PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

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

Everolimus (Afinitor) for Advanced Breast Cancer

March 25, 2013

Manufacturer Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	Afinitor in Advanced Breast Cancer
Role in Review (Submitter and/or Manufacturer):	Submitter and Manufacturer
Organization Providing Feedback	Novartis Pharmaceuticals 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.*

Novartis agrees in part with the pan-Canadian Oncology Drug Review Expert Review Committee's (pERC) initial recommendation. In general, the recommendation aligns with the pivotal BOLERO-2 clinical trial, Health Canada approved labelling, and guideline groups' recommendations for use of Afinitor in treatment algorithms.

Specifically, the pERC acknowledged the following for Afinitor:

> **Place in therapy:** For the treatment of hormone-receptor (HR) positive, HER2 negative advanced breast cancer in post-menopausal women after recurrence or progression following a non-steroidal aromatase inhibitor(NSAI), *"there is a need for therapies that delay progression and extend survival."*
>
> **Patient Values:** Afinitor aligns with patient values, as it offers patients a convenient oral option in breast cancer treatment which significantly delays disease progression without compromising quality of life vs. endocrine therapy alone.
>
> **Clinical Efficacy:** There is *"a clinically and statistically significant improvement in progression-free survival"*(11.0 months versus 4.1 months, HR=0.38, central radiological assessment)
>
> **Clinical Safety:** Afinitor has a predictable and manageable adverse event profile which is *"consistent with expectations for everolimus based on its use in other indications"* while maintaining quality of life.

In the following sections some points of clarification are provided, based on the BOLERO-2 clinical trial.

Summary of pERC Deliberations:

> *'pERC also noted that in some cases, e.g. if patients receive a dose of 7.5 mg, drug costs would double because there would be two tablets needed to achieve the desired dose.'*

Clarification: The 7.5 mg dose was not studied in the BOLERO-2 trial; there are no data to support use of this dose in the proposed indication.

Economic Evaluation:

> *'pERC also noted that in some cases, e.g. if patients receive a dose of 7.5 mg, drug costs would double because two tablets are required.'*

Clarification: The 7.5 mg dose was not studied in the BOLERO-2 trial; there are no data to support usage of this dose in the proposed indication. Management of adverse reactions may be achieved through temporary dose interruption and/or reduction (to either 5 mg or 2.5 mg) or treatment discontinuation.

Adoption Feasibility:

> *'pERC also noted that while dose reductions may occur with everolimus in practice, this would not lead to a corresponding reduction in drug costs because the cost of a 2.5 mg, 5 mg and 10 mg tablet is the same; in some cases, it may even increase drug costs.'*

Clarification: Recommended dose reductions for the management of toxicities are to 5 mg or to 2.5 mg (50% of previously administered dose); therefore, this should not result in an increase in drug costs.

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
2	Potential Next Steps for Stakeholders	3, 8	*'…population of patients to be able to receive**d** everolimus…"* Typographical error, should read, "receive."

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.pcodr.ca 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.pcodr.ca 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.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. 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.