pan-Canadian Oncology Drug Review

Registered Clinician Feedback on a pCODR Expert Review Committee Initial Recommendation

Pembrolizumab (Keytruda) for Non-Small Cell Lung Cancer

November 3, 2016

1 Feedback on pERC Initial Recommendation

Name of the drug indication(s):	Pembrolizumab
Name of registered clinician(s):	Dr. Rosalyn Juergens; Dr. Quincy Chu; Dr. Nicole Bouchard; Dr. Diane Ionescue; Dr. Natasha Leighl; Dr. Jeff Rothenstein; Dr. Paul Wheatley-Price

**pCODR may contact this person if comments require clarification. Contact information will not be included in any public posting of this document by pCODR.*

3.1 Comments on the Initial Recommendation

a) Please indicate if the registered clinician(s) agrees or disagrees with the initial recommendation:

____ agrees __X__ agrees in part ____ disagree

Please explain why the registered clinician(s) agrees, agrees in part or disagrees with the initial recommendation.
Please see below:

b) Notwithstanding the feedback provided in part a) above, please indicate if the registered clinician(s) would support this initial recommendation proceeding to final pERC recommendation ("early conversion"), which would occur within 2(two) business days of the end of the consultation period.

____ Support conversion to final recommendation.	__X__ Do not support conversion to final recommendation.
Recommendation does not require reconsideration by pERC.	Recommendation should be reconsidered by pERC.

c) Please provide feedback on the initial recommendation. Is the initial recommendation or are the components of the recommendation (e.g., clinical and economic evidence) clearly worded? Is the intent clear? Are the reasons clear?

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
		Pg 3. Potential Next Steps for Stakeholders. Initial Recommendation	Lung Cancer Canada agrees with the general recommendation but believes there are many questions related to the duration of treatment to consider.

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
			This recommendation supports funding up to two years or disease progression, depending on which occurs first. This is consistent with the data presented in Keynote 010[1]. However there are several areas where the evidence is unclear/further exploration can be made. 1) Definition of Progression. LCC agrees with the PERC decision to allow for treatment beyond RECIST parameters. Progression demonstrated through a confirmatory scan conducted four to six weeks after initial progression will allow patients who experience pseudo-progression ability to continue to derive benefit from the drug. (Pg. 8, first paragraph of Initial Recommendation Report.) 2) LCC agrees with the PAG group that more clarity is needed on optimal dosing, treatment duration and treatment discontinuation. (Clinical Guidance Report, Pg. 32; 4.3 and 4.4)
			3) **Evidence Generation to Understand Optimal Duration of Therapy** pERC noted that pembrolizumab is approved at a dose of 2 mg/kg administered intravenously over 30 minutes every three weeks until confirmed disease progression, unacceptable toxicity, or a maximum of two years (in the case of KN010) whichever comes first. There is currently no evidence to identify an optimal set or fixed duration of treatment with pembrolizumab and pERC agreed that it is important to prospectively collect such data. The Committee also agreed that treatment duration should be reassessed in the event that new evidence emerges on an optimal duration of treatment. Optimal duration of treatment is still a question that is being actively investigate and LCC agrees that duration of treatment should be reassessed once new evidence emerges. However LCC notes that, short of a new pCODR-CADTH submission. there is currently no mechanism within the pCODR-CADTH process that allows for reassessment of recommendations. This means that patients that are responding and continue to derive benefit from pembrolizumab can lose coverage at two years even if new evidence emerges to support continued treatment. Hence, in absence of a mechanism for reassessment and the deadly potential risk to patient outcomes, LCC suggests that

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			the funding recommendation be amended to allow physicians to use clinical judgement on this issue consistent with evolving evidence. In addition, this recommendation does not take into account those who relapse/progress after stopping pembrolizumab due to a) a complete response, or b) after two years. The trial protocols, including Keynote 010[1] allow for re-treatment using pembrolizumab in these cases and data suggests that patients are able to derive benefit. LCC feels that this allowance should be added to the recommendation.

Ref.

1. Lancet. 2016 Apr 9;387(10027):1540-50. doi: 10.1016/S0140-6736(15)01281-7. Epub 2015 Dec 19.

About Completing This Template

- The following template form should be used by the registered clinician(s) to submit input at the beginning of a drug review. Please note that there is a separate template for providing feedback on an initial recommendation.

- The clinician(s) **must be registered with the pCODR program** to provide input. (See https://www.cadth.ca/pcodr/registration for information on eligibility and registration.)

- The registered clinician(s) must also complete the *pCODR Clinician Conflict of Interest Declarations Template* when providing input at the beginning of a drug review (see Appendix A of this document). While CADTH encourages collaboration among registered clinicians and that feedback submitted for a specific drug or indication be made jointly, each registered clinician must complete their own separate *pCODR Clinician Conflict of Interest Declarations Template*.

- Please ensure that the input is in English, and that it is succinct and clear. Please use a minimum 11-point font and do not exceed six (6) typed, 8 ½" by 11" pages. If a submission exceeds six pages, only the first six will be considered.

- The registered clinician(s) 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. Similarly, the registered clinician(s) should not feel restricted by the space allotted on the form and can expand the tables in the template as required. The categories and questions outlined are only examples, to guide identification of relevant clinical factors for pERC's consideration. Please note that comments may be attributed to a specific individual clinician and that registered clinicians who submit input will be identified as a contributor to the specific input. CADTH's pCODR program maintains the discretion to remove any information that may be out of scope of the review.

- It is important to note that scientific published references are not required, as pCODR has access to current scientific literature through the manufacturer's submission, tumour groups, and a rigorous, independent literature search.

- The registered clinician(s) must be submitted by the **deadline date** for this drug, posted on the pCODR section of the CADTH website under *Find a Review* so that it can be available in time to be fully used in the pCODR review process. If more than one submission is made by the same registered clinician(s), only the first submission will be considered.

- In addition to its use in the pCODR process, the information provided in this submission may be shared with the provincial and territorial ministries of health and Provincial cancer agencies that participate in pCODR, to use in their decision-making.

Should you have any questions about completing this form, please email submissions@pcodr.ca