PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

Submitter or Manufacturer Feedback on a pCODR Expert Review Committee Initial Recommendation

Pomalidomide (Pomalyst) for Multiple Myeloma

July 31, 2014

INQUIRIES

Inquiries and correspondence about the pan-Canadian Oncology Drug Review (pCODR) should be directed to:

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1 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.pcodr.ca 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.pcodr.ca 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.

2 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.pcodr.ca 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.

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	POMALYST® (pomalidomide) in combination with low-dose dexamethasone for patients with multiple myeloma for whom both bortezomib and lenalidomide have failed and who have received at least two prior treatment regimens and have demonstrated disease progression on the last regimen
Role in Review (Submitter and/or Manufacturer):	Submitter and manufacturer
Organization Providing Feedback	Celgene 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 _X__ 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.*

1) We agree with the initial pERC recommendation for funding Pomalyst as a treatment for relapsed/refractory multiple myeloma after failure of bortezomib and lenalidomide.

2) We agree that the recommendation is based on a recognition of the high unmet medical need for effective treatment options in relapsed/refractory multiple myeloma in patients who have failed both bortezomib and lenalidomide.

3) We commend pERC for acknowledging the real-world barriers in Canada associated with bortezomib administration, and the recognition of the value pomalidomide could bring in circumstances where bortezomib administration is problematic.

4) We disagree with limiting the economic evaluation solely to high-dexamethasone as the appropriate comparator.

The Addendum to CADTH's Guidelines for the Economic Evaluation of Health Technologies: Specific Guidance for Oncology Products, provide the following guidance in relation to comparator selection: "Relate the choice of comparators to the study population, and the local context or practice in which the decision is being made" and "In the Reference Case, use "usual care" (i.e., the most common or frequently used care) which the intervention is intended to replace. In some cases "usual care" may include more than one relevant, widely used alternative for the same indication." The guidelines also advise that "Analysts are encouraged not to rely solely on the comparators that are used in the clinical studies. It is recommended that analysts examine the environment across Canadian jurisdictions in order to help identify the feasible, relevant, appropriate and practical comparators that used in current clinical practice."

As noted by pERC, there is currently no standard of care in Canada. "Usual care" in Canada was identified through a treatment practices survey disseminated to medical oncologists treating patients with multiple myeloma in Canada. Due to the availability of newer treatments (i.e., thalidomide, lenalidomide, and bortezomib) in the recent years, most patients would be retreated with combination regimens that include these therapies. Based upon the results of this process, usual care consisting of a composite of alternative treatment options is considered an appropriate comparator in determining economic value.

In addition to the Canadian clinical input, the published literature from other jurisdictions supports the utilization of agents beyond high-dose dexamethasone (i.e. thalidomide, lenalidomide, bortezomib) as best supportive care for relapsed/refractory multiple myeloma patients. Tarrant et al and Gooding et al each present single centre analyses of the experience of multiple myeloma patients. Following a sequence of thalidomide, bortezomib, and lenalidomide treatment, Tarrant et al., report that patients received various regimens, including thalidomide and bortezomib retreatment, while 18% received palliative care. Gooding et al., report that a number of double-refractory multiple myeloma patients were retreated with lenalidomide and bortezomib at fourth-line (27% and 10% respectively), while bendamustine-based regimens were most commonly prescribed.

Thus we believe, to obtain a balanced judgment on the economic value of pomalidomide in Canada, best supportive care requires the inclusion of novel treatments.

5) Celgene disagrees with the contextualization of pERC that the daily cost of pomalidomide could be as high as $1,500/day or $42,000/cycle. The manner in which this issue is raised seems to suggest this is a wide spread issue. To our knowledge, the use of multiple capsule strengths to achieve a target daily dose is non-existent to very rare. One of the key features that patients and physician value in pomalidomide is the benefit afforded to the patient in being able to take one capsule daily. The availability of pomalidomide in four different strengths allows patients to take the appropriate dose in one convenient capsule. We ask that pERC provide additional evidence and greater clarity on how significant of an issue this is to properly contextualize this concern. Although this is likely not intended, the way in which this issues is characterized, seems to suggest that pomalidomide is a grossly expensive therapy on a regular basis.

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.

_X_ 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
2	Summary of pERC Deliberations	Paragraph 2, Line 19	The following statement "The association between long-term lenalidomide use and second malignancy is more clear" is irrelevant given that the review concerns pomalidomide.
5	Safety	Paragraph 1, line 16	

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

3.3 Additional Comments About the Initial Recommendation Document

Please provide any additional comments:

Page Number	Section Title	Paragraph, Line Number	Additional Comments