CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

selpercatinib (Retevmo)

(Eli Lilly Canada Inc.)

Indication: RET fusion-positive non-small cell lung cancer

April 14, 2022

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0261-000
Brand name (generic)	Retevmo (Selpercatinb)
Indication(s)	Indicated as monotherapy for the treatment of metastatic RET fusion-positive non-small cell lung cancer (NSCLC) in adult patients.
Organization	Lung Cancer Canada – Clinician Group
Contact information[a]	Name: Shem Singh

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
We are very happy to hear the approval for untreated and treated patients with RET fusion even in those with ECOG >2.		

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐
If not, what aspects are missing from the draft recommendation?		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
As per testing, we have confirmation that the NGS platform implemented in Ontario will cover RET fusion. In the Atlantic provinces, RET fusion is currently standard of care for part of New Brunswick. The NGS panel including RET fusion in Nova Scotia is going through the final stages of implementation, which will provide RET testing for all the Atlantic provinces. While the testing will be available in all Canadian jurisdictions at that point, many patients will still not have access to timely testing due to health care system issues including barriers to accessing to the procedures needed to procure the required tissue for testing. This often disproportionately impacts Canadian patients living in rural settings, and we encourage CADTH to help in advocating to ensure that disparities in best care on the basis of geography and other socioeconomic barriers that make accessing the health care system for some Canadians difficult are addressed.		

[a] CADTH may contact this person if comments require clarification.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
1. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

B. Previously Disclosed Conflict of Interest		
3. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒

If yes, please list the clinicians who contributed input and whose declarations have not changed:

- Dr. Quincy Chu
- Dr. Ron Burkes
- Dr. Geoffrey Liu
- Dr. Paul Wheatley Price
- Dr. Rosalyn Juergens
- Dr. Jeffery Rothenstein
- Dr. Mahmoud Abdeslalam
- Dr. Catherine Labbé
- Dr. Kevin Jao
- Dr. Sunil Yadav

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0261-000
Brand name (generic)	Selpercatinib (Retevmo)
Indication(s)	Indicated as monotherapy for the treatment of metastatic RET fusion-positive NSCLC in adult patients
Organization	Ontario Health Cancer Care Ontario Lung Cancer Drug Advisory Committee
Contact information[a]	Name: Dr. Donna Maziak

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

[a] CADTH may contact this person if comments require clarification.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
1. Did you receive help from outside your clinician group to complete this submission?	No	☐
	Yes	☒
Yes. Ontario Health provided secretariat functions to the Lung DAC.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help who provided it.		
B. Previously Disclosed Conflict of Interest		
3. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Dr. Peter Ellis		

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0261
Name of the drug and Indication(s)	Selpercatinib for RET fusion-positive NSCLC
Organization Providing Feedback	PAG

1. Recommendation revisions Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.		
Request for Reconsideration	**Major revisions:** A change in recommendation **category** or patient **population** is requested	☐
	Minor revisions: A change in reimbursement **conditions** is requested	☐
No Request for Reconsideration	**Editorial revisions:** Clarifications in recommendation **text** are requested	X
	No requested revisions	☐

2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
In the clinical evidence section, first sentence of the fifth paragraph, PAG is requesting to include the patient numbers for the cohorts.
b) Reimbursement conditions and related reasons
1. Treatment with selpercatinib should be reimbursed when initiated in adult (≥ 18 years) patients with metastatic RET fusion-positive NSCLC who meet one of the following criteria: 1.1. for first-line treatment PAG noted that Phase II non-comparative trials were previously submitted to CADTH which demonstrated improved tumour response rates; yet these submissions received a "do not reimburse" recommendation. PAG also noted there is a relevant ongoing phase III, randomized, open label study (LIBRETTO-431) comparing selpercatinib to platinum-based (carboplatin or

cisplatin) and pemetrexed therapy with or without pembrolizumab in previously **untreated** patients with locally advanced/metastatic RET fusion-positive nonsquamous NSCLC.

The public drug programs have concerns regarding recommendations that are issued with preliminary phase 1/2 clinical trial data when phase 3 confirmatory trials are currently being conducted with planned results in the next several years. The concerns include the following:

- the preliminary estimates of effect from phase 2 trials may not be an accurate assessment of the clinical efficacy for the drug under review;
- the pharmacoeconomic evaluation incorporates data that include extrapolations (e.g. overall survival, quality of life) which contribute to considerable uncertainty in the results of the analyses. Thus, the evaluation may overestimate the value for money of the drug under review. This would also benefit from re-evaluation should the phase 3 data demonstrate different results than what was reported in the phase 1/2 data
- the public drug programs have limited ability to compel the sponsor to file the pending phase 3 data for review by CADTH to valid the assumptions that have used in the economic model.

The issues noted above could result in the public drug programs providing reimbursement for selpercatinib at a price which is not cost-effective. This creates concerns regarding the ability to reimburse drugs such as selpercatinib while ensuring that the oncology drug formularies are managed in a sustainable manner.

c) Implementation guidance

None.

