pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

Provincial Advisory Group (PAG) Feedback on a pCODR Expert Review Committee Initial Recommendation

Ponatinib (Iclusig) for Chronic Myeloid Leukemia / Acute Lymphoblastic Leukemia

October 1, 2015

3 Feedback on pERC Initial Recommendation

Name of the drug indication(s): Ponatinib (Iclusig) for CML & ALL

Endorsed by: Provincial Advisory Group Chair

Feedback was provided by eight of nine provinces (Ministries of Health and/or provincial cancer agencies) participating in pCODR.

3.1 Comments on the Initial Recommendation

a) Please indicate if the PAG (either as individual PAG members and/or as a group) agrees or disagrees with the initial recommendation:

_____ Agrees ____ Agrees in part __x__ Disagree

PAG members providing feedback disagree with pERC's initial recommendation. PAG feels that stem cell transplant is not the appropriate comparator for ponatinib in the chronic phase CML or heavily pre-treated patients.

b) Notwithstanding the feedback provided in part a) above, please indicate if the PAG 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.

PAG would like pERC to reconsider

1. The face validity of pERC's assessment of ponatinib compared to the Committee's review of bosutinib, given the higher rates and severity of toxicities and lack of quality of life data with ponatinib.
2. The cost-effectiveness compared to best supportive care as the more relevant question in the chronic phase CML setting
3. A recommendation for subgroup of patients CML/ALL with T315I mutation separately from the broader CML/ALL group of patients, if appropriate

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
1	pERC Recommendation	Paragraph 2	One year PFS and OS rates were measured in the clinical trials for both ponatinib and bosutinib. Why were the one year PFS and OS rates considered "impressive" for ponatinib but not for bosutinib?
1	pERC Recommendation	Paragraph 3	Hydroxyurea and stem cell transplant are not appropriate comparators for the chronic phase CML. Best supportive care would be the most appropriate comparator in the subgroup of patients who have been heavily pre-treated, in the absence of direct comparative data with bosutinib. It is unclear why ponatinib was deemed cost-effective when bosutinib was not, specifically for the chronic phase CML without T315I mutation and whether the cost-effectiveness applies to all subgroup of CML and ALL patients considered in the deliberations
2	Potential next steps for stakeholders	Paragraph 4	PAG agrees with the recommended restrictions on prescribing that have been suggested
2	Potential next steps for stakeholders	Paragraph 5	Clarity on the optimal sequencing of ponatinib and other therapies: Is this referring to the sequence of previous TKI use? The recommendation for ponatinib is for patients where TKI therapy is not appropriate.

3.2 Comments related to PAG input

Please provide feedback on any issues not adequately addressed in the initial recommendation based on the PAG input provided at the outset of the review on potential impacts and feasibility issues of adopting the drug within the health system.

Page Number	Section Title	Paragraph, Line Number	Comments related to initial PAG input

3.3 Additional comments about the initial recommendation document

Please provide any additional comments:

Page Number	Section Title	Paragraph, Line Number	Additional Comments
4	Summary of pERC deliberations	Paragraph 1 Lines 14-17	What is pERC's rationale to support using ponatinib in patients who do not have T315I mutation? Is there a therapeutic gap, given the significant toxicities of ponatinib and the lack of QOL data and the recently completed review of bosutinib for the same patient population? In addition, the trial is non-comparative and pERC noted that a RCT would be feasible for patients with CP-CML (the population that pERC felt ponatinib may be cost effective compared to ASCT and hydroxyurea.)
4	Summary of pERC deliberations	Paragraph 3, Line 17-19	The statement "…that ponatinib would be unlikely cost effective against bosutinib at almost three times greater drug cost…" appears to be inconsistent with the recommendation to fund conditional on cost-effectiveness being improved for bosutinib and the recommendation to fund ponatinib without that proviso
			Ontario's Disease Site Group provided feedback through its PAG member and also agrees with a restricted prescriber list, given the toxicities of the drug and the lack of widespread familiarity with its use. However, the Disease Site Group felt that pERC has understated the toxicities of ponatinib.

About Completing This Template

pCODR invites the Provincial Advisory Group (PAG) to provide feedback and comments on the initial recommendation made by the pCODR Expert Review Committee. (See www.pcodr.ca for information regarding review status and feedback deadlines.)

As part of the pCODR re view 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 pERC 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 PAG, either as individual PAG members and/or as a group, agrees or disagrees with the pERC 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 pERC 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 pERC final 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 a pERC final 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 pERC final 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 members of the PAG can provide feedback on the pERC initial recommendation; delegates must work through the PAG representative to whom they report.
    a. Please note that only one submission is permitted for the PAG. Thus, the feedback should include both individual PAG members and/or group feedback.

b) Feedback or comments must be based on the evidence that was considered by pERC in making the pERC 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 *Provincial Advisory Group (PAG) Feedback on a 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. PAG 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, PAG 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.