CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

LISOCABTAGENE MARALEUCEL (Breyanzi)

(Celgene Inc., a Bristol Myers Squibb company)

Indication: For the treatment of adult patients with relapsed or refractory (R/R) large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma (PMBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.lymphoma, primary mediastinal large B-cell lymphoma (PMBCL), and follicular lymphoma grade 3B (FL3B) after at least 2 prior therapies.

June 16, 2022

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0258-000
Brand name (generic)	Lisocabtagene maraleucel (Breyanzi)
Indication(s)	For the treatment of adult patients with relapsed or refractory (R/R) large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma (PMBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.
Organization	Ontario Health (CCO) Hematology Cancer 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	☐
The Hematology DAC feels that lis-cel use should align with the clinical trial inclusion criteria (ie, follicular lymphoma grade 3B (FL3B) and secondary CNS).		

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. Tom Kouroukis		

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0258
Name of the drug and Indication(s)	Lisocabtagene maraleucel for RR DLBCL
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
None

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
None
b) Reimbursement conditions and related reasons
None
c) Implementation guidance
None

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0258-000
Brand name (generic)	Breyanzi (lisocabtagene maraleucel)
Indication(s)	For the treatment of adult patients with relapsed or refractory (R/R) large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma (PMBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.lymphoma, primary mediastinal large B-cell lymphoma (PMBCL), and follicular lymphoma grade 3B (FL3B) after at least 2 prior therapies.
Organization	Lymphoma Canada
Contact information[a]	Name: Antonella Rizza

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
Yes, Lymphoma Canada agrees with CADTH's recommendation for liso-cel for this indication. Liso-cel provides an additional treatment option to patients with LBCL that aligns with patient preferences of improved quality of life, longer survival and longer remission and choice in treatment options. Further the availability of liso-cel would prevent unnecessary delays in treatment caused by short supply of existing CAR-T cell therapies.		

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, according to the rationale for the recommendation our patient group submission was considered particularly when highlighting the following: -Patients identified a need for treatment options that provide better survival and response outcomes, with better health-related quality of life, and les toxicity. -Patients are seeking improved access to CAR-T therapies, which is currently limited. -liso-cel may meet some of the needs identified by patients by providing an effective alternative option		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
Yes, the reasons are clearly stated.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒
No. Although pERC acknowledges and articulates that the availability of accredited centres in Canada is a barrier that should be considered, the issue of equitable access to CAR-T is not		

addressed further. Lymphoma Canada recommends that CAR-T therapy should be available equitably across all provinces so as to avoid the challenges facing an already immunocompromised population. As noted in the Access and Financial Impacts to Treatment in Canada section of our original submission, patients articulated the following challenges:

"*Travel time, required ferry ride, extra hotel stays and time away from home and children"*

"*"I likely need car T-cell therapy next and will need to travel to another province since BC does not currently offer it"*

"At this point I've have full access to treatment, however, my next relapse I would like to have full access to CAR-T in my community and covered by OHIP, which at this point that I know - it isn't"

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

Yes, Table 1 "Reimbursement Conditions and Reasons" clearly states this information. However, under the Prescribing Section (Implementation Guidance) of Table 1, Lymphoma Canada recommends that additional guidance be provided on eliminating barriers to access for those patients whom are eligible for the treatment but for whom travel, family and financial considerations are important variables patients must factor into a decision for treatment if they have to leave their home province to receive CAR-T therapy.

[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	*Antonella Rizza*
Position	*CEO*
Date	*June 15, 2022*
☒	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 Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0258
Brand name (generic)	Breyanzi (lisocabtagene maraleucel)
Indication(s)	For the treatment of adult patients with relapsed or refractory (R/R) large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma (PMBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.
Organization	Celgene Inc., a Bristol Myers Squibb Company
Contact information[a]	[redacted]

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

The stakeholder agrees with the draft recommendation and the specific rationale provided:
"Overall, survival and response endpoints were deemed meaningful by clinical experts compared to expected outcomes in patients with DLBCL not using a CAR T-cell treatment in the third line setting." (p.3/19 - Rationale for the Recommendation - 1st paragraph) and
"Given the totality of the evidence, pERC concluded that liso-cel may meet some of the needs identified by patients and clinicians when compared to similar CAR T-cell therapies approved for use in Canada, namely by providing an effective alternative option with a potentially different safety profile for most relapsed or refractory LBCL patients." (p.3/19 - Rationale for the Recommendation - 2nd paragraph)

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	☐

The recommendation has in very large part considered the stakeholder input provided to CADTH.

The summary section on the CADTH reanalysis of the PE results would, however, have benefited from increased transparency and comprehensiveness to allow external readers to properly assess and understand the range of ICERs scenarios considered by CADTH.

The section states:

- "CADTH undertook a series of exploratory analyses which indicated that the results of the model are highly sensitive to assumptions regarding pre-treatment, comparative efficacy and safety, and health state utility values. In these exploratory analyses, the ICERs for liso-cel ranged from $115,000 per QALY to more than $13M per QALY.
- There was also a scenario in which liso-cel was not on the cost-effectiveness frontier (i.e., more costly and same or fewer QALYs as other CAR-T therapies)." (p.17/19 - Table 2: Summary of Economic Evaluation - Last row in the table - CADTH reanalyses results).

This summary statement focuses on a minority of scenarios and does not reflect the range of results generated by CADTH's own reanalyses scenarios. More specifically, it does not consider that in some of these same scenarios, one of the CAR Ts, including liso-cel, dominated one or both of the other CAR-T therapies. The ICERs for liso-cel compared to salvage chemotherapy ranged from $115,771 per QALY to $151,117 per QALY. Depending on whether efficacy and safety advantages were assumed or not, the range of ICERs compared to tisa-cel varied from tisa-cel being dominated to liso-cel being dominated. The range of ICERs compared to axi-cel also varied from axi-cel being dominated to liso-cel being dominated. Out of the 10 scenarios tested, in one scenario the ICER was $13M per QALY, explained by almost no QALY difference over tisa-cel. There was also one scenario in which liso-cel was not on the cost-effectiveness frontier (i.e., more costly and same or fewer QALYs as other CAR-T therapies) and two scenarios in which liso-cel dominated over both other CAR-T therapies."

As done in other HTA recommendations, presenting the results of the probabilistic sensitivity analyses (PSA) using a scatter plot of the cost-effectiveness plane would have been useful to quickly visualize the distribution of the PSA results.

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	☐
The stakeholder agrees with the committee's recommendation that "Liso-cel should be reimbursed in patients with secondary CNS involvement as long as they fulfill all other criteria". (p.4/19 - Table 1. Reimbursement Conditions and Reasons - 4th bullet point).		

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