CADTH | pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

Submitter or Manufacturer Feedback on a pCODR Expert Review Committee Initial Recommendation

Inotuzumab Ozogamicin (Besponsa) for Acute Lymphoblastic Leukemia

July 6, 2018

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	Besponsa (inotuzumab ozogamicin) for the treatment of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)
Eligible Stakeholder Role in Review:	Submitter and Manufacturer
Organization Providing Feedback:	Pfizer Canada Inc.

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 **__X__ agrees in part** ____ disagree

Pfizer Canada carefully reviewed the pCODR Expert Review Committee (pERC) Initial Recommendation, summary of deliberation and evidence in brief. Overall, Pfizer agrees with the scope of the recommendation and the clinical assessment, and also supports the general alignment of the provincial advisory groups, clinicians and patient advocates input. That being said, Pfizer Canada has noted an issue relative to the Initial Economic Guidance document used in pERC deliberations.

Pfizer Canada believes that pERC may have deliberated on the cost-effectiveness of inotuzumab ozogamicin (InO) based on results of probabilistic analyses that were run using an influential parameter that was incorrect. Pfizer appreciates that this error occurred because it inadvertently did not inform pCODR that the body surface area (BSA) parameter needed to be modified in two places when running the probabilistic sensitivity analyses (PSA). As a result, pERC concluded that substantial uncertainty exists in the economic model, where in fact we believe that the probabilistic analysis results should have been more consistent with the deterministic analyses results. This applies to both the comparison with chemotherapy (Hyper-CVAD) and blinatumomab.

pCODR representatives clarified that the process step of "Stakeholder Feedback on a pERC Initial Recommendation" is the opportunity for Pfizer Canada to provide the appropriate input on this issue.

With information provided in the Initial Economic Guidance document, we replicated as closely as possible the Best Guess Estimate scenarios for the comparison to chemotherapy and blinatumomab. We obtained deterministic incremental cost-effectiveness ratios (ICERs) of $201,928/QALY and -$59,856/QALY, respectively. We then reran probabilistic analyses for 5000 iterations. The average probabilistic ICERs were $203,255/QALY versus chemotherapy and -$62,375/QALY versus blinatumomab. These results are very consistent with their respective deterministic ICERs. We are confident that pCODR will also obtain similarly uniform ICERs once the BSA input is adjusted in their version of the economic model.

As a result, Pfizer Canada respectfully requests that the relevant input be corrected in the economic model and that new probabilistic analyses results be presented to pERC for reconsideration for the final pERC recommendation.

3.2 Comments Related to Eligible Stakeholder Provided Information

b)

____ 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.**

Page #	Section Title	Paragraph, Line Number	Comments related to Stakeholder Information
2.	pERC Recom-mendation	Par #6; line 4	"pERC noted that there was considerable uncertainty the cost-effectiveness estimates of inotuzumab ozogamicin compared with blinatumomab due to lack of robust direct or indirect comparative effectiveness data in the submitted economic evaluation."
Pfizer Canada acknowledges the limitations of indirect treatment comparisons, but would like to reiterate that much of the reported uncertainty mentioned in this paragraph is related to an input issue when probabilistic analyses are run in the economic model.			
6. 12.	Summary of pERC delibe-rations; Economic evaluation	Par #7; line 19 Par #13; line 1	"(…) pERC agreed with the EGP's best estimate of the probabilistic ICER when compared with chemotherapy and blinatumomab"
Pfizer Canada believes that pERC may have deliberated on the cost-effectiveness of InO based on results of probabilistic analyses that were run using an influential parameter that was incorrect. This applies to both the comparison with chemotherapy and blinatumomab. As a result, we believe that the conclusions in the report will not be the same following a pERC reconsideration using a corrected PSA.			
6 12.	Summary of pERC delibe-rations; Economic evaluation	Par #7; line 25 Par #13; line 8	"(…) pERC noted that the considerable uncertainty in the model parameters (…) is demonstrated by the change in direction of the EGP's reanalysis of the probabilistic ICER (…)"
Pfizer Canada acknowledges the limitations of indirect treatment comparisons, but would like to emphasize that probabilistic analyses results have been consistently close to deterministic analyses results, and that the reported change of direction is directly linked to an input issue when probabilistic analyses are ran in the economic model.			
11.	Economic evaluation	Par #8; line 2 Par #8; line 7 Par #8; line 11	"(…) inotuzumab is likely not cost-effective compared with blinatumomab at the submitted price." "(…) with a best guess point estimate of $349,175.02 per QALY based on the probabilistic ICER." "(…) with a best guess point estimate of 126,625.47 per QALY based on probabilistic ICER."
Pfizer Canada believes that pERC may have deliberated on the cost-effectiveness of InO based on results of probabilistic analyses that were run using an influential parameter that was incorrect. This applies to both the comparison with chemotherapy (Hyper-CVAD) and blinatumomab. As a result, we believe that the conclusions of the report will not be the same following a pERC reconsideration using corrected PSA.			

About Completing This Template

pCODR invites the Submitter, or the Manufacturer of the drug under review if they were not the Submitter, to provide feedback and comments on the initial recommendation made by pERC. (See www.cadth.ca/pcodr for information regarding review status and feedback deadlines.)

As part of the pCODR review 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 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 Submitter (or the Manufacturer of the drug under review, if not the Submitter), agrees or disagrees with the 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 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 final pERC 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 final pERC 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 final pERC 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 the group making the pCODR Submission, or the Manufacturer of the drug under review can provide feedback on the initial recommendation.

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 *Submitter or Manufacturer Feedback on 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. The Submitter (or the Manufacturer of the drug under review, if not the Submitter) 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, the Submitter (or the Manufacturer of the drug under review, if not the Submitter) 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 pcodrsubmissions@cadth.ca.

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