pan-Canadian Oncology Drug Review

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

Lenalidomide (Revlimid) for Multiple Myeloma

October 22, 2013

INQUIRIES

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

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3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	REVLIMID® (lenalidomide) for the maintenance treatment of newly diagnosed multiple myeloma in patients after stem-cell transplantation
Role in Review (Submitter and/or Manufacturer):	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:

X	agrees		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 support the initial pERC recommendation for funding Revlimid as maintenance treatment of newly diagnosed multiple myeloma, following autologous stem-cell transplantation.

2) We are in agreement that the recommendation is based on a recognition of the unmet medical need for effective treatment options in the maintenance setting that improve remission duration, patient survival and quality of life.

3) We are in agreement with pERC and the Clinical Guidance Panel, that there is positive clinical value for Revlimid in the maintenance setting post-ASCT.

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

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
2	Summary of pERC Deliberations	Paragraph 4, line numbers 4-5	It would appear that the CGP and EGP assessed the reasonableness of the time horizon based on whether "on average" it makes sense for a patient to live an additional 40 years given the median age was 59 years old.

5	Cost-effectiveness estimates: influenced by overall survival and time horizon	Paragraph 5, line numbers 3-5	The intended interpretation is that the time horizon of 40 years is the maximum duration allowed for any patient to stay in the analysis, not the average time. The median age of subjects in the CALGB 100104 trial was 59 years of age with a range of 29 – 71 years. Therefore, it is reasonable to expect a small number of patients to live up to an additional 40 years since some of these patients are still young and the availability of effective treatments in relapsed/refractory multiple myeloma. In our analysis, only 5% and 1% of the lenalidomide-treated patients were predicted to have a life expectancy longer than 19 and 25 years, respectively. We also highlight that in an economic analysis conducted by the UK National Institute for Health and Clinical Excellence (NICE) Evidence Review Group (ERG) of first-line treatments (e.g., MPT and VMP) for newly diagnosed multiple myeloma used a time horizon of 30 years. This analysis was conducted in newly diagnosed patients who were not eligible for stem cell transplantation and with an average age of approximately 70 years old. This patient population tends to be much more fragile and with worse prognosis compared to the younger patients who undergo stem cell transplantation. Thus we believe that the use of 40 years is reasonable and valid.
2 5	Summary of pERC Deliberations Drug costs:higher drug costs if dose adjustments because lenalidomide priced per tablet	Paragraph 5, lines 1-5 Paragraph 1, lines 3-5	Revlimid is available as 10 mg and 15 mg capsules to allow for flexibility in dosing and to minimize use of multiple strengths to achieve target dose.
6	Adoption Feasibility	Paragraph 1, lines 2-5	Revlimid is distributed through a controlled distribution program. This program is designed to ensure that there are no cases of fetal exposure to Revlimid, and is required by Health Canada.

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