pan-Canadian Oncology Drug Review

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

Ibrutinib (Imbruvica) for Waldenström's Macroglobulinemia

Canadian Organization for Rare Disorders

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	Canadian Organization for Rare Disorders

**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. Having provided a joint initial submission, CORD agrees with the Feedback provided by Lymphoma Canada, However, given the limited space for feedback to the initial recommendation, we have agreed that CORD will submit a supplemental Feedback based unique challenges posed by Waldenstrom's macroglobulinaemia as a rare disease. We believe the negative recommendation does not adequately recognize the lack of viable treatment options for WM patients who, as noted by pERC, are at risk for multiple relapses, with limited assurance of responding to re-treatment to the same therapy.
2. As noted by pERC, it is possible to accept data from Phase II single-arm clinical trials with small patient populations where there are limited comparative options, progressive (fatal) disease and high unmet need. This is the exact situation for WM and the fact that the manufacturer is conducting additional trials that may yield more conclusive data in the future should not be a cause for penalizing the patients currently in need (and may not be eligible when future trials are completed). The evidence of clinical effectiveness is sufficient to warrant ibrutinib being available to patients who may have experienced other therapies and/or relapsed. Moreover, the fact that there were many patients identified in Canada and internationally should cited as reason to discount the CT data. The estimation of sample size for the clinical trial was deemed appropriate by the clinicians, researchers, and regulators based on known population size and availability.
3. We feel the decision not to recommend reimbursement despite the strong patient evidence of added value and need because pERC felt the clinical evidence could be better and the economic evaluation yielded uncertain long-term estimates of value is counter to pERC's Deliberative Framework. We do not feel the patient-baesd values were given independent and equal weighting but were secondary to "confirmation" by clinical and economic appraisals. The dismissal of the advantage of an oral therapy over infusion therapy for this patient population clearly ignores the impact to the patients' quality of life. Whether this information has been captured in QoL information submitted by the company from the Clinical Trials should not be a case for discounting the patient feedback.
4. CORD very strongly urges pERC to reconsider this initial recommendation.

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	SUMMMARY OF pERC RECOMMENDATIONS	1: 1-24	*Given the acknowledgement that relapse with WM is to be expected, pretreatment with rituximab may not be appropriate for some patients, and that treatment options are needed, it is unconscionable to deny access to any and all WM patients because there is not definitive evidence based on large-scale RCTs. pERC acknowledges recommending access in other cases based on data from Phase II (single-arm) trials. The hesitancy on the part of pERC is based, in part, on their knowledge that the company is conducting comparative RCTs with more patients but the reason why Health Canada approved ibrutinib on the basis of the Phase II studies is because there are few effective treatments, patients will become resistant to these treatments over time, and this creates a critical unmet need that could be filled by ibrutinib for relapsed WM patients.*
6	OVERALL CLINICAL BENEFIT	5: 8-12	The estimation of overall median survival as closer to the lower estimate of four years rather than the higher estimates of 12 years is not justified and discounts the value of additional therapies (following relapse)
8	ECONOMIC EVALUATION	6: 16-18	*pERC concluded that ibrutinib was not cost-effective (very high ICER) using Median Survival Time of 5 years when, in fact, the MST is likely closer to 10 years (or more). It would be important to test the sensitivity of this*

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
			estimate and recalculate ICER based on a more realistic 10-year MST.
9	ADOPTION FEASIBILITY		*It also important to note that a limited recommendation for relapsed WM patients who have used other treatment options and/or would benefit significantly from oral therapy (unable to tolerate IV) would have only a very small budget impact. Access on a case-by-case basis would allow for monitored access and also address the concerns raised about physician experience with monitoring and managing treatment interactions.*

1.2 Comments Related to Patient Advocacy Group Input

Please provide feedback on any issues not adequately addressed in the initial recommendation based on patient advocacy group input provided at the outset of the review on outcomes or issues important to patients that were identified in the submitted patient input. Please note that new evidence will be 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 providing is eligible for a Resubmission, please contact the pCODR Secretariat.

Examples of issues to consider include: what are the impacts of the condition on patients' daily living? Are the needs of patients being met by existing therapies? Are there unmet needs? Will the agents included in this recommendation affect the lives of patients? Do they have any disadvantages? Stakeholders may also consider other factors not listed here.

Page Number	Section Title	Paragraph, Line Number	Comments related to initial patient advocacy group input

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.