CADTH

pan-Canadian Oncology Drug Review Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation (Patient Advocacy Group)

Lorlatinib (Lorbrena) for Non-Small Cell Lung Cancer

Lung Cancer Canada

January 30, 2020

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	Lorlatinib (Lobrena). As monotherapy for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) who have progressed on: crizotinib and at least one other ALK inhibitor, or patients who have progressed on ceritinib or alectinib.
Eligible Stakeholder Role in Review (Sponsor and/or Manufacturer, Patient Group, Clinical Organization Providing Feedback	Patient Group Lung Cancer Canada

**The pCODR program may contact this person if comments require clarification. Contact information will not be included in any public posting of this document by the pCODR program.*

3.1 Comments on the Initial Recommendation

a) Please indicate if the eligible stakeholder agrees, agrees in part, or disagrees with the Initial Recommendation:

☐ agrees ☐ agrees in part ☒ disagree

The decision by pERC to provide a negative recommendation for lorlatinib as a monotherapy for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) was concerning to Lung Cancer Canada and the lung cancer community, and we feel this decision should be reconsidered.

1. Lung cancer is the most commonly diagnosed and leading killer of all cancers in Canada, with an expected 29,300 new cases and 21,000 deaths in 2019. Non-small cell lung cancer (NSCLC) represents 85% of all lung cancers, and anaplastic lymphoma kinase (ALK)-positive NSCLC makes up about 2 – 5% of this group. With just a 19%, 5 year survival rate and the known risk of progression following treatment, there is an unmet need, necessitating the need to provide patients with viable treatment options.
2. With the emergence of targeted therapies, many lung cancer patients have been able to live longer with a good quality of life. They are able to stay functional,

independent and physically active with manageable side effects, and the dosage modality makes it easier not just for the patients but also their loved ones/caregivers. Lorlatinib is a targeted therapy that has shown promise, and is what AM a stage 4 lung cancer survivor who recently celebrated her 10 year "cancerversary" is currently taking, and has been on for 3 years. Input from the initial submission showed all the patients interviewed stated they were able to maintain independence and functionality on lorlatinib. For example, TW a landscaper was able to continue working, be more involved in activities with friends and family, as well as travel quite a bit. RC said lorlatinib saved his life.

3. pERC stated that due to the limited evidence from the phase 2 trial it was not confident of the net clinical benefit of lorlatinib. Studies have shown consistency between phase 2 and 3 targeted therapy clinical trial results, and the results from the lorlatinib trial showed a response rate of 40%, an intracranial response of 50% and a median duration of response of over 14 months, this shows that lorlatinib works and it consistent with patient values. The intracranial response shows that lorlatinib is effective in fighting brain metastases which significantly affects prognosis and quality of life. With the small population of ALK positive NSCLC patients and no phase 3 trial currently being planned, this data should be strongly considered. PERC, citing uncertainty in the data, has consistently made negative funding recommendations for targeted therapy treatments submitted using phase 2 data. However it should be noted that ALL of those treatments have gone on to have positive results, either in phase 3 or follow-up studies. The certainty is solid. Phase 2 trial results in targeted therapy treatments are meaningful. It is not necessary to risk patient lives by waiting for "confirmatory" data.
4. This treatment option according to pERC aligns with patient values. Lorlatinib has manageable side effects and provides a needed additional treatment choice. ALK treatments have changed the paradigm. Why should these patients be denied the opportunity to live longer and better? Why should chemotherapy, that is well documented to have toxic side effects or supportive care which does not treat but rather manages the symptoms related to the disease be the next option for patients after progression when there currently is an option that works and can prolong patient survival. With the other choices there is an added burden on patients and caregivers to drive to clinics to get treated, longer stays in the hospital for infusions, even managing the side effects, which in turn can affect productivity and sometimes result in financial hardship for families.

b) Please indicate if the eligible stakeholder agrees, agrees in part, or disagrees with the provisional algorithm:

☐ agrees ☐ agrees in part ☒ disagree

Cost effectiveness compared to chemotherapy and supportive care can be addressed by ensuring better negotiations between the PCPA and manufacturers to facilitate a more acceptable option which would help improve adoption feasibility. This should not be a barrier to provide patients with a viable option. LCC understands these cost concerns, and would encourage the manufacturer and PCPA to negotiate with the need of these patients in mind.

c) Please provide editorial feedback on the Initial Recommendation to aid in clarity. Is the Initial Recommendation or are the components of the recommendation (e.g., clinical and economic evidence or provisional algorithm) 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 Eligible Stakeholder Provided Information

Notwithstanding the feedback provided in part a) above, please indicate if the Stakeholder would support this Initial Recommendation proceeding to Final pERC Recommendation ("early conversion"), which would occur two (2) Business Days after the end of the feedback deadline date.

