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

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

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.

April 30, 2024

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CDA-AMC in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings. **If your group has submitted input that is not reflected within this document, please contact Formulary-Support@cda-amc.ca.**

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CADTH Reimbursement Review Patient Input

Name of Drug: ciltacabtagene autoleucel (CARVYKTI)

Indication: Adult patients with relapsed-refractory multiple myeloma who have received 1-3 prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and are refractory to lenalidomide.

Name of Patient Group: Myeloma Canada

Author of Submission: Aidan Robertson [redacted]

1. About Your Patient Group

Multiple myeloma, also known as myeloma, is the 2nd most common form of blood cancer. Myeloma affects plasma cells, which are a type of immune cell found in the bone marrow. Every day, 11 Canadians are diagnosed with myeloma, yet despite its growing prevalence the disease remains relatively unknown. People with myeloma experience numerous relapses; with successful treatment the disease can enter periods of remission, but myeloma will always ultimately return and require further treatment. Myeloma patients may also become refractory to a treatment, meaning it can no longer control their myeloma, and they will require a new regimen, meaning new, and more effective treatments for myeloma are always needed. Myeloma Canada has existed for over 15 years to support the growing number of Canadians diagnosed with myeloma, and those living longer than ever with the disease access new and innovative therapies. Over the years, as a part of this mission Myeloma Canada has collected data on the impact of myeloma and its treatments on patients and caregivers by conducting surveys. The compiled data are then presented to the pERC.

www.myeloma.ca

1. Information Gathering

Myeloma Canada is sharing input received from a patient and caregiver survey regarding the CAR T-cell therapy ciltacabtagene autoleucel (cilta-cel). The survey was available in English and French, from April 5 to April 24, 2024, and was shared across Canada and internationally, via email and social media.
118 complete responses to the survey were received, 65 disqualified responses wherein a respondent's answers indicated they did not meet the eligibility requirements were removed from the dataset, leaving 53 eligible respondents from Alberta (3), British Columbia (12), Newfoundland and Labrador (2), Ontario (29), Quebec (5), and 2 from outside of Canada, both from France. Survey eligibility was determined by patient and caregiver self-report of their experience with myeloma, that they (or the person they care for) have relapsed/refractory myeloma, received 1-3 prior lines of therapy, and are refractory to lenalidomide, OR, have experience with a CAR T-cell therapy. All patients and caregivers were asked similar questions

regarding disease experience, then divided into subsets, and posed different questions based on their experience with CAR-T cell therapy and/or the treatment under review.

These subsets are:

- Patients/caregivers who meet the criteria of the indication, referred to as Subset E (37).
  Subset E respondents included 33 patients and 4 caregivers; 29 residents of an urban area and 8 residents of a rural area; 18 individuals assigned female at birth and 19 assigned male at birth. 20 respondents were between the ages of 60-69, 8 respondents were between '70-79', 5 were aged '50-59', 2 were between '40-49', and 2 were '80-89' years of age.
- All respondents with CAR T-cell therapy experience, referred to together as Subset C (16).
  Subset C respondents included 13 patients and 3 caregivers; 14 residents of an urban area and 2 residents of a rural area; 8 individuals assigned female at birth, and 8 assigned male at birth. 6 respondents were between the ages of 70-79, 6 respondents were between '60-69', 2 were aged '50-59', and 2 were '40-49' years of age.
    - Patients/caregivers with cilta-cel experience (8), referred to as Subset C.1; AND;
    - Patients/caregivers who have experience with a different CAR T-cell therapy (8), referred to as Subset C.2.

2. Disease Experience

All respondents were asked, "*Please rate on a scale of 1 - 5, how important it is for you to control various aspects related to your myeloma, or the person you care for's myeloma. 1 is "Not important", 5 is "Extremely important*". Among 53 responses, 'infections' was the most important aspect to control and was rated '5-extremely important' most frequently (27), followed by 'kidney problems' (23). By the weighted average of responses, patients and caregivers also felt mobility, and pain were slightly more important to control, though all options listed received an average rating of '4 – very important' (after rounding).

When asked "*Please rate on a scale of 1 - 5, how much symptoms associated with myeloma, or caring for someone with myeloma, impacts or limits your day-to-day activities and quality of life. 1 is "No impact", and 5 is "Severe impact".* All respondents (53) indicated that their 'ability to travel' was most significantly impacted with 11 respondents indicating '5 – severe impact', followed by 'ability to work' (8), and 'ability to exercise' (6). One patient commented on this question, "*Applies to when I had active myeloma. Post CART I have no symptoms".*

All patients and caregivers were asked '*Has multiple myeloma, or caring for someone with myeloma, resulted in any of the following psychological / social difficulties for you? Please rate on a scale of 1–5 how severely they impacted your quality of life (1 – No impact and 5 – Severe impact)'*. Respondents most frequently felt that that 'Interruption of life goals/accomplishments (career, retirement, etc.)' due to myeloma had a '5 – severe impact' (15) on their quality of life, followed by 'loss of sexual desire' (11), and 'Anxiety/worry' (6).

When asked "*If you are receiving treatment for your myeloma at the moment, please indicate how often you or the person you care for leave home to undergo tests or treatment*.", responding patients and caregivers (53) most frequently chose 'Once a month' (20) Once a week (14), Every two weeks (8), and 'Other' (8).

When asked "*What are the most significant financial implications of myeloma treatment on you and your household? If there is more than one implication, please check all that apply*.", responding patients and caregivers (53) most frequently chose 'lost income or pension funds due to absence from work, disability, or early retirement' (21) and 'travel costs' (21), followed by 'parking costs' (19), 'drug costs' (18), and 'accommodation costs' (9). Comments (6) provided by those who selected 'other' were notable. Two Subset C respondents commented that they had paid to travel to the US to receive CAR T-cell therapy. Of the 4 additional comments left by Subset E respondents, two described the cost of travel and accommodation for stem cell transplant, and one noted their insurance deductible had increased dramatically. "*I went to the USA for car T cell therapy and paid for it"; "accommodation[sic] while undergoing stem cell transplant".*

All patient respondents were asked, "*Do you need the support of a family member or caregiver to help you manage your myeloma or your treatment-related symptoms*?" Subset E patients (33) most frequently chose 'Yes' (17), followed by 'No' (13), 'Yes, but I am unable to access the help I need' (2), and 'No, but I would love to have someone to help' (1). Subset C patients (13) most frequently chose 'Yes' (8), followed by 'No' (5).

When asked *'What is most important to you as a patient/caregiver when considering a myeloma treatment? Please provide comments.",* responding patients and caregivers (47) provided comments indicating it is important that treatments are effective, have manageable side effects, and have minimal impact on quality of life. Some comments to this effect are as follows.

