CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

ciltacabtagene autoleucel (Carvykti)

(Janssen Inc.)

Indication: Relapsed or refractory multiple myeloma

April 14, 2023

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0302-000
Brand name (generic)	Carvykti (ciltacabtagene autoleucel)
Indication(s)	Relapsed or refractory multiple myeloma
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	☐
Yes, we agree with the recommendation. Ciltacabtagene autoleucel is a much needed and valuable treatment for patients with relapsed or refractory multiple myeloma who have received at least 3 prior lines, including a proteasome inhibitor, immunomodulatory agent, and an anti-CD38 antibody. Based on the CARTITUDE-1 trial, such patients treated with ciltacabtagene autoleucel achieve clinical benefit in response rates, overall survival and progression-free survival over outcomes currently achievable with standard 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	☒
Our organization did not provide initial stakeholder input		
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	☐
Reimbursement consideration should take into account that unlike other standard therapies for this heavily pretreated population, ciltacabtagene autoleucel is a one-time infusion without ongoing dose administration.		

[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	☐
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
All HSCT program 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: •		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	Christine Chen
Position	Program Director and Clinician Investigator, Princess Margaret Cancer Centre
Date	05-04-2023
☒	**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
None	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	Terrance Comeau
Position	Director of New Brunswick HSCT Program
Date	06-04-2023
☒	**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
Kite	☒	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	Kevin Hay
Position	Assistant Professor, Department of Medicine, University of British Columbia
Date	06-04-2023
☒	**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
Kite/Gilead	☒	☐	☐	☐
Novartis	☒	☐	☐	☐
BMS	☒	☐	☐	☐
Jazz Pharmaceuticals	☒	☐	☐	☐
Janssen	☐	☒	☐	☐

New or Updated Declaration for Clinician 4	
Name	Kevin Song
Position	Interim Medical Director, Leukemia/BMT Program of BC
Date	12-04-2023

☒	**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
Kite/Gilead	☒	☐	☐	☐
Celgene/BMS	☒	☐	☐	☐
Janssen	☐	☒	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0302-000
Brand name (generic)	Carvykti (Ciltacabtagene autoleucel)
Indication(s)	For the treatment of patients with relapsed or refractory multiple myeloma (RRMM), who previously received at least three prior lines of therapy including a proteasome inhibitor (PI), an immunomodulatory agent (IMiD) and an anti-CD38 antibody (3L RRMM).
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	☒

We disagree with the reimbursement condition #3. Ciltacabtagene autoleucel should be considered in patients with prior exposure to anti-BCMA antibody drug conjugates (e.g., belantamab) since these patients may still respond to cilta-cel.

The following abstract suggests evidence of response to CAR-T in patients who received prior BCMA-targeting agents.
https://ashpublications.org/blood/article/141/3/219/486575/Efficacy-and-safety-of-cilta-cel-in-patients-with

There are a number of patients across Canada who had received belantamab under clinical trial CMRG 007. CAR-T should be available as a treatment option for these patients.

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.

Re Table 2: CARTITUDE-1 trial excluded patients who have received prior treatment with any therapy targeted to BCMA
Please refer to comments in #1 above.

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: Table 1) Please refer to comments in #1 above.		

[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 secretariat support in completing this submission.		
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 • Clinician 2 • *Add additional (as required)*		

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

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0302
Name of the drug and Indication(s)	Ciltacabtagene autoleucel for multiple myeloma
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

Version: 1.0
Publication Date: TBC
Report Length: 2 Pages

Single Technology

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. Rapid Algorithm for Multiple Myeloma (PAG Leads: SK and ON) 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	
Brand name (generic)	Ciltacabtagene autoleucel (Carvykti)
Indication(s)	For the treatment of adult patients with multiple myeloma, who have received at least 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 antibody, and who are refractory to their last treatment.
Organization	Myeloma Canada
Contact information[a]	Name: Aidan Robertson [redacted]

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

pg. 5 Discussion Point 1.
Myeloma Canada is very pleased that pERC has decided to recommend the reimbursement (with conditions) of ciltacabtagene autoleucel— a CAR T-cell therapy for the treatment of triple-class refractory multiple myeloma. Though the evidence of benefit compared to standard of care remains limited and the implementation concerns are quite significant, access to cilta-cel is a critical step towards meeting the need for effective myeloma treatments in the fourth-line setting (and beyond).

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	☐

Myeloma Canada appreciates the committee including mention that myeloma patients themselves identified the need for improved access to CAR T-cell therapies. We were also glad to see the committee had taken into consideration the most important elements of our submission— such as, patients' overall desire for improved quality of life, fewer side effects, longer periods of time without any active treatment— and reflected these in the rationale of their decision. We are grateful to the committee for placing such significant value on the fact that treatment options are currently extremely limited for triple-class refractory myeloma patients, and for many, cilta-cel represents a last remaining hope.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

We acknowledge a lack of available RCT evidence from which the pERC could directly compare patient outcomes following cilta-cel treatment, with the current standard of care. We greatly appreciate the committee's consideration of multiple observational studies in their assessment, and the careful approach taken to weighing the totality of evidence pointing to cilta-cel's potential real-world efficacy in the indicated population (triple-class RRMM).
Though the reasons for the decision are clearly stated, the committee also notes that most are conditioned upon a lack of certainty in the existing real-world evidence/lack of direct RCT evidence,

thus the validity of the price calculations are subject to significant change as the body of evidence evolves. Particularly, if the positive improvements in PFS and OS seen across all five real-world datasets are validated by clinical practice, and/or the speculated beneficial effect on HRQoL for patients is realized, the cost of treatment per-QALY-adjusted life year may be significantly reduced. Does the committee have any plans to reassess the accuracy of these calculations in the future with the benefit of more data examine? What level of inconsistency between the results analyzed for this decision, and results emerging from new research, would the committee feel warranted reassessment of their current recommendation?

