Initial Recommendation* can be downloaded from the pCODR 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. PAG 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. Similarly, PAG should not feel restricted by the space allotted on the form and can expand the tables in the template as required.

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 forwarded to the pERC.

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 Secretariat.

h) The comments must be submitted via a Microsoft Word (not PDF) document to the pCODR Secretariat by the posted deadline date.

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

Note: Submitted feedback may be used in documents available to the public. The confidentiality of any submitted information cannot be protected.