> *"Access to the best treatments available. Canada seems to behind what is happening in the US for instance especially with regard to Car-T."*
>
> *"The most important thing when considering a myeloma treatment is the period of time following treatment that I will be drug free, in addition to the safety and efficacy of the treatment."*
>
> *As caregiver, my understanding of the side effects and implications of the treatment. We'll do anything necessary to keep my patient comfortable, with a reasonable quality of life. Once those tradeoffs become more of an issue, it is hard to know what we will do, so we try to concentrate on the present."*

3. Experiences With Currently Available Treatments

Subsets E and C were asked "*How many prior lines of therapy have you or the person you care for received?".* Of Subset C (16) respondents, 7 (44%) received 4 lines of therapy, 4 respondents indicated they or the person they care for, had received 6 lines of therapy or more, followed by 3 lines of therapy (3), and one respondent chose 2 and 5 lines of therapy respectively. Most Subset E respondents (37) indicated they received 3 lines of therapy (22; 59%), 12 responded 2 lines of therapy, and 3 respondents indicated they or the person they care for, had received 1 line of therapy.

When Subset E respondents (37) were asked "*Have you/the person you care for previously received treatment with any BCMA-targeted therapy? (Ex. idecabtagene vicleucel, belantamab modafin, elranatamab, teclistamab, linvoseltamab or another novel BCMA-directed myeloma treatment)",* 2 responded 'Yes', 27 responded 'No', and 8 indicated they were unsure.

Experience with other CAR T-cell therapies.

Of the 16 Subset C respondents who indicated they had experience with CAR T-cell therapy, 8 reported experience with cilta-cel (Subset C.1) and 8 reported experience with a different CAR T-cell therapy (Subset C.2). These 8 C.2 respondents indicated they had received, Zevor-cel (3), Abcema (idecabtagene vicleucel) (2), CarsGen (1), B383 (1), and one responded they did not know the name of the CAR T-cell therapy they received. Subset C.2 (8) was then posed the following questions about their experience with CAR T-cell therapy.

When asked to indicate how long ago they or the person they care for received treatment with CAR T-cell therapy, 3 C.2 respondents (8) chose 'Between 6 and 12 months ago', 2 chose 'Over a year ago' one respondent indicated 'Less than 3 months ago', one chose 'Between 3 and 6 months ago', 1 chose ', and 1 indicated 'Two or more years ago'.

When asked "*Based on your experience with CAR T-cell therapy, how would you rate the effectiveness of this treatment in helping to control myeloma for you/the person you care for? 1 being 'not effective' and 5 'extremely effective'.* Of 8 respondents, 5 chose '5 – extremely effective', 2 chose '4 – very effective', and 1 chose '2 – somewhat effective'. When asked*, "Based on your experience receiving or caring for someone receiving CAR T-cell therapy, how would you rate the overall side effects? 1 being 'not at all tolerable' and 5 'extremely tolerable.',* 3 C.2 respondents (8) chose '5 – extremely tolerable', 3 chose '3 – tolerable', one chose '4 – very tolerable'. and one chose '2 – somewhat tolerable'.

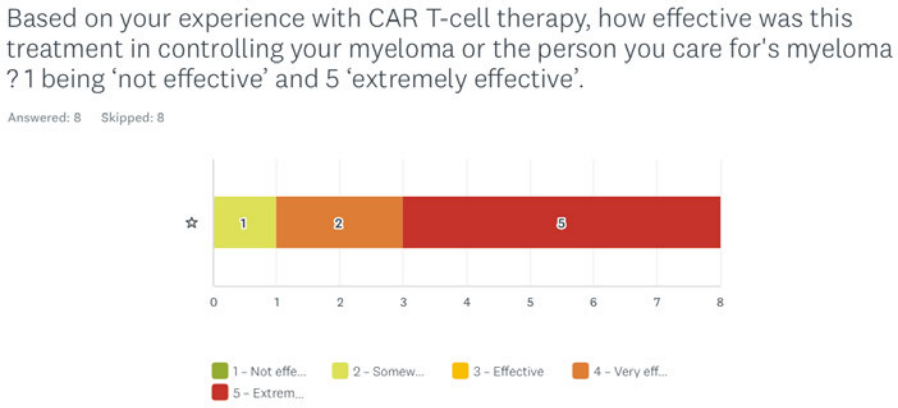


Figure 1 – Effectiveness of treatment with CAR T-cell therapy; subset C.2 (8)

When C.2 respondents (8) were asked "*For a period of time after receiving CAR T-cell therapy, it is likely you/the person you care for were not receiving active myeloma treatment (i.e. did not need any drugs to control your/their mm). How long was this treatment interruption for you/the person you care for?",* one

indicated ‘4-7 months’, one chose ‘8-10 months’, one chose ’14-16 months’, 4 indicated it was too soon to tell, and one commented “*Treatment free for 3.5 years”*.

C.2 patients (7) were asked, “*Did CAR T-cell therapy meet your expectations in treating your myeloma?*” 6 chose ‘Yes’, and one indicated it was too soon to tell. When asked, *“Did treatment with ciltacabtagene autoleucel (cilta-cel) improve your long-term health outlook?”* 6 chose ‘Yes’, and one indicated it was too soon to tell. When asked *“Did treatment with ciltacabtagene autoleucel (cilta-cel) improve your overall quality of life?”*, 6 chose ‘Yes’, and one indicated it was too soon to tell.

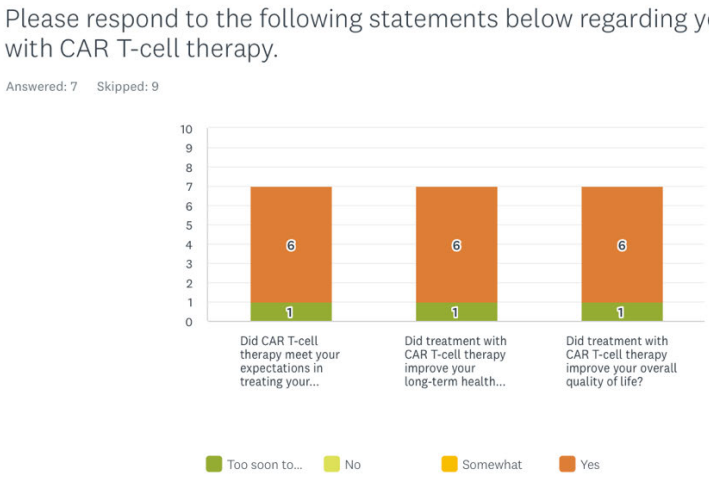


Figure 2 – Experience with CAR T-cell therapy; subset C.2 patients (7)

When asked if they or the person they care for had relapsed since receiving CAR T-cell therapy, 5 of 8 respondents chose “My/their myeloma is still in remission’, 1 responded, “My/their myeloma did come back, and I/they are currently under a new treatment’, and 2 indicated it was too soon to tell.

When asked *“Is there anything else about your experience with CAR T-cell therapy you would like us to know ? Please share your thoughts.”* 6 respondents left the following comments, most of which were very positive.

