Canada's Drug Agency
L'Agence des médicaments du Canada

CDA-AMC REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

alectinib (Alecensaro)

(Hoffman-LaRoche Limited)

Indication: Alecensaro as adjuvant treatment following tumor resection for patients with anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC).

October 18, 2024

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0350-000
Brand name (generic)	Alectinib (Alecensaro)
Indication(s)	Alecensaro as adjuvant treatment following tumour resection in adult patients with Stage IB (4 cm) - IIIA (according to AJCC/UICC 7th edition) anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer.
Organization	Lung Cancer Canada Lung Health Foundation
Contact information[a]	Winky Yau, Lung Cancer Canada [redacted] Riley Sanders, Lung Health Foundation [redacted]

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

This feedback on the draft recommendation for alectinib is on behalf of both Lung Cancer Canada and Lung Health Foundation.

The Lung Cancer Canada and Lung Health Foundation patient groups thank pERC for the positive recommendation to reimburse alectinib (Alecensaro) as indicated for the adjuvant treatment following tumour resection in adult patients with Stage IB - IIIA ALK-positive non-small cell lung cancer. The approval of alectinib within this indication as per the successful results of the ALINA clinical trial brings a very welcome expansion to the early-stage setting, in addition to the metastatic/stage IV indication that alectinib has already been publicly funded for in the years prior. This recommendation will ensure that all patients who harbour the ALK-positive mutation are able to access an important therapy that has since become standard of care for this biomarker with very efficacious results.

We do suggest amending the reimbursement condition #3.3, which currently states "Reimbursement of alectinib should be discontinued upon occurrence of any of the following:"
3.1. Disease recurrence
3.2. Unacceptable toxicity
3.3. Completion of 2 years of therapy

The two-year limit of treatment with alectinib we do not necessarily agree with, and would suggest pERC amend this condition to remove 3.3 from the conditions surrounding treatment discontinuation. Many of the patients on alectinib that LCC had spoken to via interviews in the initial submission have been on the treatment for much longer than 24 months, with a few patients still on it today, 5-6 years since starting the treatment, and are still progression-free or have been encouraged by their oncologist to continue the treatment despite minor progression because the benefits of continuing the

treatment still outweigh the risks of discontinuation. We suggest this condition be amended accordingly to allow patients access to alectinib as long as it continues to be an effective treatment. Overall, Lung Cancer Canada and Lung Health Foundation find this draft recommendation as very positive and excellent news, and hopes that CDA is able to bring this to a positive final recommendation with the suggested amendment.

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.
- 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	*October 17, 2024*
☒	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	☐	☐	☐	☐

A. Patient Group Information	
Name	*Riley Sanders*
Position	Senior Manager, Public Affairs

	Lung Health Foundation
Date	*October 17, 2024*
☒	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

4. 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.

5. 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

2. 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

6. 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 Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0350-000
Brand name (generic)	Alecensaro (alectinib)
Indication(s)	Alecensaro as adjuvant treatment following tumour resection in adult patients with Stage IB (4 cm) - IIIA (according to AJCC/UICC 7th edition) anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer.
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	☒
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 recommendation is silent on the issue of whether patients can still receive adjuvant chemotherapy. The trial randomized patients to adjuvant chemo or alectinib but chemotherapy is an established therapy and patients should not be denied this. Adjuvant chemotherapy is still effective in ALK-positive NSCLC and many clinicians will still want to have the option for adjuvant chemotherapy prior to alectinib particularly in stage II and III disease.		

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. There are also some gray areas remaining –		

1. If patients to have received neoadjuvant chemo +/- immunotherapy (for downstaging and/or before molecular testing was available) then surgery, can they be considered for adjuvant alectinib? The DAC recommends that these patients should be eligible to receive adjuvant alectinib. 2. Patients who already started/recently completed adjuvant chemotherapy (before funding is available), can they be offered adjuvant alectinib when funding becomes available?

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 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		
2. 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. OH-CCO provided secretariat support to the group in completing this submission.		
3. 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		
4. 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. Donna Maziak • Dr. Andrew Robinson • Dr. Peter Ellis • Dr. Stephanie Brule • Dr. Sara Kuruvilla • Dr. Natasha Leighl • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. Mihaela Mates*
Position	Member, OH (CCO) Lung Cancer Drug Advisory Committee
Date	*11-10-2024*

☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0350
Name of the drug and Indication(s)	Alectinib As adjuvant treatment following tumor resection for patients with anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (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
Please identify the specific text from the recommendation and provide a rationale for requesting a change in recommendation.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
Please provide details regarding the information that requires clarification.
b) Reimbursement conditions and related reasons
Please provide details regarding the information that requires clarification.
c) Implementation guidance
Please provide high-level details regarding the information that requires clarification. You can provide specific comments in the draft recommendation found in the next section. Additional implementation questions can be raised here.

- In Table 2, PAG suggested removing "other" in the sentence: "pERC agreed with the clinical experts, noting that retreatment with **other** *ALK* inhibitors may be considered for patients who experience disease recurrence 6 months or longer after the last dose of adjuvant alectinib.", so that retreatment can be considered for either alectinib or other ALK inhibitors if recurrence happens 6 months or longer from adjuvant therapy.

