CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

pralsetinib (Gavreto)

(Hoffmann-La Roche Ltd.)

Indication: Gavreto is indicated for the treatment of adult patients with rearranged during transfection (RET) fusion-positive locally advanced unresectable or metastatic non-small cell lung cancer (NSCLC).

September 16, 2022

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0283-000
Brand name (generic)	Pralsetinib (Gavreto)
Indication(s)	The treatment of adult patients with RET fusion-positive locally advanced unresectable or metastatic NSCLC
Organization	Ontario Health (CCO) Lung Cancer Drug Advisory Committee
Contact information[a]	Name: Dr. Andrew Robinson

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
The DAC raised the issue of oligoprogression and consistency with the selpercatanib recommendation. The pralsetinib recommendation says treatment should be discontinued if there is clinical progression not amenable to local therapies such as radiation. The selpercatanib recommendation has similar wording but uses the term oligoporgression. We would suggest that these are really discussing the same point and would suggest consistency in wording between similar agents.		

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 DAC.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
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. Sara Kuruvilla • Dr. Andrew G Robinson		

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0283-000
Brand name (generic)	Pralsetinib (Gavreto)
Indication(s)	Gavreto is indicated for the treatment of adult patients with rearranged during transfection (RET) fusion-positive locally advanced unresectable or metastatic non-small cell lung cancer (NSCLC).
Organization	Lung Cancer Canada – Clinician Group
Contact information[a]	[redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	X
	No	☐
Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale. The positive recommendation is in line with our views that is a valuable treatment for patients with RET Fusion positive NSCLC. The recommended inclusion criteria and exclusion criteria are in line with clinical trial design and also in line with clinical practice.		

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	X
	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	X
	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	X
	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	X
	No	☐
If not, please provide details regarding the information that requires clarification.		

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

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  - 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	x
	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	x
	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	x
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Dr. Shaqil Kassam • Dr. Mahmoud Abdelsalam • Dr. Quincy Chu • Dr. Rosalyn Juergens • Dr. Zhaolin Xu • Dr. Normand Blais • Dr. Paul Wheatley-Price • Dr. Nicole Bouchard • Dr. Kevin Jao • Dr. Catherine Labbé • Dr. Geoffrey Liu • Dr. Ron Burkes		

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0283
Name of the drug and Indication(s)	Pralsetinib 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	☐
	No requested revisions	X

2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested
None.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
None.
b) Reimbursement conditions and related reasons
None.
c) Implementation guidance
None.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0283-000
Brand name (generic)	Pralsetinib (Gavreto)
Indication(s)	Gavreto is indicated for the treatment of adult patients with rearranged during transfection (RET) fusion-positive locally advanced unresectable or metastatic non-small cell lung cancer (NSCLC).
Organization	Lung Cancer Canada – Patient Group
Contact information[a]	[redacted]

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

Lung Cancer Canada thanks pERC for the positive recommendation of pralsetinib for RET-fusion-positive NSCLC patients with metastatic or advanced disease. This marks an important milestone for this rare patient population, as stated in the Rationale for Recommendation by pERC, as there is a high unmet need and currently no targeted therapies funded in this area. There is a pressing need for additional treatment options in this patient population given the poor prognosis, high symptom burden and significant risk of metastases, particularly in the central nervous system. The positive impacts that pralsetinib has had on patients interviewed in Lung Cancer Canada's initial submission is evident, as patients reported significant improvements in their disease and symptom burden, improvements in their mobility and functionality, and ultimately, the ability and freedom to return to a lifestyle that is worthwhile and meaningful, including their return to work.

As per the results of the ARROW study, there is clinically meaningful benefit of pralsetinib to patients, across the globe, even when dosages were reduced to alleviate adverse effects. The opportunity to have this progression-free survival time is critical for patients to maximize their quality of life and be able to continue with their day-to-day lives with autonomy and dignity, and we are pleased that pERC has agreed as well.

Lung Cancer Canada agrees with the draft recommendation that pERC and CADTH has published, and do not have suggestions to make at this time.

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	☐
If not, please provide details regarding the information that requires clarification.		

[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.
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A. Patient Group Information	
Name	*Shem Singh*
Position	*Executive Director*
Date	*Sept 16/2022*
☒	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	PC0283
Brand name (generic)	GAVRETO™ (Pralsetinib)
Indication(s)	For the treatment of adult patients with rearranged during transfection (RET) fusion-positive locally advanced unresectable or metastatic non-small cell lung cancer (NSCLC).
Organization	Hoffmann-La Roche Limited
Contact information[a]	[redacted]

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

Hoffmann-La Roche Limited agrees with the CADTH pCODR Expert Review Committee (pERC) recommendation that pralsetinib be reimbursed for the treatment of adult patients with rearranged during transfection (RET) fusion-positive locally advanced unresectable or metastatic NSCLC.

Roche agrees with CADTH that "there is a need for additional treatment options in this rare patient population given the poor prognosis, high symptom burden and high risk of CNS metastases." (page 3). Roche is pleased that pERC acknowledges that "pralsetinib addresses a therapeutic need, as there are currently no targeted therapies funded for RET fusion-positive NSCLC patients" (page 3) and that "pralsetinib met the needs identified by patients in terms of stopping or delaying disease progression, having manageable side effects, improving quality of life, and allowing patients to maintain their independence and functionality." (page 3). Pralsetinib is also the only oral targeted treatment with a fixed and once-daily dose available for RET fusion-positive NSCLC, and among RET-targeted therapies it is available at a lower list price for the majority of patients. This can offer a more predictable treatment cost for the health care system, while offering greater patient convenience.

Given that CADTH was unable to derive a reliable base-case estimation of cost-effectiveness, Roche suggests that the results of the exploratory analysis should be interpreted with caution. Specifically, Roche notes the approach taken by the EGP to "assume equal overall survival for each comparator" (page 15) in their exploratory re-analyses. This approach is not only inconsistent with CADTH's recent review of another therapy for RET fusion-positive NSCLC, it also produces clinically implausible treatment effects for the comparator drugs, and furthermore contradicts the totality of evidence related to the likelihood of overall survival benefit of pralsetinib (and as expected by the clinical expert consulted). During the review, Roche acknowledged CADTH's interest in exploring alternative scenarios regarding long-term survival, and suggested potential alternative methods for conservative estimation of OS benefit instead of the EGP re-analysis summarized in Table 3 (page 16). Roche's proposed alternatives included assuming equal post-progression OS benefit, while still allowing for OS benefit pre-progression. This proposed approach was also more consistent with the re-analysis in another recent review in RET fusion-positive NSCLC. CADTH accepted this approach as a scenario analysis and it resulted in a treatment-naïve sequential ICER of $282,322/QALY – which is the lower bound of CADTH's estimated range of ICERs (page 3). Therefore, the overall

results of CADTH's exploratory analysis likely underestimate the value of pralsetinib; given the most realistic estimate of the cost-effectiveness likely falls at the lower end of CADTH's range.

Notwithstanding the economic comments, Roche supports the conversion of the draft recommendation to a final recommendation to expedite access for patients with RET fusion-positive NSCLC. Roche is committed to working with the jurisdictions via the pCPA process to ensure that patients have access to this new targeted therapy as soon as possible.

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, please provide details regarding the information that requires clarification.		

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	☐
If not, please provide details regarding the information that requires clarification.		

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