CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

LENVATINIB AND PEMBROLIZUMAB (Lenvima and Keytruda)

(Eisai Limited)

Indication: Treatment of adult patients with advanced (not amenable to curative surgery or radiation) or metastatic RCC with no prior systemic therapy for metastatic RCC.

June 9, 2022

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0268-000
Brand name (generic)	Lenvatinib and pembrolizumab (Lenvima and Keytruda)
Indication(s)	Lenvatinib, in combination with pembrolizumab, for the treatment of adult patients with advanced or metastatic RCC with no prior systemic therapy for metastatic RCC
Organization	Ontario Health (CCO) Genitourinary Cancer Drug Advisory Committee
Contact information[a]	Name: Dr. Girish Kulkarni

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

The DAC agrees that the recommendations are all very reasonable. The DAC would like to point out that the last point of Table 1 about the budget impact is a little out of context. Although it's estimated to have a significant budget impact, it should not lead to a significantly higher budget impact than all TKI/VEGFR funded indications combined. These patients will come from patients who would ordinarily be given axi/pembro (and a few ipi/nivo although probably not that many) and that means that the total money spent on first line treatment should change very little if pricing is the same or better than the other funded regimens. We're not likely to treat more patients than we previously did or currently do.

The DAC agrees that beyond differences of pricing for Lenva vs Axi, big picture these patients would likely come within the same bucket of current / anticipated IO/VEGF-TKI starts anyways, as opposed to unearthing new Ontarians who would not have been eligible for currently approved therapies. Additionally, it seems like the longer time on therapy / longer PFS for this new combo Len/Pem (vs Axi/Pem) in registration trial has been considered to some extent in the recommendation

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	☒
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	☐
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. Girish Kulkarni • Dr. Sebastien Hotte • Dr. Aly-Khan Lalani		

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0268
Name of the drug and Indication(s)	Lenvatinib and pembrolizumab for mRCC
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
None

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
In Table 2: Summary of Drug Plan Input and Clinical Expert Response, under considerations for initiation therapy, third row, in the following sentence, *"pERC considered that it would be reasonable to re-administer pembrolizumab (up to 17 additional cycles), with or without lenvatinib,"* PAG is requesting the removal of the text "with or" for consistency with the previous pERC recommendation on pembrolizumab in combination with axitinib.
b) Reimbursement conditions and related reasons
None.
c) Implementation guidance
None

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0268-000
Brand name (generic)	LENVIMA® (lenvatinib)
Indication(s)	In combination with KEYTRUDA® (pembrolizumab), for the treatment of adult patients with advanced (not amenable to curative surgery or radiation) or metastatic renal cell carcinoma (RCC) with no prior systemic therapy for metastatic RCC
Organization	Eisai Limited
Contact information[a]	[redacted]

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

Eisai Limited (Eisai) agrees with the committee's recommendation that lenvatinib combined with pembrolizumab (LEN+PEM) be reimbursed for the treatment of adult patients with advanced (not amenable to curative surgery or radiation) or metastatic RCC who have had no prior systemic therapy for metastatic disease.

As noted on pg. 7 of the recommendation, clinician experts consulted during the review considered prolonged overall survival (OS), progression free survival (PFS), reduction in metastatic lesions (ORR) and improved quality of life as the most important treatment goals. Similarly, it was noted on pg. 3 of the recommendation that patients identified a need to reduce or control disease, improve survival in advanced disease, reduce cancer symptoms, enhance health-related quality of life (HRQoL), as well as avoid deleterious side effects. The committee "concluded that LEN+PEM met some of the needs identified by patients by delaying disease progression, potentially improving overall survival, and potentially maintaining or improving (HRQoL)" (pg. 3, 3rd paragraph), as LEN+PEM demonstrated:

- The longest median progression-free survival (PFS) observed to date in first-line RCC.
- Superior overall survival (OS) compared with sunitinib.
- The highest objective and complete response (CR) rates with the lowest rates of progressive disease in first-line RCC.
- Manageable adverse events consistent with the known safety profile for each individual agent.
- Similar or improved HRQoL and disease-related symptom scores, supporting tolerability compared with sunitinib.

Of relevance, the committee also highlighted that "evidence from indirect treatment comparisons (ITC) suggested that LEN+PEM results in similar or potentially better PFS benefits compared with other combination therapies such as axitinib plus pembrolizumab (AXI+PEM) or ipilimumab plus nivolumab" (pg. 3, 2nd paragraph), with AXI+PEM being the most relevant comparator (pg. 5, 3rd bullet).

Eisai is not requesting a reconsideration of this recommendation, and as such, supports conversion of the draft recommendation to the final recommendation. Furthermore, Eisai is committed to working with the CADTH-participating plans to facilitate access to LEN+PEM in a timely manner.

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	☒
While Eisai agrees with the overall recommendation and associated reimbursement conditions, Eisai is suggesting one editorial change: the removal of the last discussion point on pg. 5. This bullet explains that, although the drug cost of LEN+PEM is lower than the drug cost of AXI+PEM, a price reduction is advised for LEN+PEM because of the longer treatment duration driven by the longer PFS with LEN+PEM. However, pERC's recommendation that there is insufficient evidence to justify a cost premium for LEN+PEM over the least expensive immunotherapy/TKI combination (top of pg. 5) is based on the premise that LEN+PEM results in similar or potentially better PFS compared to AXI+PEM, implying that PFS, and therefore treatment duration, should be similar between LEN+PEM and AXI+PEM in the real-world. Eisai believes that there is inconsistency between this point and the reimbursement condition. Therefore, Eisai respectfully suggests removing the last discussion point on pg. 5 altogether.		

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