CADTH | pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

Registered Clinician Feedback on a pCODR Expert Review Committee Initial Recommendation

Panitumumab (Vectibix) for Left Sided metastatic Colorectal Carcinoma

March 29, 2018

3 Feedback on pERC Initial Recommendation

Name of the drug indication(s):	Panitumumab/ left-sided mCRC
Name of registered clinician(s):	Dr. E Kennedy, Dr. J Biagi, Dr. B Meyers, Dr. S Welch

**pCODR 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 registered clinician(s) agrees or disagrees with the initial recommendation:

____ agrees ____ agrees in part **X** disagree

Please explain why the registered clinician(s) agrees, agrees in part or disagrees with the initial recommendation.

The current recommendation against PMAB appears to only look at the issue from the viewpoint of benefit, and not the potential for harm from this therapy in a patient with the wrong clinical characteristics (ie. right sided tumour).

PERC seem suggests that a larger trial is required to further evaluate this finding. This is extremely unlikely, and the corollary is that EGFR therapy in a right-sided tumour potential is more harmful has serious implications of future trial design.

The recommendations against PMAB extend to a number of areas:

1) Toxicity, however provided data do not compare to toxicity of chemotherapy + bevacizumab.

2) The need for RAS testing. Most centres are moving to reflex testing in multiple tumour disease sites, so RAS testing likely should be considered standard of care.

3) The downstream implications of bevacizumab in second line. This is an important consideration, but the funding of bevacizumab is likely a separate discussion.

Panitumumab has demonstrated a significant magnitude of benefit and is recommended (an EGFR mAb) along with standard chemotherapy for patients with ls RAS wild type CRC by guidelines published in Current Oncology

b) Notwithstanding the feedback provided in part a) above, please indicate if the registered clinician(s) 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.

____	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.

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	Recommendation	2, 5	There was considerable uncertainty…with panitumumab. Clarify why there is uncertainty with PFS and OS specifically. Clarify toxicity concerns.

3.2 Comments Related to the Registered Clinician(s) Input

Please provide feedback on any issues not adequately addressed in the initial recommendation based on registered clinician(s) input provided at the outset of the review on outcomes or issues important that were identified in the submitted clinician input. Please note that new evidence will be not considered during 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.

Examples of issues to consider include: Are there therapy gaps? Does the drug under review have any disadvantages? Stakeholders may also consider other factors not listed here.

Page Number	Section Title	Paragraph, Line Number	Comments related to initial registered clinician input
4	Summary of PERC deliberations	2, 5	"PERC agreed that until more robust data become available". It is highly unlikely that additional randomized studies will be completed given the effect size observed, and concern that if retrospective data is correct, use of EGFR therapy in right-sided tumour is associated with harm

3.3 Additional comments about the initial recommendation document

Please provide any additional comments:

Page Number	Section Title	Paragraph, Line Number	Additional Comments
7	Limitations	2	PEAK and PRIME are discussed. Unclear that these studies differ in OS and PFS outcomes, suggests that the former trial is simply a negative trial (whereas there was no OS benefit).
	Patient values	3	Need to be more specific about side effects associated with chemotherapy, vs EGFR therapy. Also, side effect profile of bevacizumab and QoL not mentioned as a comparator. Patient feedback on side effects are described as tolerable, but this differs from this discussion earlier (page 4) stating that the combination has considerable side effects. Concerns were also raised that patient feedback was obtained from patients with left and right-sided tumours. Unclear the point of this statement.

1 About Completing This Template

pCODR invites those registered clinicians that provided input on the drug under review **prior** to deliberation by the pCODR Expert Review Committee (pERC), to also 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 registered clinician(s) agree or disagree 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, including registered clinician(s), agree with the recommended clinical population described in the initial recommendation, it will proceed to a final pERC recommendation 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.

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.

2 Instructions for Providing Feedback

a) Only registered clinician(s) that provided input at the beginning of the review of the drug can provide feedback on the initial recommendation. If more than one submission is made by the same registered clinician(s), only the first submission will be considered.

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 during this part of the review process; however, it may be eligible for a Resubmission.

c) The template for providing *pCODR Clinician 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. Registered clinician(s) 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

registered clinician(s) 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 initial pERC recommendations 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). Comments should be restricted to the content of the initial recommendation.

g) References to support comments may be provided separately; however, these cannot be new references. New evidence is not considered during 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 by logging into www.cadth.ca/pcodr and selecting "Submit Feedback" by the posted deadline date.

i) If you have any questions about the feedback process, please e-mail submissions@pcodr.ca. Information about pCODR may be found at www.cadth.ca/pcodr.

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