☐	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.

We understand that phase 3 data has been a standard that PERC has long relied on. However as treatment innovates, so must PERC. We encourage PERC to provide a positive recommendation and ask for the collection of real –world evidence to "confirm".

As we mentioned in our initial submission, for all lung cancer patients the question typically is, "What next if my treatment fails?" In the case of ALK positive lung cancer patients, there is an option, LORLATINIB. Lorlatinib can help control the disease, delay progression, prolong survival with manageable side effects, allowing patients have a meaningful continuation of a good quality of life and this aligns with patient values. LCC encourages pERC to reconsider their decision as this treatment modality is well worth consideration.

Page Number	Section Title	Paragraph, Line Number	Comments related to Stakeholder Information

1 About Stakeholder Feedback

pCODR invites eligible stakeholders to provide feedback and comments on the Initial Recommendation made by the pCODR Expert Review Committee (pERC), including the provisional algorithm. (See www.cadth.ca/pcodr for information regarding review status and feedback deadlines.)

As part of the pCODR review process, pERC makes an Initial Recommendation based on its review of the clinical benefit, patient values, economic evaluation and adoption feasibility for a drug. (See www.cadth.ca/pcodr for a description of the pCODR process.) The Initial Recommendation is then posted for feedback from eligible stakeholders. All eligible stakeholders have 10 (ten) business days within which to provide their feedback on the initial recommendation. It should be noted that the Initial Recommendation, including the provisional algorithm may or may not change following a review of the feedback from stakeholders.

pERC welcomes comments and feedback from all eligible stakeholders with the expectation that even the most critical feedback be delivered respectfully and with civility.

A. Application of Early Conversion

The Stakeholder Feedback document poses two key questions:

1. **Does the stakeholder agree, agree in part, or disagree with the Initial Recommendation?**

   All eligible stakeholders are requested to indicate whether they agree, agree in part or disagrees with the Initial Recommendation, and to provide a rational for their response.

   Please note that if a stakeholder agrees, agrees in part or disagrees with the Initial Recommendation, the stakeholder can still support the recommendation proceeding to a Final Recommendation (i.e. early conversion).

2. **Does the stakeholder support the recommendation proceeding to a Final Recommendation ("early conversion")?**

   An efficient review process is one of pCODR's key guiding principles. If all eligible stakeholders support the Initial Recommendation proceeding to a Final Recommendation and that the criteria for early conversion as set out in the *pCODR Procedures* are met, the Final Recommendation will be posted on the CADTH website two (2) Business Days after the end of the feedback deadline date. This is called an "early conversion" of an Initial Recommendation to a Final Recommendation.

   For stakeholders who support early conversion, please note that if there are substantive comments on any of the key quadrants of the deliberative framework (e.g., differences in the interpretation of the evidence), including the provisional algorithm as part of the feasibility of adoption into the health system, the criteria for early conversion will be deemed to have **not** been met and the Initial Recommendation will be returned to pERC for further deliberation and reconsideration at the next possible pERC meeting. If the substantive comments relate specifically to the provisional algorithm, it will be shared with PAG for a reconsideration. Please note that if any one of the eligible stakeholders does not support the Initial Recommendation proceeding to a Final pERC Recommendation, pERC will review all feedback and comments received at a subsequent pERC meeting and reconsider the Initial Recommendation. Please also note that substantive comments on the provisional algorithm will preclude early conversion of the initial recommendation to a final recommendation.

B. Guidance on Scope of Feedback for Early Conversion

Information that is within scope of feedback for early conversion includes the identification of errors in the reporting or a lack of clarity in the information provided in the review documents. Based on the feedback received, pERC will consider revising the recommendation document, as appropriate and to provide clarity.

If a lack of clarity is noted, please provide suggestions to improve the clarity of the information in the Initial Recommendation. If the feedback can be addressed editorially this will done by the CADTH staff, in consultation with the pERC chair and pERC members, and may not require reconsideration at a subsequent pERC meeting. Similarly if the feedback relates specifically to the provisional algorithm and can be addressed editorially, CADTH staff will consult with the PAG chair and PAG members.

