CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

enfortumab vedotin (Padcev)

(Seagen Canada Inc.)

Indication: In combination with pembrolizumab, is indicated for the treatment of adult patients with unresectable locally advanced or metastatic urothelial cancer (mUC) with no prior systemic therapy for mUC.

November 15, 2024

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CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0353
Brand name (generic)	Padcev (Enfortumab vedotin)
Indication(s)	Enfortumab vedotin In combination with pembrolizumab, for the treatment of adult patients with unresectable locally advanced or metastatic urothelial cancer (mUC) with no prior systemic therapy for mUC.
Organization	OH (CCO) Genitourinary Cancers Drug Advisory Committee (GU DAC)
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 GU DAC agrees with the recommendation to fund but disagrees with certain aspects of the report. The GU DAC would like to request the following revisions:

Table 1 - Reimbursement conditions

- 2.1 & 2.2 – change 12 months to ≥ 6 months post completion of adjuvant or neoadjuvant chemotherapy, to align with adjuvant nivolumab.
- 4.3 – add "systemic" (i.e., treatment should not be initiated in patients with prior "systemic EV or other MMAE-based ADCs"). There are ongoing phase I trials of EV that is given through bladder instillation; these patients should not be disadvantaged from receiving systemic EV-pembrolizumab.
- 5. Diagnostic imaging conducted "as per clinical practice" instead of mandating every 2 to 3 months, as imaging may not be readily available in some areas.
- 8. Suggest clarifying that EV-pembrolizumab should not be used in combination with other anticancer drugs "in routine clinical practice" to allow for flexibility when funded standard of care drugs are used in combination with investigational agents in a clinical trial setting.

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	☐

However, see #1 for suggested revisions by the GU DAC.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒

Table 2 – Responses to Questions from the Drug Programs

- Time-limited switch – the GU DAC disagrees with pERC's statement that time-limited switch be considered "only if [patients] have not started" platinum-based first line chemotherapy. Patients who had to start alternate first line chemotherapy should be given the opportunity to switch over to EV-pembrolizumab.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒
The GU DAC notes that EV should be continued if not discontinued due to disease progression.		

[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	☒
OH (CCO) provided a 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. Girish Kulkarni • Dr. Sebastien Hotte • Dr. Chris Morash		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. Akmal Ghafoor*
Position	*Member, Genitourinary Cancers Drug Advisory Committee*
Date	*11-November-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**
Janssen	☒	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Dr. Urban Emmenegger*
Position	*Member, Genitourinary Cancers Drug Advisory Committee*
Date	*12-November-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**
Merck	☐	☒	☐	☐

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0353
Name of the drug and Indication(s)	Enfortumab vedotin (Padcev) in combination with pembrolizumab for the treatment of adult patients with unresectable locally advanced or metastatic urothelial cancer with no prior systemic therapy.
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.

In table 1, under Renewal, PAG is concerned that the 2-3 months time frame may get incorporated into funding criteria when imaging wait times are already an issue. PAG recognized that pERC and the clinical experts share the same concerns as stated in Implementation guidance. PAG requests modification of the reimbursement condition to address this concern.

In table 1, under Discontinuation, PAG notes that enfortumab continues until progression or toxicity, but requests incor ‘up to a maximum of two years of pembrolizumab’. Under Discontinuation – Implementation advice, PAG reqeusts changing treatment duration to 2 years instead of 35 cycles as some physicians may choose every 6 week dosing. In table 1, under Prescribing, PAG requests less restrictive wording for the following sentence: “Enfortumab vedotin in combination with pembrolizumab should not be used in combination with other anti-cancer drugs for with locally advanced or metastatic urothelial cancer.” PAG is concerned that patients enrolled in clinical trials on enfortumab and pembrolizumab along with study drugs may not have access to the first two drugs based on this condition.
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 d) Eligibility to re-treatment, PAG would like to confirm whether pERC agrees with retreatment with pembrolizumab, with or without enfortumab, as long as there is no disease progression on either agent and no intolerable toxicity. In table 2, under Generalizability (a. Patients on active treatment with a time-limited opportunity to switch to the drug(s) under review), PAG would like to clarify whether patients currently receiving or who finished receiving platinum-based chemotherapy can be switched to/initiated on the drugs under review.

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 update to the algorithm is requested but should only be initiated in December. 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 Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0353-000
Brand name (generic)	PADCEV (enfortumab vedotin)
Indication(s)	In combination with pembrolizumab, for the treatment of adult patients with unresectable locally advanced or metastatic urothelial cancer with no prior systemic therapy for metastatic urothelial cancer.
Organization	Pfizer Canada ULC
Contact information[a]	Name: [redacted]

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

In general, Pfizer Canada ULC (Pfizer) agrees with CDA-AMC's draft recommendation for enfortumab vedotin, in combination with pembrolizumab (EV+P), for the treatment of adult patients with unresectable locally advanced or metastatic urothelial cancer with no prior systemic therapy for metastatic urothelial cancer.

Pfizer also recognizes the feedback received from clinicians and the patient group, which indicated that EV+P will become the de facto standard of care for incurable urothelial cancer and that patients strongly prioritize health outcomes and are willing to accept more significant side effects.

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	☐

Pfizer agrees that the committee has considered the submission and accompanying feedback provided for this file. Pfizer specifically agrees with the following:

- There is a significant unmet need for new therapies that increase survival with a manageable safety profile and maintain quality of life (QoL).
- EV+P is an effective treatment with the highest reported tumor response rate in incurable urothelial cancer. Compared to standard of care (SOC) treatment with platinum-based chemotherapy, EV+P nearly doubled median overall survival (OS) in Study EV-302 and demonstrated clinically meaningful benefit in progression-free survival (PFS) and objective response rate (ORR) with high certainty.
- The safety profile of EV+P is predictable, acceptable, and clinically manageable in most patients.
- ECOG should not be too prescriptive because adequate performance status should be based on clinical judgement.

Regarding the pharmacoeconomic evaluation, Pfizer respectfully reiterates the following:

- The log-logistic distribution to model OS and the generalized gamma distribution to model PFS are appropriate assumptions that avoid assuming that treatment effect wanes immediately after trial follow-up.

- The CDA-AMC approach to model treatment duration for EV+P adds bias in favour of SOC and overestimates the costs of EV+P.

Notwithstanding the above comments on the pharmacoeconomic review, Pfizer supports the conversion of the draft recommendation to a final recommendation to expedite access to EV+P for patients with unresectable locally advanced or metastatic urothelial cancer. Pfizer is committed to working with all jurisdictions via the pCPA process to ensure that patients have timely access to EV+P.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
Pfizer agrees that the reasons for the recommendation clearly stated.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
Pfizer agrees that 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	☐
Pfizer agrees that 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.