CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

epcoritamab (Epkinly)

(AbbVie Corporation)

Indication: For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS), DLBCL transformed from indolent lymphoma, high grade B-cell lymphoma (HGBCL), primary mediastinal B-cell lymphoma (PMBCL) or follicular lymphoma Grade 3B (FLG3b) after two or more lines of systemic therapy and who have previously received or are unable to receive CAR-T cell therapy.

May 16, 2024

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0334-000-000
Brand name (generic)	epcoritamab (Epkinly)
Indication(s)	For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS), DLBCL transformed from indolent lymphoma, high grade B-cell lymphoma (HGBCL), primary mediastinal B-cell lymphoma (PMBCL) or follicular lymphoma Grade 3B (FLG3b) after two or more lines of systemic therapy and who have previously received or are unable to receive CAR-T cell therapy.
Organization	The Leukemia & Lymphoma Society of Canada (LLSC)
Contact information[a]	Name: Colleen McMillan [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
We agree that there is a currently unmet need within this patient population for additional treatments that result in longer disease remission and improved survival, disease symptom control, and improvement in HRQoL. There is a further need for easier access to new treatments that can be received closer to home and are aligned with patient's preferred treatment goals. epcoritamab may meet some of these needs including potentially extending disease remission and survival, as well as providing an alternative treatment that may be more tolerable for some patients in this setting compared with regimens that include the use of cytotoxic chemotherapy. We commend the committee for recommending that patients have access to a time limited options as this population is lacking available options right now.		

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	☐
We do believe that the committee has considered our input. We appreciate the committee's attention to our feedback, and we extend our gratitude for taking it into consideration. While we acknowledge this, we would encourage the committee, within future recommendations, to recognize the invaluable insights shared by patient groups, on behalf of patients and caregivers who possess firsthand experience with treatments under review. Patient organizations invest significant time and effort in engaging patients and caregivers, especially when Canadian experience with the treatment under review is limited or lacking. Integrating these voices directly into the committee's recommendations would not only be rewarding and encouraging for those who contribute but also enrich the decision-making process with real-world perspectives.		

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	*Colleen McMillan*
Position	*Advocacy Lead*
Date	*15-05-2024*
☒	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	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

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

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0334-000
Brand name (generic)	Epkinly (Epcoritamab)
Indication(s)	For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS), DLBCL transformed from indolent lymphoma, high grade B-cell lymphoma (HGBCL), primary mediastinal B-cell lymphoma (PMBCL) or follicular lymphoma Grade 3B (FLG3b) after two or more lines of systemic therapy and who have previously received or are unable to receive CAR-T cell therapy.
Organization	Lymphoma Canada
Contact information[a]	Name: Gurjot Basra [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.

We agree with the committee's overall recommendation that Epcoritimab be reimbursed (time limited). LBCL patients have expressed that it is important to them to have a choice of treatments that will be better tolerated and best suited to their personal clinical history, especially in the third line and beyond. From our survey data, patients who had undergone therapy with Epcoritamab experienced fewer side effects, primarily fatigue, headaches and diarrhea. Epcoritamab further offers the appealing advantage of subcutaneous administration, resulting in less time to be spent in hospitals per visit, which can improve the quality of life of patients and caregivers. Additionally, as there are many barriers in regards to access to CAR-T, Epcoritamab provides a feasible and viable option for patients as well.

The responses from patients who received treatment with Epcoritamab from our patient submission are highlighted below:

- "I would like to thank the researchers who developed this treatment"
- "Today I have practically no more pain"
- "was on treatment with Epcoritamab for 30 months, currently in complete remission"

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?

Yes, the committee has demonstrated that it has recognized the importance of the preferences of the surveyed patient population, namely that patients would like access to more options in the relapsed/refractory setting that allow them to live longer, with less symptoms and an improved quality of life.

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.

The reasons for the recommendations are clearly stated. However, reimbursement condition 5 stating that Epcoritamab should not be reimbursed when given in combination with other systemic anticancer drugs, may be limiting for patients as this can hinder the ability to tailer treatment plans to individual patient needs, compromising the chances of optimal outcomes. Instead, the decision for combination therapy should be left to the discretion of the treating clinician (hematologists or oncologists) with expertise in the management of LBCL.

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	☐

Most conditions have been listed clearly, however, condition 6 seems to suggest that despite Epcoritmab being a viable option for patients in third line and beyond, feasibility of adoption is solely dependent on the submitted price. We feel the feasibility of adoption should not be tied strictly to budgetary impacts and rather that the focus be on the manageable toxicity profile, improvement in QoL and prolonged response should take precedence.

