PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

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

Panitumumab (Vectibix) for Metastatic Colorectal Cancer

December 3, 2015

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	Panitumumab for the treatment of previously untreated treatment of previously untreated patients with non-mutated (wildtype) *RAS* metastatic colorectal carcinoma (mCRC) in combination with FOLFOX
Role in Review (Submitter and/or Manufacturer):	Submitter and Manufacturer
Organization Providing Feedback	Amgen Canada Inc.

**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 Submitter (or the Manufacturer of the drug under review, if not the Submitter) agrees or disagrees with the initial recommendation:

____ agrees __X__ agrees in part ____ disagree

Please explain why the Submitter (or the Manufacturer of the drug under review, if not the Submitter) *agrees, agrees in part or disagrees with the initial recommendation.*

1) Agree with the recommendation to fund Vectibix in the patient population described.
2) Agree with pCODR on the unmet need in this patient population and recognizing the superior clinical benefit in patients who are unable to receive bevacizumab in the first-line setting. In addition, panitumumab involves predictive biomarkers that allow the selection of patients that are more likely to benefit from therapy, while reducing exposure to treatment-related toxicity risks in patient who will not benefit from EGFRi therapy.
3) Disagree that the recommendation is limited to "patients who have a contraindication to bevacizumab and who would otherwise be treated with FOLFOX" as the description of this patient population is incomplete and should be "**bevacizumab-ineligible** due to clinical reasons such as intolerance or contraindications and who would otherwise be treated with combination chemotherapy only" as per the patient population group acknowledged by the Clinical Guidance Panel in their report.
4) Disagree that the recommendation is limited to patients who do not receive bevacizumab in 1st line RAS WT mCRC as PEAK and CALGB80405 have shown better or at least equal efficacy between EGFRi + chemotherapy and bevacizumab + chemotherapy in 1st line RAS WT mCRC.

b) Notwithstanding the feedback provided in part a) above, please indicate if the Submitter (or the Manufacturer of the drug under review, if not the Submitter) 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.

__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.

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
p.1	pERC Recommendation	Paragraph 1; line 3-6: "for treatment of patients with WT RAS mCRC in the first-line treatment setting in combination with FOLFOX, who have a contraindication to bevacizumab and who would otherwise be treated with FOLFOX"	The Clinical Guidance Panel concluded that there is a moderate net overall clinical benefit to panitumumab + FOLFOX compared to FOLFOX alone in the **bevacizumab-ineligible** population. The description of the patient population in the pERC recommendation is incomplete and should be "**bevacizumab-ineligible** due to clinical reasons such as intolerance or contraindications and who would otherwise be treated with combination chemotherapy only" to accurately reflect the patient population acknowledged by the Clinical Guidance Panel in their report.
p.4	Summary of pERC deliberations	Paragraph 4; lines 6-7: "pERC accepted the pCODR clinical guidance panel's view… could likely be extended to panitumumab plus FOLFIRI"	There is variability in the use of backbone chemotherapy in first line mCRC treatment in Canada. Amgen appreciates that pERC made reference to the fact that the clinical benefits of panitumumab + FOLFOX could likely be extended to panitumumab + FOLFIRI. Amgen supports pERC's recommendation of panitumumab in the treatment of patients with WT RAS mCRC in the first line treatment setting in combination with FOLFOX/FOLFIRI who are bevacizumab-ineligible due to clinical reasons such as intolerance or contraindications and who would otherwise be treated with combination chemotherapy only.
p.4	Summary of pERC deliberations	Paragraph 3; lines 9-11: "pERC felt the estimates of cost-effectiveness	Based on the reanalysis conducted by the EGP on the Amgen submitted model, the first 3 reanalyses (i.e. wastage, liver resection rates and utilities for best supportive care) results in ICERs that were similar to Amgen's submitted ICERs.

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
		were very likely to be significantly higher than the submitter's and thus not be considered cost-effective."	The fourth scenario, at the 95% confidence interval for hazard ratio for progression-free survival, the upper and lower values were a significant driver of the ICER, but these extreme values do not reflect how likely these hazard ratios will occur. The cost-effectiveness ratios observed in these scenarios were quantitatively different than Amgen's submitted numbers, but it does not reflect the likelihood of these extreme values becoming reality. Decision making should occur based on the most likely cost-effectiveness ratios. Amgen used the best estimates available in a PSA model to incorporate uncertainty. Although it is customary to look at extreme impact of a variable through one way sensitivity analysis, acceptance of sensitivity analyses based on these extreme values should be interpreted with caution and should take into account likelihood of occurrence. Please consider revising the sentence to include "pERC felt the estimates of CE may be higher than the submitter's and thus not be considered cost effective."
p.7	Adoption Feasibility	Paragraph 1, line 2: "It was noted the high cost of panitumumab, the need for RAS testing in the first-line setting, and the longer infusion time are key challenges."	According to the bevacizumab product monograph: "The initial AVASTIN dose should be delivered over 90 minutes as an intravenous infusion. If the first infusion is well tolerated, the second infusion may be administered over 60 minutes. If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 minutes." In the panitumumab product monograph, panitumumab is to be infused over 60 minutes; therefore, the infusion time for bevacizumab and panitumumab is similar. While Amgen does acknowledge that clinical sites may adopt infusion practices that differ from what is outlined in the product monograph as they gain experience with the various treatment regimens, we are unable to comment on routine Canadian administration practices for either drug. Amgen requests "and the longer infusion time" to be taken out of the statement.

3.2 Comments Related to Submitter or Manufacturer-Provided Information

Please provide feedback on any issues not adequately addressed in the initial recommendation based on any information provided by the Submitter (or the Manufacturer of the drug under review, if not the Submitter) in the submission or as additional information during the review.

Please note that new evidence will be 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 providing is eligible for a Resubmission, please contact the pCODR Secretariat.

Page Number	Section Title	Paragraph, Line Number	Comments related to Submitter or Manufacturer-Provided Information

3.3 Additional Comments About the Initial Recommendation Document

Please provide any additional comments:

Page Number	Section Title	Paragraph, Line Number	Additional Comments

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.