pan-Canadian Oncology Drug Review

Patient Advocacy Group Feedback on a pCODR Expert Review Committee Initial Recommendation

Ibrutinib (Imbruvica) for Waldenström's Macroglobulinemia

Lymphoma Canada

November 3, 2016

1 Feedback on pERC Initial Recommendation

Name of the drug indication(s):	Ibrutinib for R/R Waldenstrom's macroglobulinaemia
Name of registered patient advocacy	Lymphoma Canada

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

1.1 Comments on the Initial Recommendation

a) Please indicate if the patient advocacy group agrees or disagrees with the initial recommendation:

____ agrees ____ agrees in part _**X**_ disagree

Please explain why the patient advocacy group agrees, agrees in part or disagrees with the initial recommendation.

1. Waldenström's macroglobulinemia (WM) is an incurable cancer. The vast majority of WM patients will continue to relapse following each course of therapy, therefore there is a great need for multiple effective therapies for this patient population. Currently, WM patients in Canada have very few effective treatment options with tolerable side effects available to them upon disease relapse. The standard treatments currently used to treat relapse are either marginally effective or are cytotoxic treatments with limited duration of response. They also require hospitalization for delivery, putting an extra burden on patients and their caregivers. Almost all respondents (98.5%) to our surveys feel there is a need for additional therapies.
2. As the pERC noted, Imbruvica's ability to control symptoms, with fewer toxic side effects than available therapies, in an easy to take-at-home pill format, is extremely important to patients and their quality of life.
3. Dr. M. Cheung is one of only two members of the pERC who has extensive clinical experience and expertise with lymphoproliferative diseases (the other being Dr. C. Moltzan). However, Dr. Cheung did not participate in deliberations and voting on the initial recommendation for this review. We feel that it is extremely important that Dr. Cheung be involved in the pERC deliberations given the complexity of the disease and treatment landscape for WM.

b) Notwithstanding the feedback provided in part a) above, please indicate if the patient advocacy group 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.	_**X**_	Do not support conversion to final recommendation.
	Recommendation does not require reconsideration by pERC.		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
2	Summary of pERC deliberations	Paragraph 2, lines 7 and 20	pERC noted the lack of complete response (CR) in patients following ibrutinib treatment. Unlike other indolent lymphomas, CRs are uncommon in WM - CRs of only 5-15% are achieved with chemotherapy + rituximab and are exceedingly rare with monotherapy. The CGP agreed that PFS is a meaningful and appropriate endpoint for the ibrutinib trials and also stated that two year PFS of 69% and OS of 95% represented excellent disease control in a heavily pre-treated patient population.
2	Summary of pERC deliberations	Paragraph 2, lines 18-20	pERC noted that "…outcomes observed with ibrutinib in terms of objective response and PFS were similar to those seen in the literature with currently available treatments." Of the studies cited in the clinical guidance report, bortezomib and bendamustine are the only single agents with reported ORR, MRR and PFS approaching those of ibrutinib in the relapsed/refractory WM population (references 4 and 18). Of these two agents, only bendamustine is publicly reimbursed in Canada for WM. A study evaluating BR in WM (reference 29) was the only study of combination therapy in relapsed/refractory WM cited by the pERC. Therefore, based on the evidence cited in the clinical guidance report, there are currently ONLY two therapeutic options available to WM patients in Canada with comparable responses to ibrutinib in the relapsed/refractory setting – Bendamustine and Bendamustine+rituximab. The disease course in the vast majority of patients involves multiple symptomatic disease recurrences that require treatment. Highly effective new treatment options, in addition to the very few that are currently available to Canadian patients, are a continued need for this patient population due to their ongoing therapy cycle of treatment, remission, retreatment, remission, etc.

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
2	Summary of pERC deliberations	Paragraph 1, line 12	pERC noted that "Current treatment of WM upon relapse or progression depends on agents used in initial treatment, and whether re-treatment with rituximab is considered appropriate..." Retreatment with rituximab upon relapse is not feasible in many patients as typically there is a loss of efficacy upon retreatment and a proportion of WM patients (higher than with other B-cell malignancies) will develop worsening infusion-related reactions as treatment with rituximab continues, leading to treatment discontinuation.

1.2 Comments Related to Patient Advocacy Group Input

Page Number	Section Title	Paragraph, Line Number	Comments related to initial patient advocacy group input
7	Patient values on treatment: Improved overall survival, slower disease progression, and availability of additional treatment options	Paragraph 1	From our survey, 152 of 240 patients felt that their current therapy was able to adequately manage their disease symptoms. However, at least 36.3% had relapsed after treatment (15% of patients did not know whether they had relapsed). Current therapy managed symptoms for a limited time before relapse. 70 had received two or more lines of therapy, up to and including a total of 6 lines of therapy, to date. On average, patients were diagnosed 3 years ago. The longer a patient had WM, the more likely they were to have had multiple lines of therapy. The more lines of therapy the patient had, the more they commented on their lack of response and shorter duration of response and/or increasing adverse reactions to available treatments. These responses clearly highlight the need among patients for additional effective therapies with manageable side effects. While patients would like any new therapy to bring about remission, patients indicated their immediate focus was an improved quality of life and life extension.

About Completing This Template

pCODR invites those registered patient advocacy groups that provided input on the drug under review **prior** to deliberation by the pCODR Expert Review Committee (pERC), to also 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 patient advocacy groups agree or disagree 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, including registered patient advocacy groups, 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 registered patient advocacy groups that provided input at the beginning of the review of the drug can provide feedback on the initial recommendation.

- Please note that only one submission per patient advocacy group is permitted. This applies to those groups with both national and provincial / territorial offices; only one submission for the entire patient advocacy group will be accepted. If more than one submission is made, only the first submission will be considered.
- Individual patients should contact a patient advocacy group that is representative of their condition to have their input added to that of the group. If there is no patient advocacy group for the particular tumour, patients should contact pCODR for direction at www.cadth.ca/pcodr.

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 during this part of the review process; however, it may be eligible for a Resubmission.

c) The template for providing *pCODR Patient Advocacy Group Feedback on a 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. Patient advocacy groups 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 to their group. Similarly, groups 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 initial pERC recommendations **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 new references. New evidence is not considered during 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 by logging into www.cadth.ca/pcodr and selecting "Submit Feedback" by the posted deadline date.

i) Patient advocacy group feedback must be submitted to pCODR by **5 P.M. Eastern Time** on the day of the posted deadline.

j) If you have any questions about the feedback process, please e-mail pcodrinfo@cadth.ca. For more information regarding patient input into the pCODR drug review process, see the *pCODR Patient Engagement Guide*. Should you have any questions about completing this form, please email pcodrinfo@cadth.ca

Note: Submitted feedback is publicly posted and also may be used in other documents available to the public. The confidentiality of any submitted information at this stage of the review cannot be guaranteed.