

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

Disclaimer: The views expressed in this submission are those of the submitting organization or individual. As such, they are independent of CADTH and do not necessarily represent or reflect the view of CADTH. No endorsement by CADTH is intended or should be inferred.

By filing with CADTH, the submitting organization or individual agrees to the full disclosure of the information. CADTH does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no identifying personal information or personal health information is included in the submission. The name of the submitting stakeholder group and all conflicts of interest information from individuals who contributed to the content are included in the posted submission.



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 lyn	nphom	а
	(DLBCL) or high-grade B-cell lymphoma (HGBL) that is refrac	ctory to	
	first-line chemoimmunotherapy or that relapses within 12 mor	nths of	first-
	line chemoimmunotherapy.		
Organization	Ontario Health (Cancer Care Ontario) Hematology Cancer Dr	rug	
	Advisory Committee		
Contact information ^a	Name: Dr. Tom Kouroukis		
Stakeholder agreement w	th the draft recommendation		
	gree with the committee's recommendation.	Yes No	
	eholder agrees or disagrees with the draft recommendation. W	/henev	er
possible, please identify the	specific text from the recommendation and rationale.		
Expert committee conside	eration of the stakeholder input		
2. Does the recommendati	on demonstrate that the committee has considered the	Yes	\boxtimes
stakeholder input that y	our organization provided to CADTH?	No	
If not, what aspects are mis	sing from the draft recommendation?		
Clarity of the draft recomm	nendation		
3 Are the reasons for the	recommendation clearly stated?	Yes	\boxtimes
	-	No	
If not, please provide details	s regarding the information that requires clarification.		
1 Have the implementation	n issues been clearly articulated and adequately	Yes	
addressed in the recom		No	
	regarding the information that requires clarification.		
,, , , , , , , , , , , , , , , , , , , ,			
(Table 2)			
Do: Conorolizability			
Re: Generalizability Patients anywhere along the	e course of moving toward ASCT should be considered to swite	ch to C	AR-
T provided all other criteria			, u v
F If any line by the f		Vaa	
	mbursement conditions clearly stated and the rationale	Yes	
for the conditions provi	ded in the recommendation?	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.

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 <u>Procedures for CADTH Drug Reimbursement Reviews</u> 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	\boxtimes
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 enclyre only	Na	
2. Did you receive help from outside your clinician group to collect or analyze any	No	\boxtimes
information used in this submission?	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	No	
submitted at the outset of the CADTH review and have those declarations remained	Yes	\times
unchanged? If no, please complete section C below.		
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 Up	dated 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.

	Check Appropriate Dollar Range			ge
Company	\$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				

Name	Please state full name
Position	Please state currently held position
Date	Please add the date form was completed (DD-MM-YYYY)
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Company	\$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 op	dated 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)				
\boxtimes	I hereby certify that I have the authority to disclose all relevant information with respect to any			respect to any	
	matter involving this clinician or clinician group with a company, organization, or entity that may			entity that may	
	place this clinician or clinician g	roup in a real, p	otential, or perce	eived conflict of in	terest situation.
Conflict of	Interest Declaration				
List any co	Interest Declaration mpanies or organizations that have who may have direct or indirect i		rug under review		•
List any co	mpanies or organizations that have		rug under review		•
List any cor years AND	mpanies or organizations that hav who may have direct or indirect i	nterest in the di	rug under review Check Approp \$5,001 to	oriate Dollar Rang	ge In Excess of
List any cor years AND Company	mpanies or organizations that hav who may have direct or indirect i any name	nterest in the di \$0 to 5,000	rug under review Check Approp \$5,001 to 10,000	priate Dollar Rang \$10,001 to 50,000	ge In Excess of

New or Up	dated 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)				
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Conflict of	Interest Declaration				
	any companies or organizations that have provided your group with financial payment over the past two rs AND who may have direct or indirect interest in the drug under review.				
			Check Approp	riate Dollar Rang	je
Company		\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Add company name					
Add compa	Add company name				
Add or rem	nove rows as required				

