pan-Canadian Oncology Drug Review

Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation (Manufacturer)

Nivolumab (Opdivo) Hepatocellular Carcinoma

November 29, 2018

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	Opdivo™ (nivolumab) for the treatment of adult patients with advanced (not amenable to curative therapy or local therapeutic measures) or metastatic hepatocellular carcinoma who are intolerant to or have progressed on sorafenib therapy
Eligible Stakeholder Role in Review (Submitter and/or Manufacturer, Patient Group, Clinical Group):	Submitter and manufacturer
Organization Providing Feedback	Bristol-Myers Squibb Canada

**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

Bristol-Myers Squibb Canada disagrees with the pERC initial recommendation to not recommend reimbursement of nivolumab (OPDIVO™) for the treatment of adult patients with advanced (not amenable to curative therapy or local therapeutic measures) or metastatic hepatocellular carcinoma (HCC) who are intolerant to or have progressed on sorafenib therapy.

Bristol-Myers Squibb Canada respectfully requests pERC to reconsider the reimbursement of Opdivo especially for patients with HCC who are intolerant or who have discontinued sorafenib due to intolerance and/or toxicity. The unmet medical need for these patients is enormous given that there are no treatment options reimbursed. As emphasized by the pERC, nivolumab offers a potentially clinically effective therapy in a disease setting where other available options are limited and may be associated with potentially significant toxicity.

Indeed, the other option for patients with HCC is regorafenib. However, the approved indication by Health Canada (*https://pdf.hres.ca/dpd_pm/00045652.PDF*) and the pERC recommendation (*https://www.cadth.ca/sites/default/files/pcodr/pcodr_regorafenib_stivarga_hcc_fn_rec.pdf*) exclude patients with HCC who are intolerant to sorafenib.

A targeted review of the literature suggests that, among recent clinical trials assessing second line systemic treatment for HCC, up to 20% of patients had discontinued their prior sorafenib therapy due to intolerance or toxicity associated with sorafenib(*Zhu AX, Kudo M, Assenat E, et al. Effect of everolimus on survival in advanced hepatocellular carcinoma after failure of sorafenib: The EVOLVE-1 randomized clinical trial. JAMA. 2014;312:57-67*). This suggests that up to 20% of patients with HCC who are eligible for a systemic therapy, do not have access to any therapy due to intolerance to sorafenib.

Nivolumab is the first and only PD-1 therapy approved by Health Canada for the treatment of patients with HCC including patients with intolerance to sorafenib.

For all these reasons, BMS kindly requests that pERC recommends the reimbursement of Opdivo for patients with HCC intolerant or who have discontinued sorafenib due to intolerance and/or toxicity. Otherwise, this very small group of patients will be left without any therapeutic options despite that nivolumab is approved by Health Canada for them.

By doing so, the pERC's recommendation would help to address the substantial unmet medical need of this small group of patients.

Bristol-Myers Squibb Canada is committed to working with the provinces to facilitate access to Canadian patients with HCC.

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

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.	☒	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 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

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 pcodrsubmissions@cadth.ca.

Note: Submitted feedback may be used in documents available to the public. The confidentiality of any submitted information cannot be protected.