pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

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

Enzalutamide (Xtandi) for Metastatic Castration-Resistant Prostate Cancer

July 23, 2013

3 Feedback on pERC Initial Recommendation

Name of the drug indication(s): Enzalutamide (Xtandi) for metastatic castration-resistant prostate cancer

Endorsed by: Provincial Advisory Group Chair

Feedback was provided by seven of the 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

PAG generally agrees with the pERC recommendation of enzalutamide being a "reasonable therapeutic alternative" to abiraterone. However, PAG requested the statement be revised for greater clarity to "enzalutamide would be an alternative to abiraterone for some patients in the post-docetaxel setting rather than being an add-on therapy to abiraterone treatment". This would be consistent with pERC's comments on Adoption Feasibility.

In addition, PAG would like the potential sequential use of enzalutamide in patients with disease progression on abiraterone be addressed in the Potential Next Steps for Stakeholders (in a similar fashion as with the initial recommendation for pazopanib mRCC resubmission).

pERC has indicated that enzalutamide was marginally cost-effective compared with best supportive care. However, the cost-effectiveness was also compared with abiraterone and PAG requested clarity on the term "marginal" when a threshold for incremental cost-effectiveness ratios has not been determined by pCODR and specifically in the context of the next steps for stakeholders.

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.

__X__ Support conversion to final recommendation.
Recommendation does not require reconsideration by pERC.

_____ Do not support conversion to final recommendation.
Recommendation should be reconsidered by pERC.

All PAG members providing feedback supported the conversion of the pERC initial recommendation to a pERC final recommendation.

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
3	Summary	Last one , line 2 and 3	Pull this sentence up to PERC recommendation as buried but this is clinically relevant – alternative NOT add on to abiraterone

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
2	Summary of pERC Deliberations	Paragraph 1; line 9	Add "or cabazitaxel"
3	Summary of pERC deliberations	Paragraph 2, Line 4	Can a more definitive statement be made on sequencing to ensure consistency amongst provinces in their funding policies – e.g., pERC is not able to make any recommendations on sequencing of treatments post-docetaxel since there are no studies evaluating this question.
4	Comparator Information: uncertainty in results of indirect comparison of abiraterone	Paragraph 1: line 4	Consider listing some of the specific limitations with the indirect comparison
5	Economic model submitted: cost utility	Section title	Should this read ": cost-effectiveness" which is consistent with the paragraph below?
6	Adoption feasibility	Paragraph 1; line 8	Remove "be". Also, please further elaborate on how not requiring concomitant use of prednisone could help facilitate the implementation of enzalutamide.

3.3 Additional comments about the initial recommendation document

Please provide any additional comments:

Page Number	Section Title	Paragraph, Line Number	Additional Comments
4	Safety	Paragraph 2, last line	Although patients with a history of a seizure or any condition that may predispose to seizure were excluded from the AFFIRM study, seven patients in the enzalutamide group experienced a seizure compared to no patients in the placebo group, highlighting a potential safety issue with enzalutamide that may require further exploration or post-marketing surveillance.

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.