The Final pERC Recommendation will be made available to the participating federal, provincial and territorial ministries of health and provincial 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) The following stakeholders are eligible to submit Feedback on the Initial Recommendation:
   - The Sponsor making the pCODR Submission, or the Manufacturer of the drug under review;
   - Patient groups who have provided input on the drug submission;
   - Registered clinician(s) who have provided input on the drug submission; and
   - The Provincial Advisory Group (PAG)

b) The following stakeholders are eligible to submit Feedback on the provisional algorithm:
   - The Sponsor making the pCODR Submission, or the Manufacturer of the drug under review;
   - Patient groups who have provided input on the drug submission;
   - Registered clinician(s) who have provided input on the drug submission; and
   - The Board of Directors of the Canadian Provincial Cancer Agencies

c) 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.

d) The template for providing *Stakeholder Feedback on pERC Initial Recommendation* can be downloaded from the pCODR section of the CADTH website. (See www.cadth.ca/pcodr for a description of the pCODR process and supporting materials and templates.)

e) At this time, the template must be completed in English. The Stakeholder 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.

f) 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 provided to the pERC for their consideration.

g) 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, and should not contain any language that could be considered disrespectful, inflammatory or could be found to violate applicable defamation law.

h) 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 program.

i) The comments must be submitted via a Microsoft Word (not PDF) document to pCODR by the posted deadline date.

j) If you have any questions about the feedback process, please e-mail pcodrsubmissions@cadth.ca

Note: CADTH is committed to providing an open and transparent cancer drug review process and to the need to be accountable for its recommendations to patients and the public. Submitted feedback will be posted on the CADTH website (www.cadth.ca/pcodr). The submitted information in the feedback template will be made fully disclosable.

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Ontario Lung Association

January 30, 2020

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Name of the Drug and Indication(s): Eligible	Lorlatinib (Lorbrena)
Stakeholder Role in Review (Sponsor and/or Manufacturer, Patient Group, Clinical	Patient Group
Organization Providing Feedback	Ontario Lung Association

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3.1 Comments on the Initial Recommendation

a) Please indicate if the eligible stakeholder agrees, agrees in part, or disagrees with the Initial Recommendation:

☐ agrees ☐ agrees in part ☒ disagree

The Ontario Lung Association disagrees with pERC's Initial recommendation not to reimburse Lorlatinib, as this creates a barrier to an effective "end of line" treatment for patients with aggressive lung cancer.

Our patients are continuously requesting greater treatment options to consider and choose from. Improvement of Quality of Life has been documented as a high-priority from the patients we work with. Lorlatinib provides this improvement to patients, but without reimbursement, a barrier is created for hopeful patients to access this new treatment.

Cost of medications and access to new treatments has been an ongoing theme that patients continue to highlight in discussions and requests. Many are on fixed incomes and need new treatments options to become available that are less expensive or fully reimbursed.

pERC bases its decision to 'not reimburse' on the lack of evidence demonstrating the clinical benefit and cost effectiveness of lorlatinib in comparison to other treatment options, including chemotherapy and best supportive care. We again would like to stress that patients with aggressive lung cancer value treatment options that help relieve many of their adverse symptoms. While the relative benefits and alignment with patient values of the drug under question were recognized by pERC throughout their report, we believe this was not given enough weight in the basis of the decision made.

pERC notes in its initial recommendation under 'adoption feasibility' (page 11) that in some jurisdictions in Canada, oral medications are not funded in the same mechanism as intravenous cancer medications which limits ease of treatment. However, we would like to acknowledge that in Ontario specifically, oral cancer drugs can be funded for some populations under the Ontario Drug Benefit and other access programs such as Trillium. pERCs negative recommendation will limit access to end of line treatment for patients eligible for drug reimbursement under these programs.

b) Please indicate if the eligible stakeholder agrees, agrees in part, or disagrees with the provisional algorithm:

☐ agrees ☐ agrees in part ☐ disagree

n/a

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☐ 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.

If the eligible stakeholder does not support conversion to a Final Recommendation, please provide feedback on any issues not adequately addressed in the Initial Recommendation based on any information provided by the Stakeholder 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 program.

Additionally, if the eligible stakeholder supports early conversion to a Final Recommendation; however, the stakeholder has included substantive comments that requires further interpretation of the evidence, including the provisional algorithm, the criteria for early conversion will be deemed to have not been met and the Initial Recommendation will be returned to pERC for further deliberation and reconsideration at the next possible pERC meeting.

Page Number	Section Title	Paragraph, Line Number	Comments related to Stakeholder Information
4	Pgh 1	Pgh 1 line 1	The Ontario Lung Association is in alignment with Lung Cancer Canada in the request for pERC to issue conditional approval for Lorlatinib, in order to enable the collection of third line data.

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