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0261-000
Brand name (generic)	Retevmo (Selpercatinib)
Indication(s)	Indicated as monotherapy for the treatment of metastatic RET fusion-positive non-small cell lung cancer (NSCLC) in adult patients.
Organization	Lung Cancer Canada – Patient Group
Contact information[a]	Name: Shem Singh

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐

Lung Cancer Canada thanks pERC for recommending selpercatinib for the treatment of adult RET-positive NSCLC patients. Undoubtedly, this positive recommendation will allow for patients to receive equitable access to this treatment that otherwise may not have had the opportunity to.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐

Overall, LCC believes the recommendation demonstrates thorough consideration of our organization's input provided to CADTH. In LCC's initial submission, we highlighted the importance of having targeted therapy available as a treatment option for patients with a targetable mutation such as RET-fusion, because of the invaluable improvements it can have on patients' quality of life. As discussed in our initial submission, selpercatinib helped patients maintain and improve their functionality to a level similar to before diagnosis, helped them regain their independence that was lost from previous systematic treatments, allowed some to even return to work, and make goals for the future.

Within discussion point 3 in the recommendation, pERC noted uncertainty in the clinical data for health-related quality of life, overall survival, and progression-free survival. Although the data from the phase 1/2 LIBRETTO-001 trial may seem preliminary, the patients interviewed by LCC showed a positive and promising response, with very drastic improvements in their disease symptoms and ability to maintain long-term disease stability, some patients remained in remission for up to 4 years. With the ongoing phase III trial for selpercatinib as mentioned, this will generate even more real world evidence (RWE) and in turn with reimbursement of selpercatinib, provide more evidence in the efficacy of selpercatinib in this patient population with more certainty.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

LCC believes the rationale for the recommendation is clearly stated and takes into consideration the perspectives of patients, clinicians, and evidence from the LIBRETTO-001 trial. As discussed in

LCC's initial submission, it is imperative that patient values are considered as ultimately, the reimbursement of selpercatinib will impact patients the most. LCC thanks pERC for recognizing that there are currently no targeted therapies available for RET-fusion positive NSCLC patients, with selpercatinib being the very first therapy available for this population. As discussed above, the ongoing phase III trial will also generate more RWE overtime for clinical data with more certainty.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐

LCC agrees all implementation issues are clearly articulated and addressed within the recommendation.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒

Overall, the reimbursement conditions for selpercatinib were adequately rationalized and stated in the recommendation; however, condition 6 (Pricing) within the conditions discusses the cost-effectiveness of selpercatinib to be highly uncertain. pERC mentions a drastic price reduction of 70-93% is required for selpercatinib to be cost-effective at this $50,000 per QALY threshold.

To reiterate what LCC stated in Section 8 of our initial patient input submission, CADTH has lowered the QALY threshold for cost effectiveness to $50,000, which is consistent with non-cancer drugs. Lung Cancer Canada believes the comparison is unreasonable, especially as cancer treatments with personalised medicine (such as selpercatinib and other targeted therapies) have smaller groups and fewer patients, making $50,000 per QALY an unreasonable threshold. It also undermines the premise of separate deliberations for cancer vs non-cancer drugs. It is expected that cancer treatments will cost more than, for example, an antibiotic or a proton pump inhibitor. Lowering the threshold QALY devalues innovation in life-threatening or complex diseases, and creates an unreasonable barrier in accessing life-saving treatments for cancer patients. We ask CADTH to re-evaluate the threshold QALY for cancer treatments in recognition that cancer is a life-threatening disease with far reaching impact on society.

In addition, condition 8 (Access to RET testing) notes there should be adequate RET testing available in jurisdictions across Canada in order to identify the eligible patient population for selpercatinib. There is still unequal access to testing across the provinces, especially for those in rural communities and with socioeconomic barriers, though we are moving in the right direction with Ontario and Nova Scotia soon to finalize RET as standard of care in NGS testing. The incorporation of testing for biomarkers such as RET in panel testing as they become available should be part of the standard of care and will help reduce testing costs. We encourage CADTH to help advocate for universal access to testing across the country to mitigate the barriers in accessing the treatment patients need.

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Shem Singh*
Position	*Executive Director, Lung Cancer Canada*
Date	*14-04-2022*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☒

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0261-000
Brand name (generic)	RETEVMO™ (selpercatinib)
Indication(s)	As monotherapy for the treatment of metastatic RET fusion-positive non-small cell lung cancer (NSCLC) in adult patients
Organization	Eli Lilly Canada Inc.
Contact information[a]	Name: [redacted] Title: [redacted] Email: [redacted] Phone: [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐

Eli Lilly Canada Inc. (Lilly) agrees with the CADTH pCODR Expert Review Committee's (pERC) initial recommendation that RETEVMO™ (selpercatinib) be reimbursed for the treatment of metastatic RET fusion-positive NSCLC in adult patients. Lilly supports the conversion of the initial recommendation to a final recommendation to expedite access for adult patients with RET fusion-positive NSCLC.

Lilly is pleased with pERC's recognition of an unmet need for adult patients with RET fusion-positive NSCLC and that selpercatinib addresses an important therapeutic need, as there are currently no targeted therapies available in this population.

Lilly also agrees that selpercatinib treatment demonstrated clinically meaningful benefits, including high central nervous system (CNS) response rates, and had manageable side effects, which met the needs identified by patients.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐

Lilly agrees that pERC has considered the input provided to CADTH in its deliberation.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

Lilly agrees that the reasons for the recommendation are clearly stated.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐

Lilly agrees that the implementation issues are clearly articulated and adequately addressed.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

Lilly agrees that the reimbursement conditions and associated rationales are clearly stated.

[a] CADTH may contact this person if comments require clarification.