CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

axicabtagene ciloleucel (Yescarta)

(Gilead Sciences Canada Inc.)

Indication: Diffuse large B-cell lymphoma (DLBCL) or high-grade B-cell lymphoma (HGBL)

January 19, 2023

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0293-000
Brand name (generic)	Yescarta (Axicabtagene ciloleucel)
Indication(s)	For the treatment of adult patients with diffuse large B-cell lymphoma (DLBCL) or high-grade B-cell lymphoma (HGBL) that is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy.
Organization	Ontario Health (Cancer Care Ontario) 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	☐
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. (Table 2) Re: Generalizability Patients anywhere along the course of moving toward ASCT should be considered to switch to CAR-T provided all other criteria are met.		
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.

Re: Feasibility of adoption

- Incremental budget impact of axi-cel was stated to be expected to be >$40 million in all 3 years. The Hematology DAC wanted to seek clarification on the $ figure under Budget Impact (page 15) and whether the “three-year total of $347,640,982” represents an incremental budget impact.

[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	☒
If yes, please detail the help and who provided it. OH-CCO provided secretariat support 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, Dr. Jordan Herst		

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	

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	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
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	☐	☐	☐	☐

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	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
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	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
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			
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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	PG0293-000
Brand name (generic)	Yescarta (axicabtagene ciloleucel)
Indication(s)	Diffuse large B-cell lymphoma (DLBCL) or high-grade B-cell lymphoma (HGBL)
Organization	Cell Therapy Transplant Canada (CTTC)
Contact information[a]	Kirk R. Schultz – CTTC President

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation?	Yes	☒
	No	☐
Axicabtagene ciloleucel is now considered a valuable salvage therapy for relapsed DLBCL. Based on the ZUMA-7 trial, a significantly higher portion of patients are being cured with axicabtagene ciloleucel therapy than with standard of care chemotherapy/transplant.		

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

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  - 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	☐
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
All HSCT or BMT centre directors have had an opportunity to provide input on this response and it has been reviewed by the CTTC Board of Directors.		
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: • Kristjan Paulson • Mona Shafey • Nicole Prokopishyn • Kevin Song • Guy Cantin • Mohamed Elemary		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	Kirk R. Schultz
Position	Professor of Pediatrics, University of British Columbia; President, Cell Therapy Transplant Canada
Date	16-Jan-2023
☒	**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**
Bristol Myers Squibb – Member of DSMB for CAR T cell Trials in Leukemia	☐	☒	☐	☐
Novartis – Ad Board	☒	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	Kylie Lepic
Position	Associate Professor, McMaster University; Medical Director, Hamilton Health Sciences
Date	19-Jan-2023
☒	**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**
Novartis	☒	☐	☐	☐
Jazz Pharmaceuticals	☒	☐	☐	☐

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0293
Name of the drug and Indication(s)	Axicabtagene ciloleucel for diffuse large B-cell lymphoma (DLBCL) or high-grade B-cell lymphoma (HGBL)
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	PG0293-000
Brand name (generic)	Yescarta (axicabtagene ciloleucel)
Indication(s)	For the treatment of adult patients with relapsed or refractory large B-cell lymphoma (LBCL), who are candidates for autologous stem cell transplant (ASCT)
Organization	Lymphoma Canada
Contact information[a]	Name: Sarah Eisinga, Manager of Patient Programs, Research and Advocacy

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 Yescarta for this indication. Yescarta 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 Yescarta 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, it was acknowledged Lymphoma Canada provided perspective into the patient experience and highlighted the following from a recent survey: - Patients desire treatments with longer survival, longer remission, better quality of life and fewer side effects - Access to CAR T-cell therapies is currently limited in Canada, which imposes significant challenges to patients travelling out-of-province to receive treatment - Axi-cel provides another available treatment option for this patient population, which is important as 91% of survey respondents felt a need for more therapy options for DLBCL		

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 highlighted the barriers to access to CAR-T in Canada and the disproportionate impact on racialized or marginalized groups, the impact of travel for Yescarta needs to be addressed through increased provincial infrastructure and staff for CAR-T therapy. Almost all lymphoma patients		

are immunocompromised and therefore face significant challenges when travelling out of province for medical treatment. Solutions to these barriers need to be addressed.		
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 who 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

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A. Patient Group Information	
Name	*Sarah Eisinga*
Position	*Manager of Patient Programs, Research & Advocacy*
Date	*January 19, 2023*
☒	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	☐
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐

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**
Gilead				X
Novartis			X	
Bristols Myers Squibb			X	

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0293-000
Brand name (generic)	Yescarta (axicabtagene ciloleucel)
Indication(s)	Diffuse large B-cell lymphoma (DLBCL) or high-grade B-cell lymphoma (HGBL)
Organization	Cell Therapy Transplant Canada (CTTC)
Contact information[a]	Kirk R. Schultz – CTTC President

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation?	Yes	☒
	No	☐
Axicabtagene ciloleucel is now considered a valuable salvage therapy for relapsed DLBCL. Based on the ZUMA-7 trial, a significantly higher portion of patients are being cured with axicabtagene ciloleucel therapy than with standard of care chemotherapy/transplant.		