New or Up	dated 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				
	ist any companies or organizations that have provided your group with financial payment over the past two ears AND who may have direct or indirect interest in the drug under review.				
-	who may have all cot of mall cot i		rug under review.		
-			8	riate Dollar Rang	Je
Company		\$0 to 5,000	8		in Excess of \$50,000
Company Add compa			Check Approp \$5,001 to	riate Dollar Ran <u>c</u> \$10,001 to	In Excess of
	any name	\$0 to 5,000	Check Approp \$5,001 to	riate Dollar Ran <u>c</u> \$10,001 to	In Excess of \$50,000



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 ly (HGBL)	ympho	ma
Organization	Cell Therapy Transplant Canada (CTTC)		
Contact information ^a	Kirk R. Schultz – CTTC President		
Stakeholder agreement with	th the draft recommendation		
	gree with the committee's recommendation?	Yes No	
the ZUMA-7 trial, a significa	ow considered a valuable salvage therapy for relapsed DLBCL ntly higher portion of patients are being cured with axicabtagen standard of care chemotherapy/transplant.		d on
Expert committee conside	eration of the stakeholder input		
2. Does the recommendati	on demonstrate that the committee has considered the	Yes	\boxtimes
stakahaldar input that y	our organization provided to CADTU2		
stakenoider input that y	our organization provided to CADTH?	No	
· · · ·		No	
Clarity of the draft recomm			
Clarity of the draft recomm	nendation	Yes	
Clarity of the draft recomm			
Clarity of the draft recomr 3. Are the reasons for the	nendation recommendation clearly stated?	Yes No	
Clarity of the draft recomr 3. Are the reasons for the 4. Have the implementatio	nendation recommendation clearly stated? n issues been clearly articulated and adequately	Yes No Yes	
Clarity of the draft recomr 3. Are the reasons for the	nendation recommendation clearly stated? n issues been clearly articulated and adequately	Yes No	
Clarity of the draft recomr 3. Are the reasons for the 4. Have the implementatio addressed in the recom	nendation recommendation clearly stated? n issues been clearly articulated and adequately mendation?	Yes No Yes	
Clarity of the draft recomr 3. Are the reasons for the 4. Have the implementatio addressed in the recom 5. If applicable, are the rein	nendation recommendation clearly stated? n issues been clearly articulated and adequately	Yes No Yes No	

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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.

1. Did you receive help from outside your clinician group to complete this submission? No 2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? No All HSCT or BMT centre directors have had an opportunity to provide input on this response and it has be 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 No	⊠ □ □ n
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? No All HSCT or BMT centre directors have had an opportunity to provide input on this response and it has be reviewed by the CTTC Board of Directors. B. Previously Disclosed Conflict of Interest	
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reviewed by the CTTC Board of Directors. B. Previously Disclosed Conflict of Interest	n
3. Were conflict of interest declarations provided in clinician group input that was No	
submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	\boxtimes
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 Up	dated 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.

		Check Approp	oriate Dollar Rang	ge
Company	\$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		\boxtimes		
Novartis – Ad Board	\boxtimes			

New or Up	New or Updated Declaration for Clinician 2						
Name	Kylie Lepic						
Position	Associate Professor, McMaster University; Medical Director, Hamilton Health Sciences						
Date	19-Jan-2023						
List any co	I hereby certify that I have the matter involving this clinician or place this clinician or clinician g Interest Declaration mpanies or organizations that hav who may have direct or indirect i	clinician group roup in a real, p ve provided you	with a company, potential, or perce ur group with finar	organization, or e eived conflict of int ncial payment ove	entity that may erest situation.		
			Check Approp	riate Dollar Rang	je		
Company							
Novartis		\boxtimes					
Jazz Pharn	naceuticals	\boxtimes					

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0293
Name of the drug and	Axicabtagene ciloleucel for diffuse large B-cell lymphoma (DLBCL)
Indication(s)	or high-grade B-cell lymphoma (HGBL)
Organization Providing	PAG
Feedback	

1. Recommendation revisions Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.					
Request for	Major revisions: A change in recommendation category or patient population is requested				
Reconsideration	Minor revisions: A change in reimbursement conditions is requested				
No Request for	Editorial revisions: Clarifications in recommendation text are requested				
Reconsideration	No requested revisions	х			

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.



