pan-Canadian Oncology Drug Review

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

Ixazomib (Ninlaro) for Multiple Myeloma

Myeloma Canada

June 29, 2017

1. Feedback on pERC Initial Recommendation

Name of the drug indication(s):	Ixazomid (Ninlaro) for the treatment of adult patients with multiple myeloma who have received at least one prior therapy including and have high-risk cytogenetics or have received at least two prior therapies.
Name of registered patient advocacy group:	Myeloma 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

Myeloma Canada is of the opinion the pERC recommendations and comments are not supported by the clinical evidence demonstrated in the TOURMALINE-MM1 trial. This phase III, randomized and double blind trial represents the highest level of evidence possible a cancer agent can be ascribed to demonstrate clinical evidence. This trial was published in a very reputable journal and its main endpoint showed a statistically significant difference in the median progression free survival (PFS) in the ITT between ILd and Ld of 6 months. By comparison, the same end-point in the high-risk population (as demonstrated by cytogenetic abnormality) was almost 11 months. While Myeloma Canada cannot comment, nor is it our place to do so, on the statistical analyses presented by the manufacturer, we can state that a difference of 6 months and 11 months of being free of cancer symptoms is a definite net clinical benefit. It means being able to attend life events, see significant loved ones achieve important events or milestones, or simply to be a productive citizen.

In the recent past pERC has rejected a myeloma treatment based on the lack of a robust Phase III comparative trial with best standard of care. In this instance ixazomib did meet all these requirements in addition to reaching statistical significance in their IIT and high-risk population for their primary end-point and at the a-priori defined interim analysis time point. These results have been good enough to consider ixazomib in combination with lenalidomide and dexamethasone to be an effective treatment for myeloma patient as reported in many scientific conferences (ASH, EHA, ASCO) and publication (NEJM).

The pERC committee noted there were some benefits of an all oral regimen therapy for patients, but failed to truly appreciate its impact on patients' lives. To be clear, this means a significant decrease of hospital visits for patients and those having to accompany them. The ability to take their cancer treatment at home, which has an important impact on their self-worth and being in control of their lives and not to have their cancer treatment dictate their quality of life. Yes, this oral regimen does not eliminate clinic visits or blood tests, but it definitely helps to lessen the emotional burden of receiving an injected treatment in a cancer centre.

pERC also noted that an appropriate alternative option is the use of the triplet therapy of carfilzomib with lenalidomide and dexamethasone (CLd) or if patients are not eligible for triple therapy be given Cd. However, both these regimens, although having receive a positive pERC recommendations, are not available for patients as they are not reimbursed by provincial drug plans. Therefore, they are not a suitable alternative. In addition, although very effective, IV carfilzomib is a terribly inconvenient drug for patients to take, because of the time required to travel to a clinic, the twice-weekly schedule that is disruptive for some patients and especially for those who are frail, high risk and/or living far away from a clinic.

Myeloma Canada finds the comments pertaining to an adherence problem with an all oral regimen (because patients would have to take their ixazomib and lenalidomide on different schedules) presumptuous and baseless. The summary of the recommendations goes on to further dismiss finding a way to implement a funding recommendation based on this perceived scheduling issue for patients. Cancer patients (in part motivated by their caregivers) are some of the most compliant patients ever, as their lives depend on their treatments. Furthermore, Myeloma Canada learned from the manufacturer of ixazomib that their patient assisted program was specifically designed to align with that of lenalidomide to have the same pharmacy distribution, patient navigator and management oversight to avoid any miscommunication or double communication channels with the patients. This advantage is something that patients will appreciate and demonstrates an attention to maintaining patient adherence and engagement.

In addition, to highlight potential additional workload of pharmacy and clinic staff to counsel patients on this oral regimen (ILd) as being an issue, without measuring these outcomes, is inappropriate. pERC describes itself as an evidence based body that reviews and considers evidence to make decisions. Where is the evidence to make this statement? Taking a few moments to explain how to take an all oral cancer treatment regimen, accompanied by a Patient Support Program (paid for by the manufacturer) compared to a full day or even 2-hour chair time in a cancer centre would by far be less resource intensive.

Myeloma Canada agrees that the addition of a triple combination therapy in this patient population will have a significant budgetary impact. However, this is where the PCPA can exercise its function and negotiate with the manufacturer to achieve a more reasonable cost for the cancer agencies and drug plans across the country.

It is unfortunate and disapointing that pERC, despite the more significant need in the high-risk population - and in the presence of highly positive data in this population – did not make a recommendation for funding in this population.

In recent years myeloma patients have benefited from bortezomib and lenalidomide treatment-based regimens, and because of these, are enjoying significantly longer and higher quality lives. These treatments, although effective can only go so far in extending these patients' lives as they inevitably relapse and need additional treatments to keep their myeloma at bay. New and effective treatments, like this one, are imperative as myeloma patients will be dying sooner than needed without these options.

Just last week, one of our own warriors lost her life at way too young age. A young, vibrant 40-year-old women with high risk myeloma past away after a four-year fight. Unfortunately, she was refused ixazomib by her insurance company. Had she been able to get access she might have had a chance to spend more time with her family and loved ones. We understand this is not an outcome of pERC's recommendations, but this is the reality of myeloma patients.

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?

No feedback as requested here to provide.

1.2 Comments Related to Patient Advocacy Group Input

No feedback as requested here to provide.

1.3 Additional Comments About the Initial Recommendation Document

Please provide any additional comments:

Page Number	Section Title	Paragraph, Line Number	Additional Comments
3	pERC rec' summary	Para 2 Lines 4-6	Can pERC explain by which data or supporting facts they concluded that the administration schedule of a triplet therapy would be challenging for patients?
3	pERC rec' summary	Para 4 Line 4	Can pERC explain why the adherence to the administration schedule may be a limitation to the implementation of a funding decision and that the additional work load that is expected by the pharmacy and clinic staff may be a barrier to a possible evidence building / risk sharing reimbursement scheme, in particular when these have not been assessed?
9	Adoption Feasibility	Para: 1 Line: 13	The PAG committee noted that a relevant comparator in this setting would be CLd, and that indirect evidence was provided by the submitter, can more information be provided to clarify this statement.
26 -27	Clinical guidance report - Factors Related to Patient Population section	Para: 1	"*Given the multiple treatments that will be available, PAG is seeking guidance on the appropriate place in therapy of ixazomib in combination with lenalidomide and dexamethasone and sequencing of all treatments available*." Can pERC explain how evaluating the treatment sequencing would be feasible without having all of available treatments (and reimbursed) included for a real-world evidence comparative study to confirm this. Also, it is not clear as to which treatments they are referring to.

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.