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.

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A. Patient Group Information	
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 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	☐	☐	☐	☐

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  - 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	☐
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
All HSCT or BMT centre directors have had an opportunity to provide input on this response and it has been reviewed by the CTTC Board of Directors.		
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: • Kristjan Paulson • Mona Shafey • Nicole Prokopishyn • Kevin Song • Guy Cantin • Mohamed Elemary		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	Kirk R. Schultz
Position	Professor of Pediatrics, University of British Columbia; President, Cell Therapy Transplant Canada
Date	16-Jan-2023
☒	**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				
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Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Bristol Myers Squibb – Member of DSMB for CAR T cell Trials in Leukemia	☐	☒	☐	☐
Novartis – Ad Board	☒	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	Kylie Lepic
Position	Associate Professor, McMaster University; Medical Director, Hamilton Health Sciences
Date	19-Jan-2023
☒	**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				
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Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis	☒	☐	☐	☐
Jazz Pharmaceuticals	☒	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0293
Brand name (generic)	YESCARTA (axicabtagene ciloleucel)
Indication(s)	For the treatment of adult patients with DLBCL or HGBL that is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy
Organization	Gilead Sciences Canada Inc. (Sponsor)
Contact information[a]	[redacted]

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

We agree with the committee's recommendation to *Reimburse with Conditions* and are pleased that CADTH and pERC have recognized the need for axi-cel to be funded in the second line setting for patients with LBCL. To provide greater clarity to stakeholders, there are sections of the rationale that would benefit from additional context. Therefore, **we are submitting the following request as a request for reconsideration for editorial revisions**.

Page 5 (Discussion Points) Bullet 6, Page 15 (Budget Impact): "Although the sponsor assumed lower market uptake rates within their analysis, the CADTH base-case demonstrates that, with higher rates of uptake, the three-year budget impact could be over $347 million." This statement does not provide readers with sufficient context regarding the key assumptions used to derive the CADTH base-case. Please add the following text, as per the draft CADTH pharmacoeconomic review report (page 35):

"CADTH conducted a re-analysis by adjusting the projected market share of axi-cel to 77.4%, 87.6% and 93.8% in Years 1, 2, and 3, respectively based on feedback sought from CADTH clinical experts."

In addition to the above, please consider making the following additional editorial revisions to improve the clarity of the draft recommendation:

Page 5 (Discussion Points, Bullet 2): "Patients indicated that there is a need for treatments that prolong survival and OS was a key secondary outcome in the ZUMA-7 study. The OS data … did not reach statistical significance."

And Page 11 (Clinical Evidence, Efficacy Results, Overall survival): "OS was a key secondary outcome in the ZUMA-7 study. … At the interim OS analysis, the hazard ratio (HR) for death was 0.730 (95% confidence interval [CI]: 0.530, 1.007; 1- sided stratified log-rank p-value=0.0270)."

These statements reference the primary OS analysis and highlight the immaturity of that data. To provide readers with more context, inclusion of the updated OS analysis would be helpful. We

request the inclusion of the following wording, as per the draft clinical review report (Page 54): “The update to the interim OS analysis with additional survival data was consistent with the OS interim analysis originally conducted. The stratified HR was 0.708 (95% CI: 0.515, 0.972; p = 0.0159).”

Page 11 (Clinical Evidence, HRQoL): “There was a clinically meaningful difference (based on the trial-specified threshold of ±10 points)[16] in mean change of scores from baseline … compared to SOC.”

The statement in this section does not provide the reader clarity on whether the observed difference was statistically significant. We request the following (underlined) modification to this statement: “There was a clinically meaningful (based on the trial-specified threshold of ±10 points)[16] and statistically significant difference in mean change of scores from baseline … compared to SOC.”

Page 13 (Critical Appraisal), “The HRQoL tools were not validated in patients with LBCL.”
This statement does not provide readers enough context regarding the general validity of the HRQoL tools used. We request the inclusion of the following wording, as per the draft clinical review report (Page 71) be used: “Although the EORTC QLQ-C30 and EQ-5D-5L, are comprehensive, and widely used instruments designed to measure HRQoL in the general population, as well as in patient groups with diverse chronic diseases, both are currently not validated for patients with LBCL.”

Other Feedback:
In addition to the request for reconsideration, we would also comment that we strongly disagree with CADTH estimate of the potential budget impact of axi-cel. We believe that the CADTH estimate is vastly inflated and that this is the driven by unrealistically high market share assumptions. The CADTH market share assumptions represent an extremely optimistic market uptake that are not based on any objective data. The CADTH market share assumptions ignore the fact that there are capacity constraints in the Canadian healthcare system that limit the number of LBCL patients that can be treated with CAR T. Moreover, these capacity constraints are highly unlikely to be relieved within the near future, contrary to the assumptions made by CADTH.

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	☐

Specific sections of the rationale that would benefit from additional context to provide greater clarity to readers regarding elements of the rationale for the recommendation and suggested revisions are detailed above.

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.