PG0293-000 Yescarta (axicabtagene ciloleucel) For the treatment of adult patients with relapsed or refractory cell lymphoma (LBCL), who are candidates for autologous ste transplant (ASCT) Lymphoma Canada Name: Sarah Eisinga, Manager of Patient Programs, Research Advocacy th the draft recommendation ree with the committee's recommendation.	m cell	}-
Yescarta (axicabtagene ciloleucel) For the treatment of adult patients with relapsed or refractory cell lymphoma (LBCL), who are candidates for autologous ste transplant (ASCT) Lymphoma Canada Name: Sarah Eisinga, Manager of Patient Programs, Research Advocacy th the draft recommendation	m cell	}-
For the treatment of adult patients with relapsed or refractory cell lymphoma (LBCL), who are candidates for autologous ste transplant (ASCT) Lymphoma Canada Name: Sarah Eisinga, Manager of Patient Programs, Research Advocacy th the draft recommendation	m cell	}-
cell lymphoma (LBCL), who are candidates for autologous ste transplant (ASCT) Lymphoma Canada Name: Sarah Eisinga, Manager of Patient Programs, Research Advocacy th the draft recommendation	m cell	3-
Name: Sarah Eisinga, Manager of Patient Programs, Research Advocacy th the draft recommendation	and	
Advocacy th the draft recommendation	n and	
ree with the committee's recommendation		
	Yes No	
on demonstrate that the committee has considered the	Yes	X
our organization provided to CADTH?	No	
n a recent survey: nents with longer survival, longer remission, better quality of life therapies is currently limited in Canada, which imposes signifi- s travelling out-of-province to receive treatment her available treatment option for this patient population, which	e and cant n is	ıd
endation		
	Yes	\boxtimes
ecommendation clearly stated?	No	
stated.		
issues been clearly articulated and adequately	Yes	
	No	X
ed the barriers to access to CAR-T in Canada and the disprope	ortiona	te
	nal treatment option to patients with LBCL that aligns with patients of life, longer survival and longer remission, and choice in the ty of Yescarta would prevent unnecessary delays in treatment. The cell therapies. The therapies of the stakeholder input the the committee has considered the first organization provided to CADTH? Imphoma Canada provided perspective into the patient experient a recent survey: Therapies is currently limited in Canada, which imposes signifies travelling out-of-province to receive treatment there available treatment option for this patient population, which survey respondents felt a need for more therapy options for DL endation clearly stated? Stated.	ration of the stakeholder input Yes on demonstrate that the committee has considered the ur organization provided to CADTH? Yes with organization provided to CADTH? No mphoma Canada provided perspective into the patient experience and a recent survey: No ments with longer survival, longer remission, better quality of life and therapies is currently limited in Canada, which imposes significant a travelling out-of-province to receive treatment her available treatment option for this patient population, which is survey respondents felt a need for more therapy options for DLBCL endation Yes example and Yes issues been clearly articulated and adequately Yes

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	Yes	X			
for the conditions provided in the recommendation?	No				
Yes, Table 1 "Reimbursement Conditions and Reasons" clearly states this information. How under the Prescribing Section (Implementation Guidance) of Table 1, Lymphoma Canada recommends that additional guidance be provided on eliminating barriers to access for tho who are eligible for the treatment but for whom travel, family and financial considerations a important variables patients must factor into a decision for treatment if they have to leave th province to receive CAR-T therapy.	se pati re				