Outstanding Implementation Issues

In the event of a positive draft recommendation, drug programs can request further implementation support from CADTH on topics that cannot be addressed in the reimbursement review (e.g., concerning other drugs, without sufficient evidence to support a recommendation, etc.). Note that outstanding implementation questions can also be posed to the expert committee in Feedback section 4c.

Algorithm and implementation questions
1. Please specify sequencing questions or issues that should be addressed by CADTH (oncology only)
1. An update to the algorithm is needed (rapid algorithm). 2.
2. Please specify other implementation questions or issues that should be addressed by CADTH
1. 2.
Support strategy
3. Do you have any preferences or suggestions on how CADTH should address these issues?
May include implementation advice panel, evidence review, provisional algorithm (oncology), etc.

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0350
Brand name (generic)	ALECENSARO (alectinib)
Indication(s)	For adjuvant treatment following tumour resection for patients with stage IB (tumour ≥ 4 cm) – IIIA ALK-positive 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	☐

Roche agrees with the draft recommendation.

Rationale: Alectinib offers clinically meaningful improvements in median disease-free survival for patients with resectable ALK-positive NSCLC. It is a much needed treatment that dramatically improves over the current standard of care in Canada, all while being cost effective at traditional willingness-to-pay thresholds.

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	☐

Yes, in general, the recommendation demonstrates that the committee has considered the input Hoffmann-La Roche Limited has provided to CADTH.

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

In general, reasons for the recommendation are fairly clear throughout the report. However, Roche would like to suggest some wording that may help to improve clarity even further.

Within the Rationale for Recommendation section, there is a potential lack of clarity around the importance of disease-free survival in resectable ALK-positive NSCLC patients, and the associated

benefit demonstrated with alectinib through the ALINA trial. Example instances where clarity can be improved include:

Page 3, Rationale for Recommendation, first sentence:

- The current wording in the recommendation never explicitly states the results of the ALINA trial are statistically significant and clinically meaningful
- Roche suggests changing the wording to: "*One phase III, open-label, randomized controlled trial (RCT; ALINA) demonstrated that adjuvant treatment with alectinib resulted in ~~added clinical~~* **a statistically significant and clinically meaningful** *benefit in the primary end point disease-free survival (DFS) compared to adjuvant platinum-based chemotherapy in adult patients who had complete resection of their histologically confirmed stage IB (tumour ≥ 4 cm) − stage IIIA ALK-positive NSCLC (stages as per AJCC 7th edition)*"

Page 3, Rationale for Recommendation, second paragraph on patient input:

- Context around OS in this setting is missing from this paragraph. While it is true patients wish to prolong life, the current wording around pERC's interpretation does not convey to a reader the important context (which is discussed under Page 5, Discussion Points, first bullet) where the setting of early disease is unlikely to have mature OS and DFS/CNS-DFS are considered clinically important
- Suggest modifying the paragraph to include wording that aligns with the Discussion Points Overall Survival bullet to provide additional clarity
- "*pERC concluded that alectinib may meet some of these needs, such as improving DFS and CNS-DFS. pERC was ~~uncertain~~* **unable to definitively conclude** *whether alectinib would prolong overall survival (OS) because there were only 2 (1.5%) deaths in the alectinib group and 4 (3.1%) deaths in the chemotherapy group as of the data cut-off date (median follow-up of 27.8 months;* X)." **However, pERC acknowledged alectinib is indicated for early-stage ALK-positive NSCLC; therefore, mature data for OS is unlikely to be available in this setting and outcomes such as DFS and CNS-DFS are considered clinically important**.

In addition, the wording in the final paragraph of the Rationale for Recommendation around cost-effectiveness is inconsistent with the conclusions from the Pharmacoeconomic Review Report. Using wording from CADTH's Pharmacoeconomic Review Report (pages 9 and 20), the following changes are suggested to the recommendation report:

Page 3, Rationale for Recommendation, final paragraph on cost-effectiveness: "*~~Alectinib might be cost-effective at a willingness-to-pay (WTP) threshold of $50,000 per QALY gained~~* **The CADTH base case results align with those of the sponsor's submitted analysis, indicating that alectinib is cost-effective at a willingness to pay (WTP) threshold of $50,000 per QALY gained, relative to CHT,** *for adult patients with completely resected stage IB (tumour size ≥ 4cm) to IIIA (according to the AJCC 7th edition) ALK-positive NSCLC. Price reductions ~~would~~* **may be required to** *decrease the uncertainty associated with this recommendation."*

Page 5, Discussion Points, final sentence under the Economic analysis bullet: "*pERC observed that while the base case ICER estimate remains below the $50,000 per QALY gained willingness-to-pay threshold,* **indicating alectinib is a cost-effective treatment,** *results from scenario analyses point to the need for a price reduction."*

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
Yes, the implementation issues have been clearly articulated and adequately addressed in the recommendation.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
Yes, in general, the reimbursement conditions are clearly stated and the rationale for the conditions are provided in the recommendation.		

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