> “*This is an amazing treatment, with huge potential for myeloma patients, and should be further developed and enhanced in future. Also this therapy and similar therapies need to be accessible to patients.”*
>
> *“This treatment should become standard of care earlier in the treatment regimen. Waiting for more than 2 lines of therapy jeopardizes the patient’s other major organs, like heart & kidneys as well as neutropenic& thrombocytopenic issues from multiple lines of therapy. With MM it is important to nip it in the butt asap & CART is showing evidence of doing this.”*
>
> *“I’m 4 months after Car-T cell therapy. I’ve resumed many of my activities. I’m really in a good place and enjoying life again. I’m hopeful this ‘remission’ period will last. Without Car-T, I felt my prospects were not good.”*
>
> *“Wonder treatment. Should be as widely available as possible.”*
>
> *“my biggest issue since my Car-t has been thrombocytopenia and low neutrophils. I receive Filgastrim every 2-3 weeks to boost my neutrophils.”*
>
> *“J’ai été sélectionnée grâce à ma condition physique de sportive Je suis un programme de rééducation musculaire et cardiaque, de cette façon, j’ai récupéré plus vite au niveau physique, ce qui me permet de*

lutter contre tous les effets secondaires du Myélome Je pense qu'il faut prescrire de la rééducation aux patients en sortie ou de Greffe ou de thérapie CAR-T"

4. Improved Outcomes

When Subset E respondents (37) were asked "*How desirable to you is an estimated minimum 1.25 years of extended life without you/the person you care for needing active treatment to control your/their myeloma?"* The majority of respondents (28) chose "Extremely desirable", 2 chose 'Very desirable', 3 chose 'Desirable', 1 chose 'Somewhat desirable', 1 indicated they did not know, and 2 selected 'Other'.

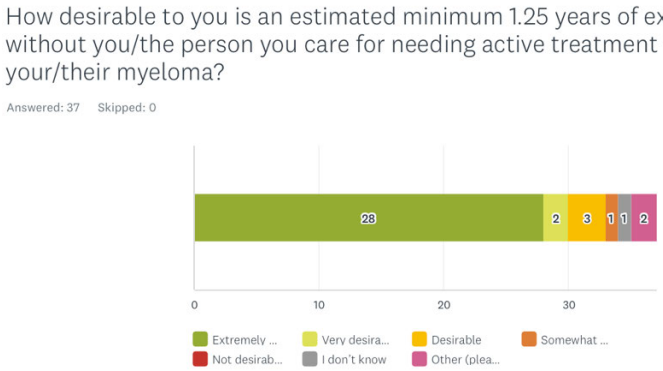


Figure 3 – Desirability of minimum 1.25 years extended life without active treatment (Subset E; 37)

Subset E was asked, "*Which side effects of ciltacabtagene autoleucel (cilta-cel) are most concerning to you as a patient/caregiver? Please rate each of the potential side effects listed below on a scale of 1 (least worrisome) to 5 (most worrisome)."* By weighted average of responses (37), the side effect rated to be most worrisome was 'Cytokine Release Syndrome' (3.76), followed by 'Infections' (3.59), and 'Neutropenia' (3.50).

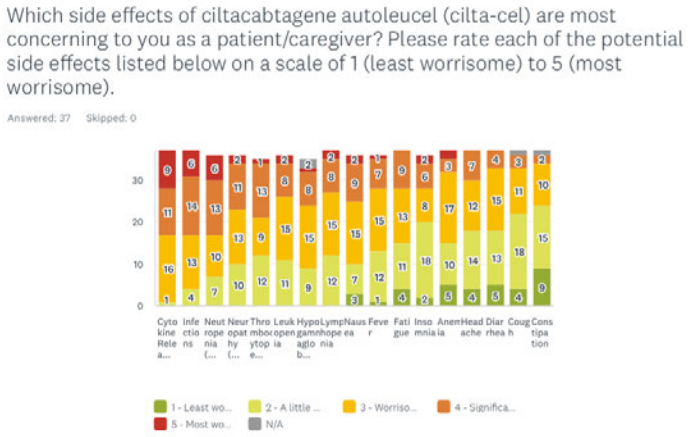


Figure 4 – Perception of cilta-cel side effects (Subset E; 37)

When asked "*Compared to other treatment options available to you/the person you care for, how worrisome do you find the overall side effect profile for ciltacabtagene autoleucel (cilta-cel)? …Please rate on a scale of 1-5 where 1 is 'not at all worrisome' and 5 is ' extremely worrisome*'", respondents (35) most

frequently chose ‘3 – somewhat worrisome’ (15), followed by ‘4 – significantly worrisome’ (9), ‘2 – slightly worrisome’ (8), ‘1 – not at all worrisome” (2), and ‘1 - extremely worrisome’ (1).

When Subset E patients (33) were asked “*Do you feel that treating your myeloma with ciltacabtagene autoleucel (cilta-cel) could improve your quality of life?”* 18 chose ‘Yes’ and 15 chose ‘I don’t know’.

Subset E patients (33) were asked “*Do you feel that ciltacabtagene autoleucel (cilta-cel) treatment could improve your long-term health outlook?”* 20 chose ‘Yes’, 1 chose ‘No’, and 12 chose ‘I don’t know’.

Subset E patients and caregivers were asked “*If you/the person you care for were eligible to receive ciltacabtagene autoleucel (cilta-cel) treatment, what do you believe the advantages and/or disadvantages could be for you?”* were given a list of factors and asked to indicate if they felt there would be an increase or decrease in that area. Respondents (36) provided the following answers for each factor: Treatment side effects (Increased: 10, No change: 5, Decreased: 7, I am unsure: 14), Control of myeloma and its symptoms (Increased: 21, No change: 0, Decreased: 5, Unsure: 10); Frequency of trips to the hospital or cancer centre for treatment (Increased: 9, No change: 6, Decreased: 13, Unsure: 8); Tolerability of the treatment’s mode of administration (Increased: 5, No change: 10, Decreased: 5, Unsure: 16); and Quality of life (Increased: 1, Decreased: 1, Unsure: 16).

