Canada's Drug Agency
L'Agence des médicaments du Canada

CDA-AMC REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

ciltacabtagene autoleucel (Carvykti)

(Janssen Inc.)

Indication: For the treatment of adult patients with multiple myeloma, who have received 1 to 3 prior lines of therapy including a proteasome inhibitor and an immunomodulatory agent, and who are refractory to lenalidomide.• For the treatment of adult patients with multiple myeloma, who have received at least three prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 antibody, and who are refractory to their last treatment.

October 18, 2024

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0302-000
Brand name (generic)	Ciltacabtagene autoleucel (Carvykti)
Indication(s)	For the treatment of adult patients with multiple myeloma, who have received 1-3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and are refractory to lenalidomide.
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	☐

Yes. Myeloma Canada is pleased that pERC has decided to recommend the conditional reimbursement of ciltacabtagene autoleucel for relapsed/refractory myeloma patients previously treated with a proteasome inhibitor, an immunomodulatory agent, and refractory to lenalidomide.

Though the implementation issues are significant and numerous, publicly funded access to ciltacabtagene autoleucel is a critical step towards meeting the unmet need for new classes of effective myeloma treatments with minimal impact on quality of life, at earlier lines of therapy.

We recognize that cost-effectiveness is highly uncertain due to the complexity of determining appropriate comparators but are concerned about the implications of the recommendation on ongoing pCPA negotiations. If the negotiation concludes with a price reduction within the range previously recommended by pERC for ciltacabtagene autoleucel at the fourth line of therapy (72-80%), it may fall outside the range recommended for RRMM (80%-88%). If this would necessitate re-negotiation or discourage provincial drug plans from listing ciltacabtagene autoleucel at the higher (negotiated) price, patients would face an additional delay in accessing treatment.
We agree that at present, based on limited comparative data, lack of health system/manufacturing capacity, and the diversity of treatment experience amongst patients at the same line of therapy, ciltacabtagene autoleucel should not supplant one specific treatment's place in therapy, but be an additional treatment option available to clinicians.

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. Myeloma Canada was glad to see the committee has 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 also grateful to the committee for acknowledging that many available treatment options have a high travel burden, often requiring weekly or biweekly trips to the hospital/cancer centre, which have a significant impact on patients' and caregivers' quality of life.

Clarity of the draft recommendation

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

Yes. The therapeutic landscape for myeloma is in a state of constant change, and we appreciate the pERC's acknowledgement that earlier and combined use of existing therapies is leaving a growing number of patients with fewer effective treatment options after their first or second relapse. Especially considering the ongoing reviews of DVRd and IsaVRd at the first line of therapy in TE and TI patients, this trend is likely to continue, making the earlier availability of new options like ciltacabtagene autoleucel increasingly necessary.

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

Myeloma Canada appreciates the committee's articulation of the numerous ethical and equity concerns inherent in delivering highly specialized, costly, and resource-intensive treatments like ciltacabtagene autoleucel (and CAR T-cell therapies in general) across geographic boundaries. The difficultly of delivering ciltacabtagene autoleucel in outside of major academic centres, and drawbacks of potentially exacerbating 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. As noted by the pERC these considerations must be balanced through the implementation process.

pg. 5 point 8. pERC noted in their final point under 'feasibility of adoption' "*Due to the resource-intensive nature of CAR T-cell therapy and currently limited human resources and logistical constraints, a standardized process to prioritize utilization should be developed to promote treatment for the optimal clinical benefit in an ethical and equitable manner*".
Myeloma Canada again firmly agrees with the committee regarding the necessity of developing guidance for prioritizing patient access to CAR T-cell therapy; to ensure that while the manufacturing capacity, and infrastructure to deliver CAR T in locations across Canada is under development, a coordinated, resource-sharing, effort across the provincial/territorial heath systems to manage growing demand would play a key role in making therapies like ciltacabtagene autoleucel more widely accessible to patients outside of urban centres.
Myeloma Canada, and members of our patient/caregiver community would greatly appreciate any opportunity to contribute to, or comment on any pan-Canadian CAR T prioritization guidance document. We recognize this is not an issue unique to myeloma, certain factors like geographic location will likely be widely applicable, and a disease agnostic prioritization framework may be the most logical place to start. Yet, considering the complexity of myeloma and its therapeutic space, we feel it will be crucial to ensure that clinical experts in myeloma review any such framework, and are provided the opportunity to include further myeloma-specific prioritization guidance, or produce a modified myeloma-specific version.

