pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

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

Brentuximab (Adcetris) for Hodgkin Lymphoma - Resubmission

February 21, 2018

Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	ADCETRIS®; post-autologous stem cell transplant consolidation treatment in HL
Eligible Stakeholder Role in Review (Submitter and/or Manufacturer, Patient Group, Clinical	Manufacturer
Organization Providing Feedback	Seattle Genetics, 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

Economic Evaluation Deliberative Quadrant

Seattle Genetics does not agree with the re-analysis of the economic evaluation performed by the EGP. Please refer to the detailed comment in section 3.2.

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

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.

_x___ Support conversion to Final Recommendation.	____ Do not support conversion to Final Recommendation.
Recommendation does not require reconsideration by pERC.	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.

Page Number	Section Title	Paragraph, Line Number	Comments related to Stakeholder Information
pCODR Initial Economic Guidance Report Page 5	1.4 Detailed Highlights of the EGP Reanalysis	Paragraph 1, Changes to the submitted economic model outlined in the three bullet points	**<u>Economic Evaluation Deliberative Quadrant</u>** Seattle Genetics does not agree with the re-analysis of the economic evaluation performed by the EGP for the reasons outlined below in order of significance. 1. **Time horizon**. The EGP decision to use a 15-year time horizon biases the analysis against finding that ADCETRIS is cost-effective. **We respectfully request that the final pERC recommendation indicate that use of a 15- or 20-year horizon may significantly underestimate the current Canadian lifespan of HL patients.** Leading Canadian clinicians/investigators in the treatment of patients with HL have stated that HL patients' life expectancy is at least 40-45 years and that 65 years is not unrealistic: *a.* British Columbia: *"For me the bottom line is that in the real world it is sensible to project results out to at least 45 years and, since deaths from Hodgkin lymphoma very seldom occur after 10 years, even longer projections are reasonable."* *b.* Ontario: *"…if we're looking at curative therapy, these are younger patients so probably up to 40-50 years becomes ultimately realistic (but the number of SCT patients followed that long is still going to be pretty low…)".* 2. **Treatment duration**. We don't agree that 16 cycles is the correct base case assumption. In the trial, patients used a median of 15 cycles. It is best to base treatment duration on actual vs. planned, since actual is a closer estimate of real life use. If anything, outside of a trial situation, the actual number of cycles could be even lower with expected real world compliance. 3. **Use of independent assessment of outcomes**: PCODR's choice can be justified because it was the primary approach accepted by the FDA and would be supported by most clinical trial experts as the least prone to bias; however, use of investigator assessments in the submitted model

was preferred because there were more points of assessment over a longer time horizon.

In line with the clinicians' estimates that 45 years would be much more representative of the lifespan of an individual with HL, the economic evaluation has been re-run with a 45-year horizon while also incorporating the EGP preferred parameters of 16 cycles and independent assessment of outcomes. The results are presented in the table below in contrast with the submitted base case results and with the EGP re-analysis using a 15-year horizon. The dramatically different results based on changing only the duration of the lifetime horizon shows how **the assumption of a significantly shortened lifespan (that is not consistent with Canadian clinical experience) biases the results against ADCETRIS.**

Analysis	Δ C	Δ E QALYs	ICUR (QALY)
Base case – 65 year horizon	$113,900	4.33	$26,303
Re-analysis of 45-year horizon with 16 cycles and independent assessment of outcomes	**$171,686**	**4.15**	**$41,362**
EGP – 15 year horizon best estimate of the three parameters	$123,999	0.89	$139,286

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 submissions@pcodr.ca.

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