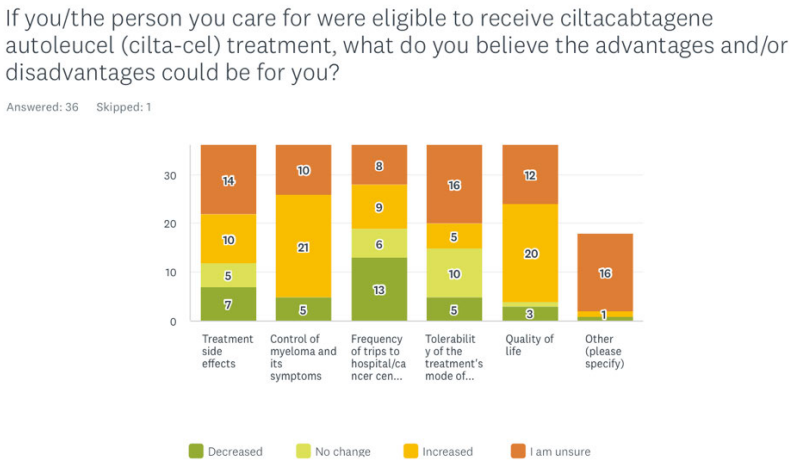


Figure 5 – Perceived advantages/disadvantages of treatment with cilta-cel; subset E (36)

When Subset E patients (33) were asked “*With what you know today, which option would you consider first as your next treatment? (Presuming your doctor has confirmed that the below treatments are appropriate for you).”*, 16 chose ‘I don’t know’, 9 responded ‘Ciltacabtagene autoleucel (cilta-cel)’, and 2 respondents each chose of ‘Other treatment suggested to you’, ‘A different CAR T-cell therapy’, ‘A clinical trial’ and ‘A bispecific antibody’.

Subset E caregivers (4) were posed a similar question “*With what you know today, which treatment option would you be most interested in, as a caregiver? (Presuming the person you care for and their doctor agree all options below are appropriate)”,* 2 responded ‘Ciltacabtagene autoleucel (cilta-cel)’, and 1 respondent each chose ‘A different CAR T-cell therapy’ and ‘I don’t know’.

When Subset E was asked “*Is there anything else you would like to say about potential ciltacabtagene autoleucel (cilta-cel) treatment ? Please share your thoughts.”* 15 respondents left comments indicating

many are excited about the potential of treatment with cilta-cel, while some are uncertain about the potential side effects and long-term benefit to their health. Some comments to this effect are as follows:

"I am hopeful that CAR T becomes available sooner than later as my treatment options are becoming limited"

"need to know what would/could be done to mitigate the side effects, especially the infections"

"If it increases PFS with minimal side effects… please bring it on, as an available option."

"Great to have a new option to control myeloma and its symptoms."

"Cela fait des années que ce suis tout ce qui se fait sur les CAR-T et celui-ci a démontré des résultats exceptionnels. J'espère de tout coeur qu'il sera accessible bientôt. D'autant plus, qu'après 6 ans sur le lenalidomide, je dois envisager à très court terme une autre option. Je suis en forme et je crois que je pourrais obtenir d'excellent résultats avec ce CAR-T. Merci."

5. Experience With Drug Under Review

Of the 16 Subset C respondents who indicated they had experience with CAR T-cell therapy, 3 were currently waiting to receive cilta-cel and 5 had already received it. These 8 respondents (6 patients, 2 caregivers) were posed the following questions about their experience with cilta-cel.

When Subset C.1 was asked to indicate how long ago they or the person they care for received treatment with ciltacabtagene autoleucel (cilta-cel), 1 respondent indicated 'Less than 3 months ago', 2 chose 'Between 3 and 6 months ago', one chose 'Between 6 and 12 months ago', and one indicated they did not remember, the remaining 3 have not yet received cilta-cel.

When Subset C.1 was asked "*Based on your experience with ciltacabtagene autoleucel (cilta-cel), how would you rate the effectiveness of this treatment in helping to control myeloma for you/the person you care for? 1 being 'not effective' and 5 'extremely effective'.* Of 5 respondents, 3 chose '5 – extremely effective', 1 chose '4 – very effective', and 1 chose '3 – effective'.

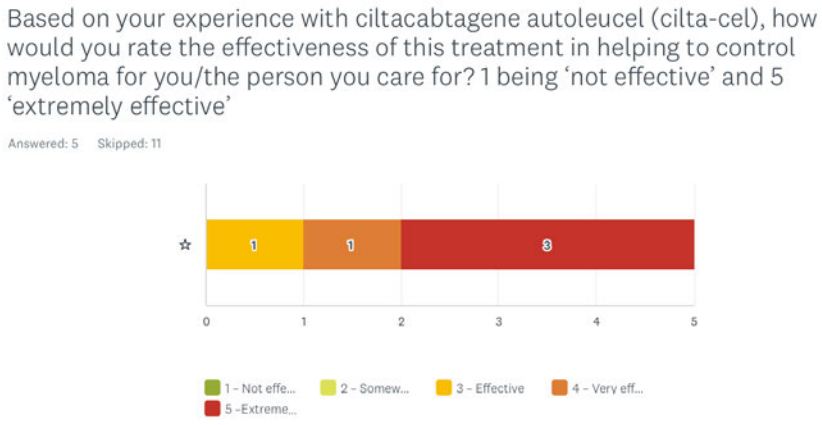


Figure 6 – Effectiveness of treatment with cilta-cel; subset C.1 (5)

When asked, *"Based on your experience receiving or caring for someone receiving ciltacabtagene autoleucel (cilta-cel), how would you rate the overall side effects? 1 being 'not at all tolerable' and 5 'extremely tolerable,'* one C.1 (5) respondent chose '5 – extremely tolerable' 2 chose '3 – tolerable' and 2 chose '2 – somewhat tolerable'.

Subset C.1 was asked, "*Which of the most frequent cilta-cel side effects listed below have you/the person you care for experienced? Please select all that apply and rate the side effects' severity on a scale of 1 'very unbearable' to 5 'very bearable'.*" By weighted average of responses (5), the side effect rated to be least bearable was 'Neurotoxicity' (2.00), followed by 'Cough' (2.00), and Neuropathy (2.25).

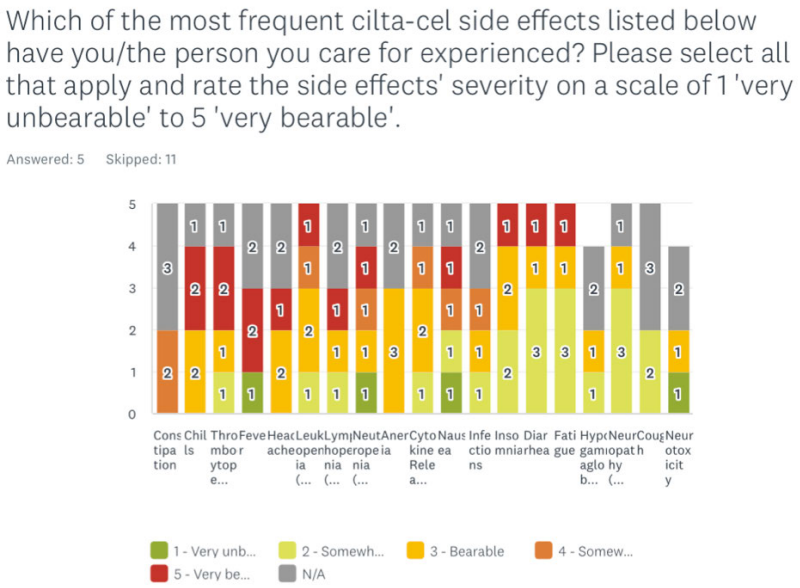


Figure 7 – Experience of cilta-cel side effects (Subset C.1; 5)

When asked, "*For a period of time after receiving ciltacabtagene autoleucel (cilta-cel), it is likely you/the person you care for were not receiving active myeloma treatment (i.e. did not need any drugs to control your/their mm). How long was this treatment interruption for you/the person you care for?",* one of 5 Subset C.1 respondents indicated '4-7 months', one chose '1-3 months', one commented that there had been no interruption, and 2 indicated it was too soon to tell.