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒

pg. 10 Implementation Issues - Table 2
Question/Issue 1: We agree completely with the pERC and clinicians' assessment that at present, the Canadian health system's ability to deliver cilta-cel to eligible patients would be very limited, localized, and thus has little chance of meeting the projected demand for cilta-cel treatment, while — presenting a "major barrier" to CARVYKTI uptake.

Issue/Question 3: Myeloma Canada appreciates the committee's nuanced discussion and clear articulation of the numerous ethical and equity concerns inherent in delivering highly specialized, costly, and resource-intensive treatments like cilta-cel (and CAR T-cell therapies in general) across geographic boundaries. The drawbacks of potentially exacerbating of existing disparities in access to healthcare and services, coexist alongside the wide-ranging potential benefits of a one-time treatment on HRQoL particularly for rural/remote patients, and are both important considerations for

pg. 6 Discussion Points
pERC noted in their final point there is an "ongoing need to develop pan-Canadian guidance outlining fair and equitable priority-setting criteria for patient access" to CAR T-cell therapies. Myeloma Canada again firmly agrees with the committee regarding the necessity of developing national guidance for CAR T-cell therapy implementation; and to ensure that while the infrastructure to efficiently deliver CAR T-cell therapies in an increasing number of locations across Canada is being built, a coordinated, resource-sharing, effort across the provincial/territorial heath systems to manage demand would play a key role in making therapies like cilta-cel more widely accessible to patients outside of major academic centres. Myeloma Canada, and members of our patient/caregiver community would be very grateful for any opportunity to contribute to, or comment on this pan-Canadian CAR-T guidance document.

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

pg. 10 Table 2 *"pERC noted that patients should have generally received an anti- CD38 antibody to be eligible for ciltacabtagene autoleucel, but agreed with the clinical experts that there is a time-limited need to* ***consider*** *patients who were not able to access an anti-CD38 antibody."*

The committee's response to Issue/Question 3 acknowledges the existence of a *"time-limited need to* ***consider*** *[these] patients";* but we are unsure what the exact intended meaning of 'consider' is in this context. Patients unable to access an anti- CD38 antibody are not mentioned amongst the conditions for cilta-cel reimbursement, nor in the accompanying 'implementation guidance' in Table 1 (pg. 4). Is the committee stating it needs to conduct a separate reimbursement review to 'consider' funding cilta-cel for this small subset of the RRMM patient population? Or is the committee agreeing that clinicians need to consider treating those unable to access an anti- CD38 antibody, with cilta-cel— and presumably seek funding for it through an exceptional access program?

Due to the need for this group of patients to receive treatment in a timely manner, and as pERC noted, it is likely a very small group; what approach does the committee recommend these patients, or their hemo/oncologists seek access to/funding for cilta-cel?

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

Appendix 1. Conflict of Interest Declarations for Patient Groups

A. Patient Group Information	
Name	*Aidan Robertson*
Position	*Health Policy & Advocacy Assistant*
Date	*14-04-2023*
☒	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	☐
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	PG0302
Brand name (generic)	CARVYKTI™ (ciltacabtagene autoleucel)
Indication(s)	For the treatment of adult patients with multiple myeloma, who have received at least 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 antibody, and who are refractory to their last treatment.
Organization	Janssen Inc.
Contact information[a]	[redacted]

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

Janssen agrees with the recommendation to reimburse with conditions CARVYKTI™ for the treatment of adult patients with multiple myeloma, who have received at least 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 antibody, and who are refractory to their last treatment.

Consistent with Janssen's feedback on the draft review reports, Janssen emphasizes the value of the LocoMMotion[1] study described on page 16 of the draft recommendation. LocoMMotion is a trial intentionally designed in the absence of a comparator arm against which the benefits and harms of CARVYKTI™ could be compared. The prospective design and alignment with CARTITUDE-1 ensured that eligibility criteria and definitions of all clinically important baseline characteristics and endpoints were identical in both studies, which allowed for the most robust comparisons possible between CARVYKTI™ and existing treatment options on progression free survival and overall survival.

Janssen thanks CADTH for the review of CARVYKTI™ in multiple myeloma. Janssen supports conversion to final 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	☐

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☐

	Yes	☐

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	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.

Sponsor's References

1. Mateos MV, Weisel K, Martin T, et al. Adjusted comparison of outcomes between patients from CARTITUDE-1 versus multiple myeloma patients with prior exposure to PI, IMiD and anti-CD38 antibody from the prospective, multinational LocoMMotion study of real-world clinical practice. *Haematologica*. Dec 22 2022;doi:10.3324/haematol.2022.280482