CADTH

pan-Canadian Oncology Drug Review Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation (Sponsor)

Niraparib (Zejula) for first line Ovarian Cancer

April 29, 2021

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	ZEJULA (Niraparib)
Eligible Stakeholder Role	Manufacturer
Organization Providing Feedback	GlaxoSmithKline Inc.

** CADTH may contact this person if comments require clarification. Contact information will not be included in any public posting of this document by CADTH.*

3.1 Comments on the Initial Recommendation

a) Please indicate if the stakeholder agrees, agrees in part, or disagrees with the initial recommendation:

☒ Agrees ☐ Agrees in part ☐ Disagrees

Please explain why the stakeholder agrees, agrees in part or disagrees with the initial recommendation. If the stakeholder agrees in part or disagrees with the initial recommendation, please provide specific text from the recommendation and rationale. Please also highlight the applicable pERC deliberative quadrants for each point of disagreement. The points are to be numbered in order of significance.

GlaxoSmithKline Inc. (GSK) agrees with pERC's initial recommendation of niraparib as maintenance treatment of adult patients with newly diagnosed epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. GSK is aligned with the clinical criteria outlined by pERC.

Clinical Feedback

There remains a high unmet need for safe and effective treatments that can provide benefit to more newly diagnosed advanced ovarian cancer patients. As such, GSK is pleased to receive this recommendation from pERC based on the net clinical benefit observed with niraparib versus placebo, regardless of biomarker status, per the PRIMA trial results.

GSK is also appreciative of the feedback received from the CGP, PAG, registered clinicians and patient advocacy groups who have provided input and indicated that the reimbursement of niraparib would fulfill an unmet need.

Economic Feedback

GSK acknowledges CADTH's fulsome review of the submitted health economic models, however, GSK would like to comment on conclusions reached by CADTH on the economic models in the initial recommendation and the Economic Report.

Willingness to Pay (WTP) Threshold (page 13):

CADTH's assessment of the price reduction required in order to meet a $50,000/QALY WTP threshold should be interpreted with caution. There is broad recognition of the unique challenges in health economic modeling of cancer and rare diseases therapies and of certain caveats in demonstrating health economic value in these therapy areas. As such, it is a common sentiment across health economists that a WTP of $50,000/QALY may not be the appropriate threshold in all cases.[1,2]

There is inconsistency across recent pCODR recommendations with respect to whether a price reduction is proposed and at what WTP threshold(s). While some include proposed price reductions to achieve a $50,000/QALY WTP threshold, others include proposed price reductions to achieve a $100,000/QALY WTP threshold,[3] and there are examples of recent recommendations that do not include any proposed price reduction.[3] In order to provide jurisdictions further clarity and insight with which to support their decision-making, GSK believes that the discount that would yield an ICER of $100,000 per QALY should be included in this pCODR recommendation for niraparib.

Budget Impact Analysis (page 13)
GSK would like to note that CADTH's reanalyzed budget impact should be interpreted with caution, given the uncertainty reflected in CADTH's assumptions and reanalysis. Notably, the methodology considered in CADTH's reassessment differs from the base-case methodology utilized in GSK's submitted model, which was developed in alignment with the PMPRB guidelines for BIA development.[6] As well, the proportion of patients who respond to first-line platinum-based chemotherapy, which was increased in CADTH's reassessment, was based on that which is reported in the literature in the GSK-submitted model. Lastly, it should be noted that despite a conditional positive recommendation for niraparib in the recurrent setting, CADTH's reanalyzed budget impact does not consider the cost-savings achieved over the three-year time horizon should niraparib be funded in both the first-line and recurrent maintenance setting (given that as it currently stands, PARP inhibitors are only recommended for use once in the treatment algorithm).