Subset C.1 respondents (4) were asked, "*Did ciltacabtagene autoleucel (cilta-cel) meet your expectations in treating your myeloma?*" one chose 'Yes', one chose 'No', one chose 'Somewhat' and one indicated it was too soon to tell. When asked, *"Did treatment with ciltacabtagene autoleucel (cilta-cel) improve your long-term health outlook?"* one chose 'Yes', one chose 'Somewhat' and two indicated it was too soon to tell. When asked *"Did treatment with ciltacabtagene autoleucel (cilta-cel) improve your overall quality of life?"*, two chose 'Yes', one chose 'No', and one chose 'Somewhat'.

When asked if they or the person they care for had relapsed since receiving cilta-cel, 3 of 8 Subset C.1 respondents chose "My/their myeloma is still in remission' , one responded, "My/their myeloma did come back, and I/they are currently under a new treatment', and one responded "My/their myeloma has just come back, and I/they will be starting a new treatment soon", and 3 indicated it was too soon to tell.

When asked *"Is there anything else about your experience with ciltacabtagene autoleucel (cilta-cel) you would like us to know ? Please share your thoughts."* 3 Subset C.1respondents left the following comments:

> "*As Canadian was not eligible based on CADTH guidelines to receive CARVYKYI CAR-T in Canada, and is travelling to Buffalo for treatment.";*
>
> *"If you are lucky like I was, it's way easier than a stem cell transplant (of which I've had 2). Very few side effects, kept my hair, and I could eat.";*
>
> *"Experienced superficial blood clots. Experienced shortness of breath. Experienced low levels of potassium. Experienced severe muscle cramping and spasms"*

6. Anything Else?

Subset E patients and caregivers were posed questions to establish their awareness and understanding of CAR T-cell therapy. Survey responses indicated knowledge of CAR T-cell therapy is relatively widespread, as most patients and caregivers (35 of 37) had heard of CAR T and were able to correctly define it when asked (30 of 37).

The limited number of respondents with cilta-cel experience in the dataset is likely attributable to the implementation issues outlined by CADTH in their previous reimbursement recommendation for ciltacabtagene autoleucel. This is an expensive, resource intensive therapy, and survey responses indicate that access to cilta-cel is currently very difficult for Canadians, leading some patients to seek treatment outside the country.

As well, numerous comments left by both patients and caregivers show that attitudes towards CAR T-cell therapy as a potential treatment option, especially from those who were already aware of it, are generally quite favourable, and there is excitement surrounding the potential of CAR T-cell therapy for myeloma.

It appears respondents have also heard largely good things about cilta-cel. Specifically, it is notable that patients feel this therapy is worth paying for treatment in the US, which is not something frequently reported to Myeloma Canada through the drug experience surveys we have conducted in the recent past.

We would also like to mention that the two surveys Myeloma Canada has conducted on cilta-cel (in 2022 and 2024) have received an above average number of responses compared to other recently conducted drug experience surveys, even when controlling for the length of time each survey was available, and the number of times it was promoted through email/social media. This is indicative to us of the high level of interest in cilta-cel, and CAR T-cell therapy in general amongst Canadians with myeloma across time, which was again reflected in comments left through the survey.

Similarly to the results of past surveys conducted by Myeloma Canada, it was notable that cytokine release syndrome (CRS) despite causing significant concern for Subset E, (perceived to be the most concerning side effect), was considered quite bearable for Subset C.1 respondents who had actually received cilta-cel.

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PG0361
Generic Drug Name (Brand Name): ciltacabtagene autoleucel
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.
Name of Clinician Group: OH (CCO) Hematology Cancer Drug Advisory Committee
Author of Submission: Dr. Tom Kouroukis

1. About Your Clinician Group

OH(CCO)'s Drug Advisory Committees provide timely evidence-based clinical and health system guidance on drug-related issues in support of CCO's mandate, including the Provincial Drug Reimbursement Programs (PDRP) and the Systemic Treatment Program.

2. Information Gathering

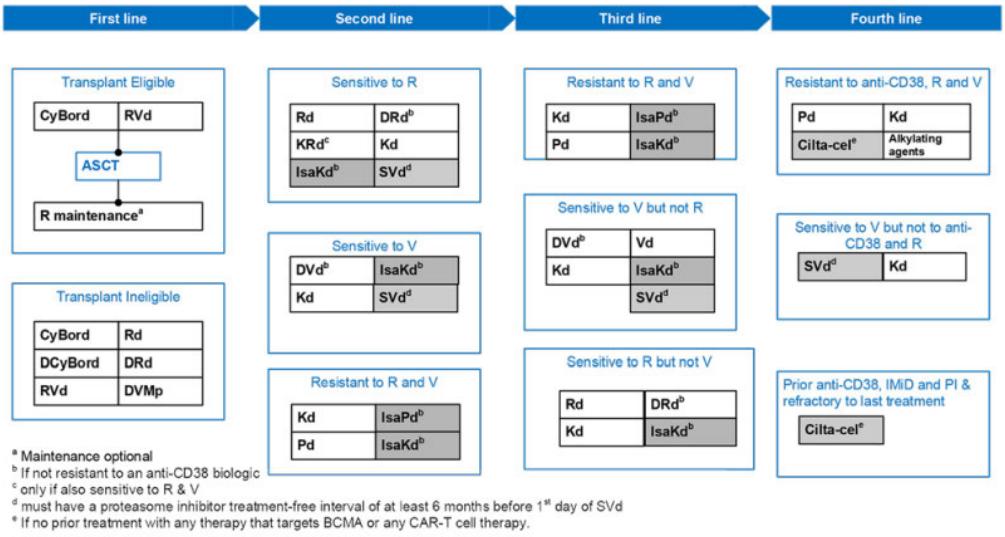
Information was gathered by videoconferencing.

3. Current Treatments and Treatment Goals

As per figure 1, there are many options available depending on first line therapy, with prior proteosome inhibitor exposure, and being lenalidomide refractory.

The treatment goals are to improve response, quality of life, disease-related symptoms, PFS, and OS.

