CADTH

pan-Canadian Oncology Drug Review Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation (Provincial Advisory Group [PAG])

Niraparib (Zejula) for Ovarian Cancer

September 3, 2020

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	Niraparib for recurrent OC
Eligible Stakeholder Role in Review (Submitter and/or Manufacturer, Patient Organization Providing Feedback	PAG

**The pCODR program 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 eligible stakeholder agrees, agrees in part, or disagrees with the Initial Recommendation:

☒ agrees ☐ agrees in part ☐ disagree

Seven jurisdictions agree. One jurisdiction agrees in part with the initial pERC recommendation for the BRCA positive patient population however for patients that are not BRCA positive, the jurisdiction would agree with HRD positive patients. Based on the toxicity profile in the HRD negative population, the jurisdiction believes there is uncertainty whether the PFS of 3 months is truly a meaningful improvement.

b) Please provide editorial feedback on the Initial Recommendation to aid in clarity. 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	First paragraph	Suggest removing "female" in definition of eligible patient population to be consistent with previous recommendations for gynecology and GU cancer indications using gender neutral language and referring to the underlying diagnosis as opposed to the gender.
2	Next Steps for Stakeholders	Time Limited Need	Should a time-limited recommendation be added to align with what was done for

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
			olaparib? For example, for patients that are not BRCA mutated who may have otherwise been eligible for treatment with niraparib.
Page 12	Summary of Deliberations	Paragraph 1, line 4	Cost of niraparib was noted to be reanalyzed by the EGP. There was mention of "correcting the dose" as of Cycle 5. Can more details be provided in the economic guidance report? A request for an editorial change to confirm there was not any loss of cost for the full dose earlier in the therapy. Unable to determine how the cost was adjusted. With orally administered therapies, if dose intensity is applied as a determinant of drug cost, often this underestimates the true cost of what was dispensed.
Page 18-19	Appendix Table of PAG Implementation Questions	Eligible Patient Population Second paragraph	If patients previously discontinued a PARP inhibitor due to intolerance or other reasons without disease progression, it would be reasonable to try a maintenance strategy after chemo, provided patients have platinum-sensitive disease and can tolerate the niraparib: (1) The trial excluded patients with a prior treatment with a PARP inhibitor. (2) The recommendation also implies support for retreatment even if the PARP was discontinued for whatever reason (e.g., patient got PARP maintenance in the front line setting for a year or more but decided to stop and take a holiday), which could have budget implications. Is the intent to allow retreatment even if the patient had received a PARP inhibitor in an earlier line setting? If yes, should this be clarified to only limit to patients who had to discontinue due to toxicity?
Page 17-18	Appendix Table of PAG Implementation Questions	Eligible Patient Population Last paragraph	For the question regarding intolerance to olaparib and eligibility to switch to nirapanib, does this only apply to patients taking olaparib after chemotherapy for recurrent disease (i.e. not the indication for olaparib following 1st line chemotherapy)?

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
		Implementation Factors Line 1	If a patient weight of 77 kg or lower results in a starting dose of 200 mg instead of 300 mg. Since this is not a flat priced agent, how would this impact upon ICER/ICUR and BIA estimates? Clarification requested on whether the economic analysis was performed using patients starting at full dose of 300 mg as this is how you interpret the ICER and future negotiations. Thus, if you have to make any adjustments at a lower dose, then will not be able to use the same economic analysis that was presented.

3.2 Comments Related to Eligible Stakeholder Provided Information

Notwithstanding the feedback provided in part a) above, please indicate if the Stakeholder 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.

Recommendation does not require reconsideration by pERC.

☐ Do not support conversion to Final Recommendation.

Recommendation should be reconsidered by pERC.

If the eligible stakeholder does not support conversion to a Final Recommendation, please provide feedback on any issues not adequately addressed in the Initial Recommendation based on any information provided by the Stakeholder 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 program.

Additionally, if the eligible stakeholder supports early conversion to a Final Recommendation; however, the stakeholder has included substantive comments that requires further interpretation of the evidence, the criteria for early conversion will be deemed to have not been met and the Initial Recommendation will be returned to pERC for further deliberation and reconsideration at the next possible pERC meeting.