Appendix 1. Conflict of Interest Declarations for Patient Groups

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A Dationt	Group Information							
Name	Sarah Eisinga							
Position	Manager of Patient Program	s Research	& Advocacy					
Date	January 19, 2023	<i>ie, 1100001.01</i>	, a , la , couoy					
	I hereby certify that I have th	ne authority	to disclose all re	levant informati	on with re	spect 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.							
R Assista	nce with Providing Feedbac	k						
	u receive help from outside		t group to com	ploto vour	No	\square		
feedba	•	your patier	it group to com	piete your	Yes			
ICCUD					163			
2. Did vo	u receive help from outside	vour patier	nt aroup to colle	ect or analyze	No	\boxtimes		
	formation used in your feed		J	· · · · · · · · · · · · · · · · · · ·	Yes			
	, , , , , , , , , , , , , , , , , , ,							
C. Previou	Isly Disclosed Conflict of Inte	erest						
1. Were	conflict of interest declaration	ons provide	d in patient gro	up input that	No			
was si	ubmitted at the outset of the	CADTH rev	view and have t	hose	Yes	\mathbf{X}		
declar	ations remained unchanged	? If no, plea	ase complete se	ection D below.				
D. New or	Updated Conflict of Interest	Declaratio	n					
3. List ar	y companies or organization	ns that have	e provided vour	aroup with fin	ancial pa	vment		
	he past two years AND who i		• •		-	-		
reviev		-			•			
				opriate Dollar F				
Company		\$0 to	\$5,001 to	\$10,001 to	In Exce			
		5,000	10,000	50,000	\$50,000			
Gilead)	X		
Novartis				X				
Bristols M	vers Squibb			Х				
		1			1			



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Contact information ^a	Kirk R. Schultz – CTTC President		
Stakeholder agreement with	ith the draft recommendation		
	gree with the committee's recommendation?	Yes No	
the ZUMA-7 trial, a significa	ow considered a valuable salvage therapy for relapsed DLBCL ntly higher portion of patients are being cured with axicabtager standard of care chemotherapy/transplant.		d on
Expert committee conside	eration of the stakeholder input		
	on demonstrate that the committee has considered the	Yes	\boxtimes
stakeholder input that y	our organization provided to CADTH?	No	
		110	
· · ·		110	
Clarity of the draft recom			
Clarity of the draft recomm	nendation	Yes	
Clarity of the draft recomm			
Clarity of the draft recomr 3. Are the reasons for the	nendation recommendation clearly stated?	Yes No	
Clarity of the draft recomr 3. Are the reasons for the 4. Have the implementatio	nendation recommendation clearly stated? n issues been clearly articulated and adequately	Yes No Yes	
Clarity of the draft recomr 3. Are the reasons for the	nendation recommendation clearly stated? n issues been clearly articulated and adequately	Yes No	
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Clarity of the draft recommon 3. Are the reasons for the 4. Have the implementation addressed in the recommon 5. If applicable, are the rein	nendation recommendation clearly stated? n issues been clearly articulated and adequately	Yes No Yes	