Figure 1: Provisional Funding Algorithm Diagram for Multiple Myeloma



[a] Maintenance optional
[b] If not resistant to an anti-CD38 biologic
[c] only if also sensitive to R & V
[d] must have a proteasome inhibitor treatment-free interval of at least 6 months before 1st day of SVd
[e] If no prior treatment with any therapy that targets BCMA or any CAR-T cell therapy.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Particularly in patients who are anti-CD38 exposed, outcomes are poor. Overall, the benefits of myeloma treatments are often of short duration. There is also no treatment-free period with the other treatments available.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

As per the criteria in the clinical trial, this could be an option as second line for transplanted patients, or likely third line for non-transplanted patients who would get daratumumab first line.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

Patients have to be reasonably fit, and able to tolerate anticipated CAR-T toxicities.

It would be expected that daratumumab-based therapy would be used prior to CAR-T. Patients with significant organ dysfunction or poor performance status would be less suited for CAR-T.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Standard myeloma response criteria. Outcomes used would be improved survival, disease control, symptom improvement.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

This is a single treatment. Therefore, there are no subsequent treatments.

Challenges often rise during the time of T-Cell collection and processing if the underlying myeloma is unstable and patients may not be fit enough to proceed with CAR-T. In such situations, the plan for CAR-T can be discontinued.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

The delivery will be at tertiary hospitals/transplant centres with expertise in cellular therapy. Potential supply issues may limit the availability of CAR-T.

6. Additional Information

Bridging may be required, and treatment will be left to physician's choice.

Non-secretory patients with myeloma should also be eligible.

7. Conflict of Interest Declarations

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 clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

   OH (CCO) provided a secretariat function to the group.

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   No.

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. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Tom Kouroukis
Position: Lead, OH (CCO) Hematology Cancer Drug Advisory Committee
Date: 11-04-2024

X **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.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
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				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Selay Lam
Position: Member, OH (CCO) Hematology Cancer Drug Advisory Committee
Date: 11-04-2024

X 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.

Table 2: Conflict of Interest Declaration for Clinician 2

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Janssen	X			
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Dr. Jordan Herst
Position: Member, OH (CCO) Hematology Cancer Drug Advisory Committee
Date: 11-04-2024

X 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.

Table 3: Conflict of Interest Declaration for Clinician 3

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				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4

Name: Dr. Pierre Villeneuve
Position: Member, OH (CCO) Hematology Cancer Drug Advisory Committee
Date: 11-04-2024

X 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.

Table 4: Conflict of Interest Declaration for Clinician 4

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				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 5

Name: Rami El-Sharkaway
Position: Member, OH (CCO) Hematology Cancer Drug Advisory Committee
Date: 11-04-2024

X 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.

Table 5: Conflict of Interest Declaration for Clinician 5

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				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 6

Name: Dr. Joanna Graczyk
Position: Member, OH (CCO) Hematology Cancer Drug Advisory Committee
Date: 11-04-2024

X 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.

Table 5: Conflict of Interest Declaration for Clinician 6

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				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 7

Name: Dr. Lee Mozessohn
Position: Member, OH (CCO) Hematology Cancer Drug Advisory Committee
Date: 11-04-2024

X 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.

Table 5: Conflict of Interest Declaration for Clinician 7

	Check appropriate dollar range*			
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				

* Place an X in the appropriate dollar range cells for each company.

CADTH

CADTH Reimbursement Review
Clinician Group Input Template

Instructions

Input from clinicians is submitted to CADTH by **groups or associations of health care professionals**. Individual clinicians who wish to provide input are encouraged to work with a group that represents their profession to prepare a group submission.

CADTH will accept input from individual clinicians only when there is no relevant group or association that could provide input for the drug under review. Individuals who wish to submit input for a drug review should first contact CADTH (at requests@cadth.ca) to confirm the absence of a relevant group or association.

Completing the Template

Please complete all applicable sections of the clinician input template.

Ensure that all contributing clinicians have completed the conflict of interest declaration in the clinician input template. Input **will not be accepted without the conflict of interest section** completed for all contributors.

Accessibility Instructions

When completing the template ensure text is compliant with below accessibility legislation:

- The Accessibility for Ontarians with Disabilities Act (AODA), states all public documents must now be compliant with Ontario's accessibility guidelines to ensure that screen readers and people with reading disabilities can access and read documents. Microsoft Word provides an Accessibility Checker for identifying and repairing accessibility issues, which is located under the Review tab and Check Accessibility sub-tab.
- Tips to ensure accessibility when completing your submission include the following:
  - **For tables**: add a table title, designate row and/or column headers, do not add tables within other tables, and cells should not be blank. See below pre-formatted AODA-compliant table as an example.

Table #: Table Title Example

<Table Heading>	<Table Heading>	<Table Heading>	<Table Heading>	<Table Heading>
<Table Body Copy>	<Table Body Copy>	<Table Body Copy>	<Table Body Copy>	<Table Body Copy>

abb = abbreviation

  - **For figures, graphs, or images:** include 1 to 2 lines of alternative text (**Alt text**: *short description of image*) to describe the contents of the figure/image for screen reader function.
  - **For links:** use descriptive hyperlinks (ex., Canadian Agency for Drugs and Technologies in Health (CADTH) Website)
  - **Colour** should not be used as the sole method for conveying content or distinguishing visual elements.

Filing the Completed Template

Delete first page of this template and all red font instructions once document is complete.

Send the completed template by using the *Submit* link next to the drug listed on the Open Calls page. The input must be filed as a Microsoft Word document by the posted deadline date for the information to be used by CADTH.

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PG0361-000
Generic Drug Name (Brand Name): Ciltacabtagene autoleucel (Carvykti)
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
Name of Clinician Group: Canadian Myeloma Research Group (CMRG)
Author of Submission: D. Reece, MD on behalf of the CMRG physicians

1. About Your Clinician Group

The Canadian Myeloma Research Group (CMRG) is a Canada-wide network of researchers aiming to develop better treatments for extending life of myeloma patients, enhancing the quality of life for those living with myeloma and related disorders and working to find a cure for these diseases and other plasma cell disorders. The three main purposes of CMRG consist of: 1) conducting investigator-initiated academic clinical trials to improve the outcome of myeloma patients; 2) maintenance of a national Myeloma Database, now consisting of over 8500 patients, to evaluate real-word patterns of treatment, outcomes, risk factors and areas for future research in myeloma; and 3) generation of consensus statements for myeloma management.

Website: cmrg.ca

2. Information Gathering

CMRG holds monthly teleconferences, and participants agreed to submit a single document for feedback to CADTH which would be signed by the physicians who agreed with the information. The initial draft of the document was prepared in consultation with the CMRG Chief Medical Officer and sent to all members to obtain input. Comments and suggestions were incorporated as appropriate. The final draft was signed by physicians who agreed with all the content and their Conflict of Interest obtained as required.