Page Number	Section Title	Paragraph, Line Number	Comments related to Stakeholder Information
1	pERC Recommendation	First paragraph	Seven jurisdictions agree. One jurisdiction agrees in part with the initial pERC recommendation for the BRCA positive

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			patient population however for patients that are not BRCA positive, the jurisdiction would agree with HRD positive patients. Based on the toxicity profile in the HRD negative population, the jurisdiction believes there is uncertainty whether the PFS of 3 months is truly a meaningful improvement.

1 About Stakeholder Feedback

pCODR invites eligible stakeholders to provide feedback and comments on the Initial Recommendation made by the pCODR Expert Review Committee (pERC). (See www.cadth.ca/pcodr for information regarding review status and feedback deadlines.)

As part of the pCODR review process, pERC makes an Initial Recommendation based on its review of the clinical benefit, patient values, economic evaluation and adoption feasibility for a drug. (See www.cadth.ca/pcodr for a description of the pCODR process.) The Initial Recommendation is then posted for feedback from eligible stakeholders. All eligible stakeholders have 10 (ten) business days within which to provide their feedback on the initial recommendation. It should be noted that the Initial Recommendation may or may not change following a review of the feedback from stakeholders.

pERC welcomes comments and feedback from all eligible stakeholders with the expectation that even the most critical feedback be delivered respectfully and with civility.

A. Application of Early Conversion

The Stakeholder Feedback document poses two key questions:

1. **Does the stakeholder agree, agree in part, or disagree with the Initial Recommendation?**

   All eligible stakeholders are requested to indicate whether they agree, agree in part or disagrees with the Initial Recommendation, and to provide a rational for their response.

   Please note that if a stakeholder agrees, agrees in part or disagrees with the Initial Recommendation, the stakeholder can still support the recommendation proceeding to a Final Recommendation (i.e. early conversion).

2. **Does the stakeholder support the recommendation proceeding to a Final Recommendation ("early conversion")?**

   An efficient review process is one of pCODR's key guiding principles. If all eligible stakeholders support the Initial Recommendation proceeding to a Final Recommendation and that the criteria for early conversion as set out in the *pCODR Procedures* are met, the Final Recommendation will be posted on the CADTH website 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.

   For stakeholders who support early conversion, please note that if there are substantive comments on any of the key quadrants of the deliberative framework (e.g., differences in the interpretation of the evidence), the criteria for early conversion will be deemed to have **not** been met and the Initial Recommendation will be returned to pERC for further deliberation and reconsideration at the next possible pERC meeting. Please note that if any one of the eligible stakeholders does not support the Initial Recommendation proceeding to a Final pERC Recommendation, pERC will review all feedback and comments received at a subsequent pERC meeting and reconsider the Initial Recommendation.

B. Guidance on Scope of Feedback for Early Conversion

Information that is within scope of feedback for early conversion includes the identification of errors in the reporting or a lack of clarity in the information provided in the review documents. Based on the feedback received, pERC will consider revising the recommendation document, as appropriate and to provide clarity.

If a lack of clarity is noted, please provide suggestions to improve the clarity of the information in the Initial Recommendation. If the feedback can be addressed editorially this will done by the pCODR staff, in consultation with the pERC chair and pERC members, and may not require reconsideration at a subsequent pERC meeting.

The Final pERC Recommendation will be made available to the participating federal, provincial and territorial ministries of health and provincial 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) The following stakeholders are eligible to submit Feedback on the Initial Recommendation:

- The Submitter making the pCODR Submission, or the Manufacturer of the drug under review;
- Patient groups who have provided input on the drug submission;
- Registered clinician(s) who have provided input on the drug submission; and
- The Provincial Advisory Group (PAG)

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 *Stakeholder Feedback on pERC Initial Recommendation* can be downloaded from the pCODR section of the CADTH 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 Stakeholder 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.

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 provided to the pERC for their consideration.

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 program.

h) The comments must be submitted via a Microsoft Word (not PDF) document to pCODR by the posted deadline date.

i) If you have any questions about the feedback process, please e-mail pcodrsubmissions@cadth.ca

Note: CADTH is committed to providing an open and transparent cancer drug review process and to the need to be accountable for its recommendations to patients and the public. Submitted feedback will be posted on the CADTH website (www.cadth.ca/pcodr). The submitted information in the feedback template will be made fully disclosable.