pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

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

Cobimetinib (Cotellic) for Metastatic Melanoma

June 30, 2016

3 Feedback on pERC Initial Recommendation

Name of the drug indication(s): Cobimetinib (Cotellic) for Metastatic Melanoma

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

All PAG members providing feedback agreed in part with the pERC initial recommendation.

There appears to be inconsistency in pERC's statement where "pERC does not recommend reimbursement" and pERC's comments in the Potential Next Steps where "pERC was unable to make a recommendation for or against cobimetinib-vemurafenib" for previously treated patients.

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.	___X__ Do not support conversion to final recommendation.
Recommendation does not require reconsideration by pERC.	Recommendation should be reconsidered by pERC.

PAG is requesting reconsideration for clarification on the intended treatment group. It is unclear whether "previously untreated BRAF V600 mutation positive" is intended to include or exclude patients previously treated with ipilimumab or other immunotherapies (such as pembrolizumab, nivolumab).

Further, the cobimetinib-vemurafenib recommendation seems inconsistent with the dabrafenib-trametinib recommendation, where a negative recommendation was specifically called out for previously treated BRAF V600 mutation-positive patients in the former, but not the latter. It is noted that both these combinations occupy the same space; PAG is requesting clarification on the reason for the differences in the recommendations.

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 & Next Steps	Paragraph 2	The sentence in the pERC Recommendation section "*pERC does not recommend reimbursement of cobimetinib plus vemurafenib for the treatment of patients with previously treated BRAF V600 mutation-positive unresectable metastatic melanoma*" seems to be inconsistent with the statement in the Next Steps "*pERC could not make a recommendation for the use of cobimetinib plus vemurafenib for the treatment of patients with BRAF V600 mutation-positive unresectable or metastatic melanoma whose disease has progressed on first-line vemurafenib*". PAG suggests the sentence in the pERC recommendation be revised to "pERC was unable to make a recommendation"
1	pERC Recommendation & Potential Next Steps for Stakeholder		One of the provincial tumour groups, through their PAG member, did not agree with the recommendation to only treat first line patients. PAG is seeking clarification on whether there is evidence or not for the use of BRAF+MEK inhibitor in patients previously treated with ipilimumab. PAG noted that there is a large number of prevalent patients who have been previously treated with ipilimumab who require treatment for disease progression.
3	Potential Next Steps for Stakeholder		PAG noted that the sequencing issue for this therapeutic area is an issue and is requesting Potential Next Steps include Sequencing of Treatments and the need for real-world evidence generation on optimal sequencing.
3	Potential Next Steps for Stakeholder		PAG noted that the optimal duration of therapy is unknown and is requesting Potential Next Steps include Evidence Generation to Understand Optimal Duration of Therapy

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
			PAG identified that the main issues are with respect to lines of treatment. Currently for a BRAF positive patient, there is the option of treating with BRAF inhibitor or ipilimumab. Some patients may also have accessed immunotherapies such as pembrolizumab or nivolumab through manufacturer patient assistance programs.
			PAG is asking whether pERC can comment on the use of BRAF+MEK inhibitor combination in patients who have received a short course of BRAF+MEK inhibitor combination for unresectable disease, and then had surgery. PAG is seeking clarity on whether these patients would still be eligible for further treatment if recurrence occurred.

3.3 Additional comments about the initial recommendation document

Please provide any additional comments:

Page Number	Section Title	Paragraph, Line Number	Additional Comments
1	pERC Recommendation	Paragraph 2	One of the provincial tumour groups, through their PAG member, indicated that patients with active brain metastases can respond to BRAF inhibitors and this population should be able to access BRAF inhibitors. However, this is based on an open-label trial on vemurafenib (Dummer et al European Journal of Cancer 2014: 50(3);611-621). If possible, PAG is seeking comments from pERC on the generalizability of this (or related) evidence to cobimentinib-vemurafenib combination.

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.pcodr.ca 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.pcodr.ca 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.pcodr.ca 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.