3. Current Treatments and Treatment Goals

- Initial Therapy: Currently, newly diagnosed Canadian myeloma patients are still divided into those who are transplant-eligible (TE), or transplant-ineligible (TI) based on age and fitness. TE patients receive bortezomib-based induction with RVD(previously CyBorD) followed by high-dose melphalan + ASCT and then lenalidomide-maintenance until disease progression. TI patients preferentially daratumumab-based regimens, typically DRd; a small proportion with renal compromise or poor marrow reserved may comment treatment with Dara-CYBORD. Less often, TI patients may receive Rd or RVd (typically “lite”) with single- agent lenalidomide also given until disease progression. Support for these algorithms comes from published phase 3 trials as well as real-world CMRG analyses. These approaches have also been endorsed by CADTH in the recent Provisional Funding Algorithm.

- Second-line therapy (after 1 prior regimen): Second-line therapy depends on whether patients have progressed on lenalidomide (which currently includes the majority of Canadian TE and TI patients). A key priority to date has been the inclusion of an anti-CD38 antibody at this time if one was not used in the first-line setting. ASCT patients on lenalidomide maintenance usually receive DVd or, more recently, IsaKd, at the time of first progression. These regimens are also utilized in the TI patient if they progressed on lenalidomide in the era before the availability of daratumumab-based regimens such as DRd as initial therapy. In the uncommon TE or TI patient who has not progressed on lenalidomide in first-line, DRd is strongly preferred as the second-line regimen (in the absence of prior daratumumab exposure). Other potential regimens in patients progressing on lenalidomide +/- daratumumab include XVd and Kd (+/- cyclophosphamide). Finally, a small number of patients with private insurance can access pomalidomide + daratumumab + dex (DPd) as an alternative to Isa-Kd in second-line if they have progressed on lenalidomide but not yet received a CD38 monoclonal antibody in initial therapy.

  Despite the preferential use of triplet regimens for second-line treatment, prior progression on first-line lenalidomide by itself constitutes an adverse risk even in the absence of other recognized high-risk features. The phase 3 trials that established the efficacy of the regimens listed above that are now an option for second-line use in Canada contained relatively low numbers of patients progressing on lenalidomide simply due to the era in which they were performed. Data on the subset of patients progressing on first-line lenalidomide has become available for many of these regimens, and consistently describes a shorter PFS than for the entire group and those without progression on lenalidomide. Specifically, the median PFS has been less than 18 months for Kd, KCd, DVd, DPd, XVd and PVd (the latter of which is not formally funded but which can occasionally be accessed via compassionate means). Real-world evidence from CRMG Database analyses confirms the suboptimal results of these regimens used in second-line after lenalidomide (references here). The longest median PFS reported in a prospective trial of relapsed/refractory patients, before the newest immunotherapeutics, was seen with IsaKd in the IKEMA trial (Martin T, et al. Blood Cancer J. 2023 May 9;13(1):72). In this study, the median PFS for all myeloma patients progressing after 1-3 prior lines of therapy was 35.7 months. However, subset analyses noted that the 18-month PFS in patients refractory to lenalidomide was only 53% compared to 77% in all patients with only 1 prior line of therapy and 68% in those with greater that 1 line (Dimopoulos MA, et al. Am J Hematol 2023;98:E15–E19). Additionally, not all individuals are eligible for this carfilzomib-based regimen due to cardiovascular, renal, or logistic issues. Due to the relatively recent funding of IsaKd, real-world Canadian results are not yet available.

- Third-line therapy (after 2 prior regimens): If patients have not yet received an anti-CD38 monoclonal antibody by the time of third-line treatment is needed, every effort is made to procure a combination containing such agents such as IsaPd. Of note, this represents a dwindling population of patients. Otherwise, POM, carfilzomib or selinexor can be administered with dex and a third agent which may have been utilized before. Funded options include POM + dex +/- cyclophosphamide (PCd), carfilzomib + dex +/- cyclophosphamide (Kd or KCd). or XVd. Again, triplet regimens are generally preferable. The median PFS with any of these regimens is less than 12 months.

- Fourth-line therapy: Until recently, the options have been extremely limited. A pomalidomide- or carfilzomib-based regimen such as Pd or Kd may be utilized if not used earlier in the third line. Additional treatment options include a regimen of bortezomib + steroids (Vd) yields a short PFS and often cannot be revisited in many jurisdictions if patients are previously refractory to proteasome inhibitors. XVd is approved and funded after1 prior line and can be used in the setting of advanced myeloma. Although cyclophosphamide can be added to many regimens or even used with steroids as a doublet (CyDex or cyclo/prednisone), the cumulative lifetime exposure to cyclophosphamide is limited to 1 to 2 years for each patient due to the risks of bladder cancer or secondary MDS/AML from this alkylating agent; the latter risk may restrict use of alternative alkylating agents

like melphalan. A CMRG database analysis indicated that the median PFS for patients who had been triple-class exposed or refractory was 4.4 and 4,6, respectively. Given these findings, palliation/best supportive care and/or local radiotherapy may be appropriate in some individuals.

Belantamab mafodotin, a BCMA antibody drug conjugate has been available via a Health Canada SAP and has been utilized in the fourth-line setting on a patient-by-patient case. There is reluctance to continue to access this drug, however, as it may preclude subsequent use of a BCMA-targeted bispecific T-cell engager monoclonal antibody (BiTE) or CAR-T cell construct.

The recent approvals of the anti-BCMA BiTEs teclistamab and elranatamab offer a longer PFS than the prior treatments listed above. These 2 agents are approved by Health Canada but are not yet funded publicly. There are ongoing drug access programs provided by pharma in Canada that allow a few select patients to receive them. These agents require special expertise during the step-up period to properly manage unique complications such as CRS and ICANS. Widespread integration of these BiTEs into provincial myeloma algorithms requires additional infrastructure in terms of more physical resources and staffing to address the specialized needs of these patients.

Similarly, the BCMA CAR-T cell construct cilta-cel is approved by Health Canada but is not yet funded in fourth-line therapy. Although supportive care considerations overlap with those of the BiTEs, cilta-cel's administration is more complex due to its need for T-cell collection, bridging therapy while waiting for CAR-T processing, lymphodelpletion therapy and CAR-T cell infusion, even though it is given only once. As with the BiTEs, resources will need to be built into the current system to accommodate: 1) the increasing proportion of patient who will receive this treatment; 2) the specific early toxicities which are more severe than those seen with the BiTEs; and 3) the need for patients to remain close to the treating centre during the early post-administration days.

