



**pan-Canadian Oncology Drug Review
Submitter or Manufacturer Feedback on a
pCODR Expert Review Committee Initial
Recommendation**

Ibrutinib (Imbruvica) for Mantle Cell Lymphoma

July 19, 2016

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s): IMBRUVICA® (ibrutinib) for the treatment of patients with relapsed or refractory mantle cell lymphoma (MCL)

Role in Review (Submitter and/or Manufacturer): Submitter and Manufacturer

Organization Providing Feedback Janssen 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 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.

Janssen Inc. agrees with the committee's decision that there is a substantial need for effective treatment options for patients with relapsed/refractory MCL (R/R MCL). The median survival for patients with R/R MCL is only one to two years. There is currently no standard of care, and available chemo-based treatments induce short remissions and patients relapse through several lines of therapy very quickly. There is an urgent need for therapies that prolong progression-free survival with an acceptable toxicity profile while improving patients' quality of life.

Ibrutinib is a targeted therapy that offers a new mechanism of action for the treatment of R/R MCL. Janssen Inc. agrees that ibrutinib is an effective treatment option for R/R MCL. It fulfills the current unmet need by demonstrating clinically meaningful and statistically significant improvement in overall response rate, progression-free survival, and quality of life, compared to temsirolimus, an agent that has shown superiority over chemo-based treatments in a randomized controlled trial. In addition, ibrutinib likely provides overall survival (OS) benefit compared to temsirolimus. The OS hazard ratio was 0.76 (95% CI: 0.53-1.09, $p=0.1324$), despite 23% of temsirolimus patients had crossed over to receive ibrutinib after a median follow-up of 20 months. Janssen therefore does not agree with using the HR =1 in the EGP reanalysis. Janssen does not agree with the statements around uncertainty of treatment duration following the use of ibrutinib in R/R MCL. To date, the median progression-free survival has been reached in two Phase II studies (PCYC-1104, MCL-2001) and the Phase III study (MCL-3001), with observed medians ranging between 10.5 months and 14.6 months. As such, Janssen firmly believes the treatment duration of ibrutinib to be

estimable with more certainty in R/R MCL.

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.

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.

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
			NO COMMENTS

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
			NO COMMENTS

3.3 Additional Comments About the Initial Recommendation Document

Please provide any additional comments:

Page Number	Section Title	Paragraph, Line Number	Additional Comments
			NO 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.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 submissions@pcodr.ca.

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