CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

ENFORTUMAB VEDOTIN (Padcev)

(Seagen Canada Inc.)

Indication: For the treatment of adult patients with unresectable locally advanced or metastatic urothelial cancer (mUC) who have previously received a platinum-containing chemotherapy and programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor therapy.

December 16, 2021

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0251
Brand name (generic)	Enfortumab Vedotin
Indication(s)	For the treatment of adult patients with unresectable locally advanced or metastatic urothelial cancer (mUC) who have previously received a platinum-containing chemotherapy and programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor therapy.
Organization	Clinicians Group/Medical Advisory Board, Bladder Cancer Canada
Contact information[a]	[redacted]

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.		

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 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		
2. 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.		
3. 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		
4. 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: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Samantha Gray*
Position	*Medical Oncologist, Horizon Health Network*
Date	*13-12-2021*
☒	**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**
Seagen – Advisory Board	☒	☐	☐	☐
Pfizer – Advisory Board	☒	☐	☐	☐
BMS – Advisory Board	☒	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Dr. Nimira Alimohamed*
Position	*Medical Oncologist, Tom Baker Cancer Centre, Alberta Health Services*
Date	*13-12-2021*
☒	**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**
Seagen – Advisory Board	☒	☐	☐	☐

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	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0251
Name of the drug and Indication(s)	Enfortumab vedotin for mUC
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 4 Summary of Economic Evaluation, in the “Treatment” row, PAG is suggesting adding the dosing information here as it would help to contextualize the per vial price to have the dosing schedule for the treatment nearby as follows *“1.25 mg/kg IV over 30 minutes on Days 1, 8, 15 every 28 days (maximum dose of 125 mg for patients >100 kg).”* In Table 4 Summary of Economic Evaluation, in the “Comparator” row PAG is requesting the following revision “A combined taxane comparator consisting of *either* docetaxel *or* paclitaxel.”
b) Reimbursement conditions and related reasons
None.

c) Implementation guidance
In Table 2 Implementation Guidance from pERC, under condition 1, PAG is requesting the statement be clarified as follows: “pERC was unable to make an informed recommendation on the use of enfortumab vedotin in patients who were not able not receive platinum-based chemotherapy due to comorbidities, or who may have received an alternate non-platinum-based chemotherapy regimen. However, there may be case-by-case exceptions made for patients who are not eligible for platinum-based chemotherapy. In this case, immunotherapy should be given first, followed by enfortumab vedotin.” In Table 2 Implementation Guidance from pERC, under condition 6, PAG noted the maximum dose of enfortumab vedotin is 125 mg (not 125 mg/kg).

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0251
Brand name (generic)	Enfortumab Vedotin
Indication(s)	For the treatment of adult patients with unresectable locally advanced or metastatic urothelial cancer (mUC) who have previously received a platinum-containing chemotherapy and programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor therapy.
Organization	Bladder Cancer Canada
Contact information[a]	[redacted]

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.		

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	*Michelle Colero*
Position	*Executive Director, Bladder Cancer Canada*
Date	*14/12/2021*
☒	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	☒
Eversana, (previously called Advocacy Solutions), experts in healthcare advocacy, provided best practices for data collection, consultation and discussions with our patient group.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☒
Eversana, (previously called Advocacy Solutions) collected the responses from our patient group and provided analysis on the results.		

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**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH SPONSOR FEEDBACK

PADCEV® (enfortumab vedotin)

Draft Recommendation

2000 ARGENTIA ROAD, PLAZA 3, SUITES 400, MISSISSAUGA, ON L5N 1V9 • TEL/TÉL: 833-944-6546 • www.seagen.com

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0251-000
Brand name (generic)	PADCEV (enfortumab vedotin)
Indication(s)	For the treatment of adult patients with unresectable locally advanced or metastatic urothelial cancer (mUC) who have previously received a platinum-containing chemotherapy and programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor therapy.
Organization	Seagen Canada Inc.
Contact information[a]	[redacted]

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

Seagen Canada Inc. (Seagen) agrees with CADTH's draft recommendation for enfortumab vedotin for the treatment of adult patients with unresectable locally advanced or metastatic urothelial cancer (mUC) who have previously received a platinum-containing chemotherapy and PD-1 or PD-L1 inhibitor therapy.

Seagen also recognizes the extensive feedback received from clinicians and patient advocacy groups. They have all indicated that the reimbursement of enfortumab vedotin would fulfill a significant unmet need for a new treatment that can extend survival in patients with unresectable locally advanced or metastatic urothelial cancer.

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	☐

Seagen fully agrees with the clinical considerations and patient-based values made by pERC while deliberating on enfortumab vedotin. Seagen specifically agrees with the following:

- There is a considerable unmet need in patients with unresectable locally advanced or metastatic urothelial cancer (UC) who have previously received chemotherapy and immunotherapy.
- Enfortumab vedotin provides an effective treatment in patients who have previously received platinum-based chemotherapy and PD-1 or PD-L1 inhibitors, that meets the needs identified by patients, including a need for treatments that halt disease progression and increase survival. Enfortumab vedotin was associated with a manageable toxicity profile.
- On a case-by-case basis, patients who are not eligible for platinum chemotherapy or have contraindications to immunotherapy could potentially be eligible for enfortumab vedotin.
- Furthermore, pERC recognized that selected patients with an ECOG PS of 2 could be considered for treatment with enfortumab vedotin, at the discretion of the treating physician.

Regarding the pharmacoeconomic evaluation, Seagen would like to comment on the conclusions reached by the CADTH reanalysis. Seagen respectfully reiterates the following:

- Disregarding the relative dose intensity as observed in EV-301 decouples dosing from efficacy and safety outcomes, introducing an assumption that there is no dose-dependent relationship between efficacy or safety outcomes and the mean dose administered.
- The Weibull distribution is the most appropriate survival extrapolation, which is well-supported by clinician input and long-term data from EV-201.

Please note that on page 14, the 28-day cost is stated as $19,491. This is incorrect and is based on suboptimal administration. Using a mean body weight of 74kg and the recommended dosage of 1.25mg/kg 3 times every 4 weeks, each administered dose is 92.5mg. The most optimized administration would be two 30mg vials and two 20mg vials, which corresponds to a cost of $5,906 per dose or **$17,718** per 28-day cycle.

Regarding the budget impact analysis, Seagen would like to comment on the conclusions reached by the CADTH reanalysis. Seagen respectfully reiterates the following:

- 100% relative dose intensity does not account for dose reductions or modifications, overestimating incurred drug costs.
- The optimal duration of avelumab maintenance is at least 2 years, and some patients will not be eligible for enfortumab vedotin until Year 3 or later in the BIA. The reanalysis assumes that a significant number of patients would immediately be eligible for enfortumab vedotin in the second-line setting in Year 1, overestimating the patient population.

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

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
Seagen is appreciative that the reasons for the recommendation are indeed clearly stated.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
Seagen agrees that the reasons for the implementation issues are indeed clearly stated.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
Seagen is once again appreciative that the reimbursement criteria for the recommendation and rationale are indeed clearly stated.		

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