pan-Canadian Oncology Drug Review

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

Daratumumab (Darzalex) for Multiple Myeloma

Myeloma Canada

December 1, 2016

1. Feedback on pERC Initial Recommendation

Name of the drug indication(s):	Daratumumab (Darzalex®) For the treatment of patients with multiple myeloma who 1) have received at least 3 prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent (IMiD); OR 2) have failed or are intolerant to a PI and who have failed or are intolerant to an IMiD
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 **clinical practices** and are in fact contradictory to the evidence presented in the Clinical Guidance report. pERC is suggesting that Best Standard Care (BSC) be used as comparator to truly evaluate the effectiveness of datumumab. However, clinicians report that the BSC therapies suggested by pERC as comparators have higher rates of toxicity and and lower effectiveness than that shown by daratumumab. The Clinical Panel suggests that it would be unethical to conduct such comparative trials.

Although the manufacturer did not present any **Quality of Life** (QoL) data for daratumumab the committee completely omitted the (QoL) data reported by the patient input. pERC also made some assumptions that are not supported by either our patient survey or by the clinician survey, with respect to the administration of daratumumab.

pERC is also concerned by the **cost implications** of daratumumab on provincial drug budget if used in combination with other treatments. pERC should acknowledge that there are mechanisms in place to prevent provinces to pay for daratumumab in these situations and PCPA can make recommendations to address this.

Myeloma Canada submits that pERC failed to fully comprehend the gravity of this stage of disease in patients. At this stage, patients have run out of options for treatment and are close to death. In particular, the statement "there is a low probability that daratumumab would be cost-effective in this population compared to other treatments" is at best conjectural and at worst insensitive. What other "cost-effective" treatments is pERC recommending for this patient population? At the very least, a recommendation should have been made for a sub-section of the indicated population.

pERC dismissed the notion by the Clinical Guidance Panel that "daratumumab may be efficacious in producing acceptable clinical responses in refractory myeloma patients, a group of patients with limited treatment options and with a poor prognosis" by referring to the good performance status of the patient enrolled in the clinical trials and the notion that daratumumab would be given as an add-on therapy. These reasons are not supported by the clinician input submissions.

One would assume that with an ICER of $92,589/QALY there is a patient population for which daratumumab would be cost-effective and warrant it being reimbursed under predetermined conditions.

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
1	pERC rec'	Para 2 Line 3-10	The patient submission results are not congruent with pERC's conclusion that "daratumumab partially aligned with patient values based on its anti-tumour activity and therapeutic intent" or that there was considerable uncertainty in the evidence available on outcomes to decision-making such as overall survival (OS), progression-free survival (PFS), and quality of life (QOL). According to the patient survey, when patients were asked to rate daratumumab's effectiveness in controlling their myeloma on a scale of 1 (not effective) to 5 (extremely effective), 58% of respondents rated effectiveness as a 5 and the overall weighted average was 4.19, n = 38. When patients were asked to rate their quality of life while taking daratumumab on a scale of 1 (poor quality of life) and 5 (excellent quality of life), 30% rated QOL as a 5, 46% rated it a 4 and the overall weighted average was 3.95, n =37.
6-7	Patient based values	Para 2 Line 4	Although the manufacturer did not include QoL data collection in the studies they submitted the Myeloma Canada patient submission does provide information on how daratumumab impacted the lives of the patients we surveyed. In fact, in the patient submission we found that "Six out of the seven respondents who were interviewed indicated that daratumumab has met their expectations in that they are responding to the treatment and that it has improved their quality of life". pERC did take note of the open-ended comments, but not of the close-ended question and did not give it any weight in their recommendations as they concluded daratumumab only partially aligned with patient-based values.

7	Patient based values	Para: 1 Line: 4	pERC makes the comment about the length of the infusion time and intensity of the early administrations of daratumumab would be a burden for patients and their caregivers. On what evidence is the pERC basing this comment? Nowhere in the patient or clinician submissions, or manufacturer's submission is this substantiated with real evidence. PAG makes a similar comment in the clinical guidance document. We believe PAG and pERC members are introducing their own personal biased opinion with respect to how the infusion schedule is putting a burden on patients. Our submission collected data from patients and shows the benefits of dartumumab outweighed its administration inconvenience. In fact, when we asked patients to rate on a scale of 1 (not at all convenient) – 5 (extremely convenient) how convenient they found it to take daratumumab, 43% rated it a 5 and 24% rated it a 4 and the overall weighted average was 3.97, and n = 37. The majority, 18, commented on the time it takes for the infusion, some thought this was positive as the infusion frequency is reduced over time, others are retired and don't mind the time that it takes. Therefore, it is difficult to objectively conclude that the infusion time is an inconvenience to these patients.
7	Economic Evaluation	Para: 4 Line 1-4	The pERC recommendation contradicts the Clinical Guidance Panel recommendations that it would be considered unethical to put patients through a BSC head to head comparative study when the toxicity and effectiveness of the suggested BSC (Pom/Dex and high dose Dex for example) have been proven to be detrimental (and unethical – as pointed by the clinical panel) to the management of these patients. To illustrate this point, the OS in the MMY2002 was 17.5 months. Comparatively, the OS was 12.7 months for Pom/Dex vs 8 months for High Dose Dex in comparative study and similar population (1). It would be unthinkable for clinicians to suggest patients be put in a BSC treatment arm.
8	Adoption feasibility	Para 2 Line 1	Drug wastages can be easily managed through cost rebates arrangements with the manufacturer so that they not pose an un-necessary burden on the healthcare system.
8	Adoption feasibility	Para 4 Line 5-6	We find it improbable that pERC could not have a better sense of the number and proportion of the multiple myeloma population potentially eligible for daratumumab given there as been at least one other product submission (carfilzomib) other than daratumumab in the similar patient population for the pERC to evaluate and test the assumptions provided by these drug manufacturers.
8	Adoption feasibility	Para 4 Line 1-14	Infusion times, pharmacy, nurse and clinician staff, drug administration resources, wastage etc. should not be cited as reasons for the pERC to influence a decision. All of these resources are necessary for this drug, yes they do add costs but these costs to the healthcare system can be reduced or eliminated through listing agreements with the PCPA negotiations.

(1) Jesus San Miguel et al. Pomalidomide plus low-dose dexamethasone versus high-dose dexamethasone alone for patients with relapsed and refractory multiple myeloma (MM-003): a randomised, open-label, phase 3 trial. Lancet Oncol 2013; 14: 1055–66

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.