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A. Patient Name	Please state full name					
Position	Please state currently held pos	ition				
Date						
	Please add the date form was I hereby certify that I have the			information with	roopoot to	001/
	matter involving this patient group in a real, potentia	oup with a comp	any, organizatio	on, or entity that n		
B. Assista	nce with Providing Feedback					
4 D'L					No	
1. Did yo	u receive help from outside you	ur patient grou	p to complete	your reedback?	Yes	
inform	u receive help from outside you ation used in your feedback? se detail the help and who provide		p to collect or	analyze any	No Yes	
inform If yes, pleas	ation used in your feedback? se detail the help and who provide	ed it.	p to collect or	analyze any		_
inform If yes, pleas C. Previou	ation used in your feedback?	ed it.				_
inform If yes, pleas C. Previou 1. Were o submi	ation used in your feedback? se detail the help and who provide sly Disclosed Conflict of Intere	ed it. st provided in pa review and ha	itient group inp ive those decla	out that was	Yes	
inform If yes, pleas C. Previou 1. Were of submin uncha	ation used in your feedback? se detail the help and who provide sly Disclosed Conflict of Intere conflict of interest declarations tted at the outset of the CADTH	ed it. st provided in pa review and ha ection D below	itient group inp ive those decla	out that was	Yes	
inform If yes, pleas C. Previou 1. Were of submin uncha D. New or 3. List an	ation used in your feedback? se detail the help and who provide sly Disclosed Conflict of Intere conflict of interest declarations tted at the outset of the CADTH nged? If no, please complete se	ed it. st provided in pa review and ha ection D below claration that have prov	tient group inp ve those decla ided your grou	put that was arations remaine p with financial	d No Yes	
inform If yes, pleas C. Previou 1. Were o submir uncha D. New or 3. List an past ty	ation used in your feedback? se detail the help and who provide sly Disclosed Conflict of Interes conflict of interest declarations tted at the outset of the CADTH nged? If no, please complete se Updated Conflict of Interest De by companies or organizations	ed it. st provided in pa review and ha ection D below claration that have prov rect or indirect	itient group inp tve those decla ided your grou t interest in the Check Appro	put that was arations remaine p with financial p drug under revi opriate Dollar Ra	d No Yes Ves payment of iew.	
inform If yes, pleas C. Previou 1. Were of submin uncha D. New or 3. List an	ation used in your feedback? se detail the help and who provide sly Disclosed Conflict of Interes conflict of interest declarations tted at the outset of the CADTH nged? If no, please complete se Updated Conflict of Interest De by companies or organizations	ed it. st provided in pa review and ha ection D below claration that have prov	itient group inp tve those decla ided your grou t interest in the	put that was irations remaine p with financial drug under revi	d No Yes d Yes payment of iew.	
inform If yes, pleas C. Previou 1. Were o submir uncha D. New or 3. List an past ty	ation used in your feedback? se detail the help and who provide sly Disclosed Conflict of Intere conflict of interest declarations tted at the outset of the CADTH nged? If no, please complete se Updated Conflict of Interest De by companies or organizations to years AND who may have di	ed it. st provided in pa review and ha ection D below claration that have prov rect or indirect	tient group inp tive those decla ided your grou t interest in the Check Appro	put that was parations remaine p with financial drug under revi opriate Dollar Ra \$10,001 to	d No Yes d Yes payment of iew. nge In Exces \$50,000	
inform f yes, pleas C. Previou 1. Were of submit uncha D. New or 3. List an past tw Company	ation used in your feedback? se detail the help and who provide sly Disclosed Conflict of Interes conflict of interest declarations tted at the outset of the CADTH nged? If no, please complete se Updated Conflict of Interest De by companies or organizations wo years AND who may have di	ed it. st provided in pa review and ha ection D below claration that have prov rect or indirect \$0 to 5,000	ided your grou t interest in the Check Appro \$5,001 to 10,000	p with financial drug under revi priate Dollar Ra \$10,001 to 50,000	d No Yes d Yes payment of iew. nge In Exces \$50,000	over the

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- 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 <u>Procedures for CADTH Drug Reimbursement Reviews</u> 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.

1. Did you receive help from outside your clinician group to complete this submission?		
	No	\boxtimes
	Yes	
	No	\boxtimes
information used in this submission?	Yes	
All HSCT or BMT centre directors have had an opportunity to provide input on this response and it has reviewed by the CTTC Board of Directors.	s beer	1
B. Previously Disclosed Conflict of Interest		
······································	No	
submitted at the outset of the CADTH review and have those declarations remained	Yes	\boxtimes
Linchanded? It no hiease complete section (Chelow		
unchanged? If no, please complete section C below. If yes, please list the clinicians who contributed input and whose declarations have not changed:		

C. New or Updated Conflict of Interest Declarations

New or Up	dated 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.

		Check Approp	oriate Dollar Rang	ge
Company	\$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		\boxtimes		
Novartis – Ad Board	\boxtimes			

New or Up	dated Declaration for Clinician	2						
Name	Kylie Lepic							
Position	Associate Professor, McMaster University; Medical Director, Hamilton Health Sciences							
Date	19-Jan-2023							
List any co	I hereby certify that I have the matter involving this clinician or place this clinician or clinician g Interest Declaration mpanies or organizations that hav who may have direct or indirect i	clinician group roup in a real, p ve provided you	with a company, potential, or perce ur group with finar	organization, or e eived conflict of inf ncial payment ove	entity that may erest situation.			
Check Appropriate Dollar Ran					je			
Company		\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000			
Novartis		\boxtimes						
Jazz Pharn	naceuticals	\boxtimes						



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	
Stakeholder agreement w	ith the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.

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, <u>we are submitting the following request as a</u> 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

Yes

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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 <u>statistically significant</u> 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?		No

Clarity of the draft recommendation						
3. Are the reasons for the recommendation clearly stated?		\boxtimes				
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	Yes	\boxtimes				
addressed in the recommendation?						
		-				
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?		\boxtimes				

^a CADTH may contact this person if comments require clarification.

 \boxtimes