Along with the prioritization considerations described by pERC "*patient prognosis, prior therapy, and/or geographic location*", the following factors may also inform prioritization decisions: presence of a caregiver to help manage continuous treatment, significant mobility/frailty issues further complicating travel, inability to access/tolerate an anti-CD38 monoclonal antibody, treatment adherence difficulties, comorbidities and their relationship to other treatment options (ex. if all other factors were equal, ciltacabtagene autoleucel may be favourable over belantamab mafodotin for patients with existing vision issues).

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

Yes. Though we have the following two concerns regarding reimbursement conditions:

1. pg. 8 *"The clinical experts indicated that ciltacabtagene autoleucel would be an additional option for the management of patients with MM who are refractory or exposed to lenalidomide."* In surveys conducted by Myeloma Canada, many patients have described being briefly exposed to lenalidomide, but taken off the treatment due to intolerance, meaning they will never become 'refractory'. These patients face the same lack of treatment options as those refractory to lenalidomide, and likely sooner in their myeloma journey. As noted by the clinical experts in the above quote, ciltacabtagene autoleucel could present an additional option for treating these patients at the second line and we are concerned that the current reimbursement conditions only include patients *refractory* to lenalidomide. This condition should be amended to be inclusive of these patients ex. *'refractory or intolerant to lenalidomide*' or an additional note added to the condition ex. *'…refractory to lenalidomide. Reimbursement may be considered in rare cases where a patient cannot receive lenalidomide (due to intolerance/allergy)* .'

2. We feel the conditional exclusion of patients previously treated with BCMA targeted therapy is unnecessary, as it will likely be accounted for by the process of patient prioritization. This condition would fall under the consideration of 'prior therapy' and in most cases we can assume prior treatment with BCMA-targeted therapy would exclude the patient from ciltacabtagene autoleucel for a number of reasons. We understand that anti-BCMA exposed patients were excluded from CARTITUDE-4, yet other CARTITUDE studies have shown ciltacabtagene autoleucel can be effective for patients with prior exposure to BCMA-targeted therapies (particularly after ADCs like belantamab mafodotin), and we feel that if after taking all prioritization factors into consideration, a clinician's assessment still determines an anti-BCMA exposed patient should receive treatment with ciltacabtagene autoleucel, this should be possible.

[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	*10-18-2024*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☒

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0302-000
Brand name (generic)	Carvykti (ciltacabtagene autoleucel)
Indication(s)	The treatment of adult patients with multiple myeloma, who have received at least three 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	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. - Re: "No prior CAR-T" exclusion should be clarified to "no prior anti-BCMA CAR-T". That is, if patients received a non BCMA CAR-T on clinical trial, they should be eligible for cilta-cel subsequently. - Patients who may still be sensitive to anti-BCMA therapy should be considered (e.g., patients who did not progress on anti-BCMA therapy/discontinued due to toxicities).		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		

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

Appendix 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 to the group 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 • Dr. Selay Lam • Dr. Jordan Herst • Dr. Joanna Graczyk • Dr. Lee Mozessohn • Rami El-Sharkaway		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. Christopher Cipkar*
Position	OH (CCO) Hematology Cancer Drug Advisory Committee member
Date	*10-10-2024*

☒	**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

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	CADTH Reimbursement Recommendation (draft)
Brand name (generic)	Carvykti
Indication(s)	For the treatment of adult patients with multiple myeloma
Organization	Canadian Myeloma Research Group (CMRG)
Contact information[a]	Name: Donna Reece, M.D.

