CADTH

pan-Canadian Oncology Drug Review

Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation

(Patient Advocacy Group)

Lutetium Lu 177 dotatate (Lutathera) for Gastroenteropancreatic Neuroendocrine Tumors

August 1, 2019

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	pCODR 10142 Lutetium Lu 177 dotatate (Lutathera) indicated for Gastroenteropancreatic neuroendocrine tumours (GEP-NETs)
Eligible Stakeholder Role in Review (Submitter and/or Manufacturer, Patient Group, Clinical Group):	CNETS Canada – A registered Patient Advocacy Group with CADTH who provided patient input into the above review.
Organization Providing Feedback	CNETS 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

pERC Recommendation text: "Treatment of adult patients with somatostatin receptor-positive (SSR+) midgut neuroendocrine tumours (NETs) whose disease has progressed on a somatostatin analog and is unresectable"

The recommendation is too narrow and does not include patients who could benefit from PRRT, reimbursement should be for treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumours (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults whose disease has progressed and is unresectable

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

☐ agrees ☐ agrees in part ☐ disagree

Please explain why the Stakeholder *agrees, agrees in part or disagrees with the provisional algorithm. Please note that comments should relate* ***only to the proposed place in therapy of the drug under review*** *in the provisional algorithm. If feedback includes New Information or about other therapies that are included in the provisional algorithm, the information will not be considered and will be redacted from the posted feedback. Substantive comments on*

the provisional algorithm will preclude early conversion of the initial recommendation to a final recommendation.

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
2	pERC Recommendation	pERC noted that 177Lu-Dotatat e, in patients with foregut and hindgut NETs, aligned with patient values in that it produced an antitumour response, with manageable side effects and offers an additional treatment option. However, the Committee was unable to draw conclusions on the net benefit of 177Lu-Dotatate for patients with foregut and hindgut NETs.	We received feedback from 69 NET patients, including 53 patients across the range of GEP-NET types on their experience of Lutathera treatment. The tremendous patient feedback informed our request that pERC issue a positive recommendation for treatment with Lutathera for Gastroenteropancreatic neuroendocrine tumours (GEP-NETs) and immediately reimburse the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults.
5	Summary of pERC Deliberations	pERC also deliberated upon the results of a non-randomized, non-comparative phase I/II study, ERASMUS, which evaluated 177Lu-Dotatate in the broader GEP-NETs population (i.e., not limited to midgut NETs), and which included patients with foregut and hindgut NETs. pERC considered that overall, results of the ERASMUS study appear to be consistent with the results from the NETTER-1 trial. pERC discussed the CGP's conclusions that it would be reasonable to	Access to PRRT/Lutathera treatment for NET cancer in Canada has been very slow. Our NET patient community was hopeful that pCODR would recommend reimbursement of Lutathera treatment for all NET patients who fit the above criteria. Our organization is deeply concerned that the recommendation as it is currently written is too restrictive, and that pCODR already has the evidence needed to be able to recommend Lutathera more broadly. Please look again at the patient testimonies, and

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
		extend treatment with 177Lu-Dotatate to other NETs, including foregut and hindgut NETs, based on the findings from the ERASMSUS study and based on the rationale of mechanism of action (biological plausibility) that the clinical benefit is unlikely to differ based on anatomic site for SSR+ disease	consider also the results of the ERASMUS trial, which showed that Lutathera is effective in a variety of NETs.
5	Summary of pERC Deliberations	Overall, pERC agreed that 177Lu-Dotatate aligns with patient values in that it is an effective treatment option that delays disease progression and has manageable side effects with no observed detriment to QoL.	It is our position that it would be unethical for cancer agencies to deny access to this treatment when ample evidence of its effectiveness is available. We ask that pERC please reconsider the Initial Recommendation and recommend access to all NET patients who could benefit from Lutathera treatment.

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.

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

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 Submitter 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 Submitter 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.