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

CDA-AMC REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

pembrolizumab (Keytruda)

(Merck Canada Inc.)

Indication: Keytruda as monotherapy is indicated for the adjuvant treatment of adult patients with Stage IB (T2a greater than or equal to 4 cm), II, or IIIA NSCLC who have undergone complete resection and platinum-based chemotherapy.

January 16, 2025

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0369-000
Brand name (generic)	Keytruda (pembrolizumab)
Indication(s)	Keytruda as monotherapy for the adjuvant treatment of adult patients with Stage IB (T2a ≥ 4 cm), II, or IIIA NSCLC, and with PD-L1 tumor proportion score (TPS) < 50% who have undergone complete resection and platinum-based chemotherapy.
Organization	Lung Health Foundation Lung Cancer Canada Canadian Cancer Survivor Network
Contact information[a]	Riley Sanders, Lung Health Foundation [redacted] Winky Yau, Lung Cancer Canada [redacted] Lindsay Timm - Canadian Cancer Survivor Network [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 pembrolizumab is on behalf of Lung Health Foundation, Lung Cancer Canada and Canadian Cancer Survivor Network.

Lung Health Foundation, Lung Cancer Canada and Canadian Cancer Survivor Network patient groups thank pERC for the positive recommendation to reimburse Keytruda (pembrolizumab) as indicated for the adjuvant treatment of adult patients with Stage IB (T2a ≥ 4 cm), II, or IIIA NSCLC, and with PD-L1 tumor proportion score (TPS) < 50% who have undergone complete resection and platinum-based chemotherapy. We are grateful pERC took into consideration our patient input submission and the values we had discussed that are important to the lung cancer patient community.

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	Riley Sanders
Position	Senior Manager, Public Affairs Lung Health Foundation
Date	January 16, 2025
☒	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**
Merck	☐	☐	☐	☒
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

A. Patient Group Information	
Name	Winky Yau
Position	Coordinator, Medical Affairs Lung Cancer Canada
Date	January 16, 2025
☒	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**
Merck	☐	☐	☐	☒
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

A. Patient Group Information	
Name	Lindsay Timm
Position	Community Engagement Manager Canadian Cancer Survivor Network

Date	January 16, 2025
☒	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

7. 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.		
8. 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

3. 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

9. 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**
Merck	☐	☐	☐	☒
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0369
Brand name (generic)	Keytruda (pembrolizumab)
Indication(s)	as monotherapy is indicated for the adjuvant treatment of adult patients with Stage IB (T2a greater than or equal to 4 cm), II, or IIIA NSCLC who have undergone complete resection and platinum-based chemotherapy
Organization	Ontario Health (Cancer Care Ontario) Lung/Thoracic 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.

- Agree this should be relevant to the indicated patients, improved DFS/OS are key endpoints.
- Agree with the recommendation to reimburse. The recommendation seems to be somewhat quiet on the issue of EGFR/ALK patients. The Lung DAC noted there is potential harm (side effects without benefit) and the possibility that patients might get immunotherapy rather than targeted therapy with osimertinib or alectinib.
- This recommendation is limited to patients with tumors PD-L1 <50% due to the manufacturer's submission. As a result the CDA review was limited to the subgroup of patients and not the entire study population. The whole trial should have been reviewed and then a more independent decision could have been made about funding a sub population of the entire study versus the whole study population. This is particularly so as the Health Canada indication is not limited by PD-L1 expression. It speaks to methodology and the integrity of the primary study question.

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.

Re: Table 2

Table 2 second point says the patients eligible to receive adjuvant pembrolizumab include patients planned for adjuvant chemotherapy or adjuvant radiation. Further down in the same box it says patients undergoing neoadjuvant or adjuvant radiation would not be eligible. This needs to be corrected. Excluding patients with adjuvant radiation reflects outdated information in the product monograph. There is safety data to give pembrolizumab either concurrent with radiation, or post chemoradiation in NSCLC. There is no sound rationale to exclude them from the trial. Few patients receive adjuvant radiation now (that have an R0 resection), they should have access.

The issue of patients with involved margins is a little more challenging as these are no longer R0 resections and that is part of the approval process. There should be an option for these requests to be reviewed and approved or not on a one on one basis

Re: the question about patients relapsing and eligibility for subsequent IO. This should have the same wording as other recommendations i.e. if a patient relapses more than 6 months post completion of adjuvant pembrolizumab they would remain eligible for first-line treatment options for recurrent NSCLC

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.

See comments in #1 and #4

Re: Table 1

The Lung DAC noted the following patients should not be excluded - patients who had neoadjuvant or adjuvant RT for any reason if they did indeed go ahead and have a complete surgical resection and adjuvant chemo.

Re: the relevance of the $50,000/QALY figure in 2025 - the number is outdated and never been adjusted for inflation.

[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. OH-CCO PDRP provided secretariat function to the group.		
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. Donna Maziak • Dr. Stephanie Brule • Dr. Peter Ellis • Dr. Mihaela Mates		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. Andrew Robinson*
Position	*Member, Ontario Health (Cancer Care Ontario) Lung/Thoracic Cancer Drug Advisory Committee*
Date	*02-01-2025*
☒	**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**

Merck	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Dr. Natasha Leighl*
Position	*Member, Ontario Health (Cancer Care Ontario) Lung/Thoracic Cancer Drug Advisory Committee*
Date	*14-01-2025*
☒	**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**
Merck	☒	☐	☐	☐
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**			
	$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 4	
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 5	
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	☐	☐	☐	☐

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0369-000
Name of the drug and Indication(s)	pembrolizumab (Keytruda) as monotherapy is indicated for the adjuvant treatment of adult patients with Stage IB (T2a greater than or equal to 4 cm), II, or IIIA NSCLC who have undergone complete resection and platinum-based chemotherapy
Organization Providing Feedback	Provincial Advisory Group (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.

In Table 1 under Initiation, PAG suggested an editorial revision: “All patients included **in** the reimbursement request population had received adjuvant chemotherapy.”

In Table 1 under Initiation (1.2), PAG suggested adding the AJCC edition following “Stage IB (T2a ≥ 4 cm), II, or IIIA NSCLC” for consistency with other recommendations.

Under Discussion Points, PAG suggested omitting the word “by” in the sentence: “[pERC] noted that although subgroup analyses **by** were prespecified…”
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 under Considerations for discontinuation of therapy, PAG suggested only keeping the treatment duration (e.g., 1 year) and omitting the number of doses as they vary based on treatment cadence/schedule. In Table 2, under considerations for Initiation of therapy (under pembrolizumab re-treatment), PAG suggested that the following sentence should include “pembrolizumab in combination with pemetrexed/platinum for patients with non-squamous disease, and with chemotherapy for those with squamous disease”: “patients in the incurable setting can receive up to 2 years of **pembrolizumab**”. PAG noted that stage IV single-agent pembrolizumab is currently only funded for PD-L1 TPS equal to or greater than 50. In the report, under Clinical evidence, PAG would like to confirm the drug under review was used every 3 or 6 weeks in the clinical trial as the current paragraph includes both dosing schedules.

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. A rapid algorithm is needed. 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.