[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	*Gurjot Basra*
Position	*Manager of Patient Programs, Research, and Advocacy*
Date	*May 14, 2024*
☒	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	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

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
AbbVie	☐	☐	☐	☒
Astra Zeneca	☐	☐	☐	☒
Gilead	☐	☐	☐	☒
Novartis	☐	☐	☒	☐
Roche	☐	☒	☐	☐
Incyte	☐	☐	☒	☐
BMS	☐	☐	☐	☒

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0334
Brand name (generic)	Epkinly (epcoritamab)
Indication(s)	For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS), DLBCL transformed from indolent lymphoma, high grade B-cell lymphoma (HGBCL), primary mediastinal B-cell lymphoma (PMBCL) or follicular lymphoma Grade 3B (FLG3b) after two or more lines of systemic therapy and who have previously received or are unable to receive CAR-T cell therapy.
Organization	OH (CCO) Hematology Drug Advisory Committee
Contact information[a]	Name: Dr. Tom Kouroukis

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. The DAC would not mandate imaging every 3 months if the patient is clinically doing well.		

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. The DAC believes there is no rationale to exclude patients with prior allogeneic stem cell transplant or solid organ transplant. Patients who have been treated with another bispecific agent should be eligible if that drug was to another target. This drug would be an option as a bridge to CAR-T.		
	Yes	☒

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	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. OH (CCO) provided a secretariat function to the group.		
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: • Dr. Tom Kouroukis • Dr. Pierre Villeneuve		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
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	

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0334
Name of the drug and Indication(s)	Epcoritamab for Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, DLBCL transformed from indolent lymphoma, high grade B-cell lymphoma, primary mediastinal B-cell lymphoma or follicular lymphoma Grade 3B after two or more lines of systemic therapy and who have previously received or are unable to receive CAR-T cell 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	☐
	No requested revisions	x

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.
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.

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. An update to the algorithm is needed (rapid algorithm) 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

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0334-000
Brand name (generic)	Epcoritamab
Indication(s)	For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS), DLBCL transformed from indolent lymphoma, high grade B-cell lymphoma (HGBCL), primary mediastinal B-cell lymphoma (PMBCL) or follicular lymphoma Grade 3B (FLG3b) after two or more lines of systemic therapy and who have previously received or are unable to receive CAR-T cell therapy.
Organization	AbbVie Corporation
Contact information[a]	[redacted]

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

Yes, AbbVie agrees with the positive draft recommendation.

Rationale: pERC recognized the ORR, CR, OS, PFS and DOR observed in the EPCORE-NHL-1 trial was compelling, durable, and clinically meaningful for patients. Epcoritamab is an innovative treatment option that leads to improved outcomes for R/R LBCL patients with a high unmet need. In addition, the convenience and efficiencies offered by subcutaneous administration of epcoritamab monotherapy in a disease area with primarily IV treatment alternatives was recognized.

Given the time-limited reimbursement recommendation, AbbVie is proud to commit to submitting phase 3, EPCORE-DLBCL-1 trial data once available to confirm 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	☐

Yes, the draft recommendation generally demonstrates that the committee has considered the input AbbVie has provided to CADTH.

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

Yes, the reimbursement conditions are clearly stated in general and the rationale for the conditions are provided in the recommendation. However, AbbVie has some feedback on the following:

Reimbursement Conditions and Reasons, Pricing Section in Table 1 (pg. 6)

CADTH has stated the following as a reimbursement condition: *"The ICER for epcoritamab is $120,435 per QALY gained when compared with rituximab based chemoimmunotherapy (costs informed by the R-GemOx regimen), in patients who had not previously received CAR-T therapy but did not include a post-progression benefit for patients who received epcoritamab. A price reduction of 60% would be required for epcoritamab to achieve an ICER of $50,000 per QALY gained compared to rituximab based chemoimmunotherapy (not including Pola-BR)."*

This is a scenarios analysis and is not aligned with the CADTH reanalysis base case stated in the Economic Evidence section (pg. 22) "*In the CADTH reanalysis comparing epcoritamab to R-CIT in patients who had not previously received CAR-T therapy, epcoritamab was more costly ($300,784 versus $150,374) and more effective (2.21 versus 0.50 QALYs), resulting in an ICER of $87,735 per QALY gained. A price reduction of approximately 45% is required for epcoritamab to be considered cost-effective at a $50,000 per QALY willingness-to-pay threshold."* Furthermore, this is not aligned with pERC's recommendation as part of the Pharmacoeconomic Review Report (pg. 9) dated March 28, 2024, where again CADTH notes "*A price reduction of approximately 45% is required for epcoritamab to be considered cost-effective at a $50,000 per QALY willingness-to-pay threshold*".

AbbVie requests the conditions table to be updated with the base case price reduction as stated in the Economic Evidence section of the Draft Recommendations, as well as in the Pharmacoeconomic Review Report.

Economic Evidence Section, Key Limitations (pg. 22)
CADTH states that Pola-BR has restricted funding status across Canada. However, based on listing criteria in public formularies, Pola-BR is generally funded in line with the Health Canada approved indication across CADTH jurisdictions. Further clarification is required on "restricted funding status".

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