References:

1. Marseille E, Larson B, Kazi DS, Kahn JG, Rosen S. Thresholds for the cost–effectiveness of interventions: alternative approaches. Bulletin of the World Health Organization. 2014 Dec 15;93:118-24.
2. Neumann PJ, Cohen JT, Weinstein MC. Updating cost-effectiveness—the curious resilience of the $50,000-per-QALY threshold. New England Journal of Medicine. 2014 Aug 28;371(9):796-7.
3. pan-Canadian Oncology Drug Review. Pembrolizumab (Keytruda) HNSCC – pERC Final Recommendation. December 2020.
https://www.cadth.ca/sites/default/files/pcodr/Reviews2020/10216PembrolizumabHNSCC_FnRec_EC22Dec2020_final.pdf
4. pan-Canadian Oncology Drug Review. Entrectinib (Rozlytrek) ROS1-positive NSCLC – pERC Final Recommendation. January 2021.
5. Common Drug Review. Pharmacoeconomic Review Report for Nucala (mepolizumab). March 2019.
https://www.cadth.ca/sites/default/files/pcodr/Reviews2021/10206EntrectinibROS1NSCLC_FnRec_EarlyConv_ApprovedbyChair_EC27Jan2021_final.pdf
6. PMPRB. Budget Impact Guidelines. https://www.canada.ca/en/patented-medicine-prices-review/services/reports-studies/budget-impact-analysis-guidelines.html

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
10	Need and burden of illness: Need for additional treatment options in	Paragraph 2, Lines 9-10	The phrase 'platinum-sensitive' is used clinically to describe a duration of response to platinum-based chemotherapy that is 6 months or longer.

	patients with BRCA-wt		In order to avoid confusion between 1L and recurrent populations. CADTH may consider updating the statement to read: "Therefore, there remains a significant unmet need for effective treatments that may extend remission in the majority of patients with newly diagnosed ~~platinum-sensitive~~ advanced ovarian cancer **who are in a complete or partial response to platinum-based chemotherapy."**
12	Economic Evaluation	Paragraph 3, Bullet 1	The methodology used to estimate the overall population (i.e. full Health Canada indication) in the pharmacoeconomic model was employed to account for the exclusion of stage III NVRD ovarian cancer patients following primary debulking surgery. As such, CADTH may consider updating the statement to read: "The PRIMA trial only enrolled a small proportion of patients with stage III NVRD ovarian cancer following neoadjuvant chemotherapy and interval debulking surgery and excluded patients with stage III disease and NVRD following primary debulking surgery. To estimate the overall population…"
13	Economic Evaluation	Paragraph 1, Lines 3-4	CADTH should consider adding the discount that would yield an ICER of $100,000 per QALY, in order to give jurisdictions a range of information to support their decision-making.

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 recommendation ("early conversion"), which would occur two business days after the end of the feedback deadline date.

☒	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.

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 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.

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

Template for Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation

1 About Stakeholder Feedback

CADTH invites eligible stakeholders to provide feedback and comments on the pan-Canadian Oncology Drug Review Expert Review Committee (pERC) initial recommendation.

As part of the CADTH's pan-Canadian Oncology Drug Review (pCODR) process, pERC makes an initial recommendation based on its review of the clinical benefit, patient values, economic evaluation and adoption feasibility for a drug. The initial recommendation is then posted for feedback from eligible stakeholders. All eligible stakeholders have 10 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.

CADTH 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 disagree with the initial recommendation, and to provide a rationale for their response. Please note that if a stakeholder agrees, agrees in part or disagrees with the initial recommendation, they 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 the key guiding principles for CADTH's pCODR process. 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 *Procedures for the CADTH Pan-Canadian Oncology Drug Review* are met, the final recommendation will be posted on the CADTH website two 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 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 CADTH staff, in consultation with pERC, and may not require reconsideration at a subsequent pERC meeting.

The final 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

- The following stakeholders are eligible to submit feedback on the initial recommendation:
    - The sponsor and/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
    - CADTH's Provincial Advisory Group (PAG)
- 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.
- The template for providing stakeholder is located in section 3 of this document.
- 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.
- Feedback on the initial recommendation should not exceed three 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.
- 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, and should not contain any language that could be considered disrespectful, inflammatory or could be found to violate applicable defamation law.
- References may be provided separately; however, these cannot be related to new evidence.
- 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 must be disclosable and will be posted on the CADTH website.
- The template must be filed with CADTH as a Microsoft Word document by the posted deadline.
- If you have any questions about the feedback process, please e-mail requests@cadth.ca