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation. However, please see the comments in Section 5 regarding the conclusion of the economic analysis.	Yes No	☒ ☐
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.		
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. From a myeloma clinician's point of view, the selection of Vd (bortezomib + dexamethasone) as a comparator for the economic analysis, described in the Rationale for the Recommendation section on page 3, is of uncertain practical relevance. Our CMRG real-world data indicates that Vd was the second-line regimen in only 142/3569 (3.9%) Canadian patients treated between 2010-2022 (McCurdy A, et al; *Blood* 2023; 142 [suppl 1]: 3364; poster details available on request). For third-line therapy, Vd was utilized in only 16/1126 (1.4%) patients (Louzada M, et al. *Clinical Lymphoma, Myeloma and Leukemia* 2023; 23 [suppl 2]: S127; poster details available on request). Except for newly diagnosed transplant-ineligible patients who receive DRd, every effort is made to treat second- and third-line patients with combination therapy using an anti-CD38 monoclonal antibody. Even for non-anti-CD38 regimens utilized in the second-line setting, a more relevant comparator would be either selinexor-Vd (SVd) or carfilzomib-dex (Kd) rather than Vd; both SVd and Kd have been endorsed by the CDA and are funded across Canada. Importantly, for both the ENDEAVOR and BOSTON trials that led to their approvals, Vd was the control arm and was demonstrated to be inferior. Thus, Vd is **not** considered a SOC option unless a more efficacious option is contraindicated.		

All of the CMRG physicians expressed concern that the choice of Vd in the economic analysis—an inexpensive but clinically inferior and rarely used regimen--might negatively impact the recommendation to fund cilta-cel and, therefore, negatively affect the outcome of relapsed myeloma patients in Canada.

[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.		
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: • Donna Reece, MD • Darrell White, MD • Hira Mian, MD • Suzanne Trudel, MD • Arleigh McCurdy, MD • Julie Stakiw, MD • Sindu Kanjeekal, MD • Nizar Bahlis, MD • Nicole Laferriere, MD • Peter Anglin, MD • Satish Gopalakrishnan, MD • Guido Lancman, MD • Chris Venner, MD • Vishal Kukreti, MD • Kevin Song, MD • Sita Bhella, MD • Stephe Parkin, MD		

- Rami Kotb, MD
- Ibraheem Othman, MD
- Bethany Montieth, MD
- Mohammed Aljama, MD
- Rayan Kaedbey, MD
- Richard Leblanc, MD
- Michael Chu, OM
- Marc Lalancette, MD
- Anthony Reiman, MD

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	☐	☐	☐	☐

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0361
Name of the drug and Indication(s)	Ciltacabtagene autoleucel For the treatment of adult patients with multiple myeloma who have received 1 to 3 prior lines of therapy including a proteasome inhibitor and an immunomodulatory agent, and who are refractory to lenalidomide.
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	X
	No requested revisions	☐

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. - In Table 1 (Prescribing), PAG identified a minor typo in the following sentence: "Treatment with cilta-cell (cilta-cel) is a one-time therapy."
c) Implementation guidance

Please provide high-level details regarding the information that requires clarification. You can provide specific comments in the draft recommendation found in the next section. Additional implementation questions can be raised here.

Outstanding Implementation Issues

In the event of a positive draft recommendation, drug programs can request further implementation support from CADTH on topics that cannot be addressed in the reimbursement review (e.g., concerning other drugs, without sufficient evidence to support a recommendation, etc.). Note that outstanding implementation questions can also be posed to the expert committee in Feedback section 4c.

Algorithm and implementation questions
1. Please specify sequencing questions or issues that should be addressed by CADTH (oncology only)
1. 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 Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0361
Brand name (generic)	Ciltacabtagene autoleucel (CARVYKTI®)
Indication(s)	For the treatment of adult patients with multiple myeloma, who have received 1 to 3 prior lines of therapy, including a proteasome inhibitor and an immunomodulatory agent, and who are refractory to lenalidomide
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 Inc. agrees with the recommendation to reimburse CARVYKTI® (ciltacabtagene autoleucel) for the treatment of adult patients with multiple myeloma, who have received 1 to 3 prior lines of therapy, including a proteasome inhibitor and an immunomodulatory agent, and who are refractory to lenalidomide.

