



**pan-Canadian Oncology Drug Review
Stakeholder Feedback on a pCODR Expert
Review Committee Initial Recommendation
(Patient Advocacy Group)**

**Pembrolizumab (Keytruda) for Squamous Non-
Small Cell Lung Cancer**

Lung Cancer Canada

January 3, 2020

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	For the treatment of patients with metastatic squamous NSCLC in combination with carboplatin and either paclitaxel or nab-paclitaxel, in adults with no prior systemic chemotherapy treatment for metastatic NSCLC
Eligible Stakeholder Role in Review (Sponsor and/or Manufacturer, Patient Group, Clinical Organization Providing Feedback)	Patient Group _____ Lung Cancer 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

The decision by pERC to provide a negative recommendation for the treatment of patients with metastatic squamous non-small cell lung cancer (NSCLC) in combination with carboplatin and either paclitaxel or nab-paclitaxel, in adults with no prior systemic chemotherapy treatment for metastatic NSCLC was a surprise to Lung Cancer Canada and the lung cancer community, and we feel strongly that this recommendation should be reconsidered as this is a group with a high unmet need and very few treatment options.

1. Lung cancer is the leading killer of all cancers in Canada, with a 5-year net survival of 19%. Squamous (NSCLC) account for approximately 25 to 30% of all lung cancers. It is an aggressive form of lung cancer and is associated with a shorter survival compared to non-squamous NSCLC of even lower than 19%. The standard first-line therapy is platinum-based chemotherapy or pembrolizumab (for patients with programmed death ligand 1 [PD-L1] expression on $\geq 50\%$ of tumor cells, of which a majority of this group of patients do not have). Only a very small

number of these patients are able to be treated with pembrolizumab. Squamous NSCLC patients are at a disadvantage due to the following:

- Have no targetable mutations and thus no targeted therapy treatments. This is unlike non-squamous NSCLC patients who also have targeted mutations and more treatment options.
 - Have limited treatment options, majority of which only get chemotherapy.
 - Are a population with a high-unmet need.
2. pERC provided a negative recommendation based on an inability to establish long term benefits due to the duration of the follow-up from the KEYNOTE407 clinical trial. The median follow up for this treatment was 7.8 months before it was stopped, while non-squamous NSCLC that had a median follow up of 10.5 months received a positive recommendation. Also of note is a recent update at ESMO showing a median follow up of 14.3 months.
 3. It should be noted that the KEYNOTE407 was a Phase 3, double blind, randomized trial. pCODR has criticized the use of Phase 2 single arm studies, so why would you not recommend a treatment that had results from a trial that is considered the gold standard.
 4. The results from the trial showed benefits in overall survival (OS) and progression free survival (PFS), and risk of death was lowered by 36%. These improvements, pERC noted, align with patients values, so why shouldn't this group of patients particularly a group who are at a disadvantage in terms of treatment options not be given access to a viable treatment option.
 5. Even previous submissions with equal or lower hazard ratios have been given positive recommendations. Where is the equity in that, and why the inconsistency in giving positive recommendations.
 6. These patients cannot afford to wait for a resubmission. The data is already here, available and strong. These patients just don't have the time, so why should they be made to wait. They need access to this treatment now.

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

- agrees agrees in part disagree

The best clinical practice dictates that patients should be able to benefit from current and future advances and innovations in cancer treatment.

- 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

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.

- | | | | |
|--------------------------|---|-------------------------------------|--|
| <input type="checkbox"/> | Support conversion to Final Recommendation.
Recommendation does not require reconsideration by pERC. | <input checked="" type="checkbox"/> | Do not support conversion to Final Recommendation.
Recommendation should be reconsidered by pERC. |
|--------------------------|---|-------------------------------------|--|

The typical treatment for squamous NSCLC patients is chemotherapy and in few cases immunotherapy. The KEYNOTE407 trial has shown that the addition of pembrolizumab to chemotherapy resulted in improved overall survival and progression-free survival for patients. This is a meaningful benefit, especially for patients who do not have time or other viable options.

These patients are quite sick, so why do we wait when we can improve their lives now.

LCC asks pERC to reconsider their recommendation for this group of patients as it offers them the chance to live, and live longer, and this aligns with patient values.

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 be 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 Sponsor 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 Sponsor 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.



**pan-Canadian Oncology Drug Review
Stakeholder Feedback on a pCODR Expert
Review Committee Initial Recommendation
(Patient Advocacy Group)**

**Pembrolizumab (Keytruda) for Squamous Non-
Small Cell Lung Cancer**

Ontario Lung Association

January 3, 2020

Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s): Pembrolizumab (Keytruda)/ Squamous Non-Small Cell Lung Cancer

Eligible Stakeholder Role in Review (Sponsor and/or Manufacturer, Patient Group, Clinical Organization Providing Feedback) Patient Group

Ontario Lung Association

**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

Choice is of the utmost priority for patients. They would like greater treatment options to consider and choose from, and many indicate they would be willing to try additional and / or combination treatments if the adverse effects were no worse than what they were currently experiencing. The ability to function on a day-to-day basis and experience some real quality of life is so very important to the patients we work with - they would like to be well enough to enjoy time with family and friends for whatever time they may have left.

Cost of medications has been an ongoing theme that continually comes up in our discussion with patients about possible treatments. Many are on limited incomes and would like available treatments to be less expensive or at no cost to them.

Multiple appointments, delays in accurate diagnosis and therefore delays in accessing treatments, combined with what they describe as limited treatment options, really speaks to the need for movement in our health care system towards increasing available and affordable options for treating patients living with lung cancer.

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

agrees agrees in part disagree

The Ontario Lung Association disagrees with the provisional algorithm. The pERC recommendation acknowledges: (1)the observed short-term benefits (overall survival (OS) and progression-free survival (PFS)) of this treatment, (2)that this treatment option offers this improvement in short-term OS with no detriment in quality of life, and (3)this treatment aligns with patient values in that it provides another treatment option with no negative impact on quality of life.

However, the recommendation goes on to state that long-term benefit could not be established due to the short duration of follow up (7.8 months).

This disease is aggressive and patients should have access to all innovative therapies and treatments that could prove beneficial to them at a reduced cost or no cost basis.

There is a desire for more respiratory and lung cancer specialists and a better coordinated health system. Patients would like the ability to do treatments at home, removing the need for the patient or the caregiver to take time off of work. This would also lead to less disruption of the daily routine. Quality of life, not just extension of life, is a theme that continually came through from patients.

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
			Editorially, the Initial Recommendation is clear.

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.

- | | | | |
|--------------------------|---|-------------------------------------|--|
| <input type="checkbox"/> | Support conversion to Final Recommendation.
Recommendation does not require reconsideration by pERC. | <input checked="" type="checkbox"/> | 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	pERC Recommendation	Paragraph 2 Lines 5-11	There is an unmet need for cost-effective advancements in treatment options for patients living with Squamous Non-Small Cell Lung Cancer. Patients have shared with us that they are willing to try new medications and combinations but also have acknowledged cost as a significant barrier due to low income. We have received feedback from multiple patients who have stressed the importance of both new and affordable treatment options.

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 rationale 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 be 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 Sponsor 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 Sponsor 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.