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	☐

In Janssen's view, the extensive feedback to CDA's economic review was not sufficiently addressed by the economic review report. Therefore, Janssen emphasises that significant uncertainty remains in the economic conclusions made in the recommendation; specifically, due to the following issues:

Issue 1: Exclusion of relevant comparators from the economic assessment and benchmarking the economic value of CARVYKTI® primarily against bortezomib-dexamethasone (Vd):

- Given that multiple therapeutic options exist for the target indication (*please see CADTH provisional funding algorithm for Multiple myeloma, PH0047-000, Figure 1*), Janssen conducted a full economic evaluation of CARVYKTI® against all comparators for which data was available (DVd, IsaPd, SVd, Kd, Vd, and Pd, with IsaKd as a scenario) using the best available current evidence.
- However, CDA's economic review focused only on a subset of older, obsolete comparators, which could be included within the sequential analysis format, thereby excluding triplet therapies routinely used in clinical practice today. Sequential analysis is only valid when all relevant comparators can be included. While Janssen agrees that ITCs (MAIC and IPTW) will be prone to different biases, the complete exclusion of relevant comparators for which evidence has been provided is neither consistent with CADTH PE guidelines, nor with clinical practice. As such the conclusions of CDA's economic reanalysis do not fully represent the economic value of CARVYKTI® in the current treatment landscape.

- Indeed, the reliance on Vd as the comparator used as the benchmark in CDA's assessment of the ICER is not supported by the evidence gathered by CDA itself to inform the clinical appraisal in this very HTA assessment (*please see CDA Clinical Review Report, PG0361-000, section: Standard of Therapy, pg 22-24, and Table 4*).
- Additionally, there are existing concerns with face validity associated with the sequential analysis approach, which was recognized by both CDA and the Sponsor's pharmacoeconomic reports. Given these issues, reporting a single ICER based solely on the sequential analysis significantly undermines economic value of CARVYKTI® in the 1-3 prior line (PL) setting.

Issue 2: The handling of subsequent therapy costs in CDA's reassessment of PE and BIA model:

- Janssen acknowledges the uncertainty identified in modeling subsequent therapy costs and limitation of the model in this regard. However, CDA's assumption that multiple myeloma (MM) patients at the 1-3 PL setting do not receive any subsequent therapy and do not incur additional treatment costs following progression is inappropriate and exacerbates limitations identified by the CDA in the submitted model. This approach fails to reflect the existing clinical management of MM and misrepresents the place in therapy of CARVYKTI® at earlier lines, where patients can initiate a variety of subsequent treatment options upon progression, and therefore does not reflect the reimbursement request at the 1-3 PL setting.
- Moreover, this assumption is inconsistent with the clinical evidence which informs the model. As an example, 98% of all patients that progressed on Kd in CANDOR received subsequent therapy (39% of which was CD-38 mab-based). As such, the clinical benefits of any subsequent therapy will be captured in the OS data used to project the clinical benefits. Removing only the costs of subsequent therapy but retaining the clinical benefit introduces bias into the analysis and leads to conclusions that are incongruent with clinical reality.
- This assumption also discounts the treatment-free interval of CARVYKTI® relative to therapies with a relatively shorter median PFS, and therefore does not reflect the economic impact of CARVYKTI® at the 1-3 PL setting, where patients now have a greater number of therapeutic options upon progression. As such, the CDA's revised model does not accurately represent the technology being assessed.
- Finally, as discussed in the feedback provided by Janssen, despite pointing out similar limitations in other assessments at the 1-3PL setting, CDA did not exclude subsequent therapy in the most recent submissions in this therapeutic space. A more balanced approach would have been to explore this in a scenario analysis instead of the base-case. Indeed, according to the CADTH PE guidelines *"The reference case describes a set of recommended methods that a researcher should follow for all evaluations, to increase the comparability of results across evaluations. The purpose of the reference case is to aid decision-making by promoting uniformity and transparency and enabling the comparison of results for different technologies and different decisions."*

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		