- Clinical trials are key to improving survival of Canadian patients through early access to promising agents in this setting but clinical trial participation is markedly limited by: 1) strict eligibility criteria such as platelets over 75 x 10^9/L or near-normal renal function that may be challenging to meet in advanced myeloma; 2) the decision by pharma to open promising trials in only a few Canadian sites, or, as in the case of some CAR-T cell studies, to bypass Canada completely in favor of European or US sites; 3) the policy of pharma to offer a time-limited trial spot for only few days so if a patient is not available immediately, the opening is removed and given to a centre in another country; 4) slow trial accrual to promising agents undergoing evaluation in a phase 1 study as DSMB reviews need to take place before a new cohort can be opened.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Myeloma remains incurable despite the introduction of new agents over the last 2 decades. Patients eventually become refractory to all available funded anti-myeloma agents. At this point, the symptom burden for patients is high with bone pain/destruction, anemia and other cytopenias, renal damage, hypercalcemia and a high risk of infection. The highest unmet need in myeloma continues to be adequate treatment for patients who have progressed despite exposure to effective agents. In the past, this group largely consisted of those who had already received the three major classes drugs -- an IMID, PI and anti-CD38 monoclonal antibody ("triple-class exposed or triple-class refractory"). Initially, these 3 agents were given in sequential regimens, and the unmet need was most apparent after 3 or more lines of treatment. However, with the movement of combinations of three major drug class to the first- and second-line setting, exposure (and resistance) to multiple drug classes now occurs much earlier in the disease course. Specifically, the funding of RVd induction in TE and DRd in TE patients as first-line regimens means that patients may be triple-class exposed/refractory after 2 lines of therapy (or even 1 line in the case of the few patients in Canada who can access daratumumab plus RVd (DVD) before ASCT via clinical trials or private insurance).

Importantly, as discussed above, more information has become apparent that, despite the clear benefits of lenalidomide as part of first-line therapy, progression on this potent agent even as single-agent maintenance leads to shorter PFS outcomes of 11-18 months with virtually all traditional second-line regimens (including those containing an anti-CD38 monoclonal antibody) compared to the results without such exposure. With subsequent regimens, periods of myeloma control become progressively shorter. In summary, the unmet need in myeloma has shifted much earlier in the disease course and warrants the use of the more powerful immunotherapies earlier in sequencing. From a clinical perspective, Canadian hematologists perceive that drug exposure, rather than lines of therapy, more accurately defines the need for access to the innovative immunotherapeutics in order to forestall the development of refractory myeloma and its detrimental effects on patient quality of life, caregiver burden and a shortened lifespan.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

The drug in question would be appropriate for myeloma patients previously treated with a PI and IMiD and refractory lenalidomide after 1-3 prior treatment lines. Based upon the latest phase 3 trial data, the results with cilta-cel -- with its novel mechanism of action -- far exceed that of any previous standard of care regimen for this group, including the standard regimens used more often in Canada, as discussed above. The availability of cilta-cel in the proposed setting would pertain primarily to patients who have had 2 prior lines; they may or not may not have already received an anti-CD3 monoclonal antibody as well in the current treatment environment. Importantly, given the inferior prognosis of progression on lenalidomide, patients would have access cilta-cel after 2 prior lines, rather than having to be treated with another regimen (of minimal benefit) simply to fulfill the criteria of “3 prior lines” now needed to access CAR-T therapy under current funding proposals. Requiring an extra suboptimal regimen only exposes the patient to unnecessary side-effects but also places an unwanted burden on the health care system. Moreover, patients may become too unwell to receive cilta-cell later as the disease may be progressing so quickly after that extra line to withstand the several-week period for T-cell collection and manipulation, thereby losing their chance for this modality.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

The least suitable patients would include frail patient as well as those with rapidly proliferating disease, ongoing infection, significant organ dysfunction and/or with pre-existing pancytopenia.

Patients with a good performance status, minimal or no comorbidities, low tumor burden and adequate organ function and blood counts are the most likely to have the best outcomes.

Patients with other disease-related adverse prognostic factors, such as extramedullary disease and high-risk cytogenetics, do not fare significantly worse and should be eligible for cilta-cel. Chronological older age alone *per se* does not seem to be an exclusion factor. From a practical point of view, patients whose disease is progressing at a rate anticipated to allow them to remain stable and relatively well during the 4–5-week time period necessary for CAR-T cell processing would be the best suited for this treatment in order to avoid death prior to cell therapy product delivery.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Responses are based on the monoclonal protein marker in the serum and/or urine, bone marrow biopsy and in some instances imaging studies (standardized International Myeloma Working Group Criteria, IMWG). These are aligned with those used in the trial, which also included the emerging parameter of marrow minimal residual disease (MRD).

Clinically meaningful responses usually correlate with achievement of at least a partial remission (PR) by IMWG Consensus Criteria. A PR or better is accompanied by an improvement in symptoms (cessation of bone destruction with less pain, fractures and need for radiotherapy), improvement in energy level and better ability to perform activities of daily living. Notably, cilta-cel produces unprecedented rates of responses that are deeper than a PR compared to standard regimens. Specifically, the rates of stringent complete responses (CR) and CR are on the order of 70-75% compared to 20% with standard therapy. Response status in myeloma is generally assessed every 1-3 months depending on clinical stability and regimen used for therapy.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Cilta-cel therapy represents a single infusion and therefore patients who meet eligibility criteria should receive the agent. Conventional factors for drug discontinuation such as progressive disease or adverse events are therefore not applicable in this context given the one-time design of CAR-T cell therapy.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

This therapy is appropriate for a major medical facility with expertise in other cellular therapies for hematologic malignancies. There needs to be close interaction between a specialized inpatient service, an ICU familiar with immunosuppressed cancer patients, and an outpatient facility experienced in handling complex and urgent hematologic problems. Appropriate coordination with the Emergency Department to expedite care of patients recently discharged following this treatment is also required.

The identification and planning of patients for cilta-cel therapy will require careful matching of available resources with the potential numbers of patients with relapsed myeloma. Treated patients may required an inpatient bed for about 2 weeks (or longer if complications occur) and may require readmission. They potentially require ancillary measures to treat CRS, neurotoxicity, and infections, and may need ICU support. Specialized training is required for staff, and the medical centre's infrastructure and clinical pathways must be modified to meet the safety standards for cilta-cel treatment and subsequent follow-up. These realities are expected to limit the numbers of myeloma patients that can be treated. Effector Cell Therapy Committees/programs will likely need to establish guidelines for each institution or jurisdiction.

Due to the numbers of potential myeloma patients that may benefit from cilta-cel, efforts are underway to allow the option of outpatient treatment for some, or all, of the phases of this complex therapy. This will necessitate the development of strict SOPs, staff training at multiple levels, patient education and accommodation for patients who do not live close to the medical centre. Pathways for rapid admission to a centre with expertise in this field must be readily available at all times.

6. Additional Information

Is there any additional information you feel is pertinent to this review?

<Enter Response Here>

7. Conflict of Interest Declarations

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 clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

   No

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   No

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. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Ibraheem Othman
Position: Hematologist at ABCC, Regina
Date: 30-04-2024

☒ **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.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Add company name	X	X	X	X

Declaration for Clinician 2

Name: <Arleigh McCurdy
Position: <MD
Date: 30-04-2024

☑ 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.

Table : Conflict of Interest Declaration for Clinician

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Janssen		X		
Sanofi	X			
GSK	X			
Pfizer	X			
Forus	X			
Amgen	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Dr. Jason Hart
Position: Hematologist/Medical Oncologist
Date: 30 Apr 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.

NO CONFLICT OF INTERESTs to Declare.

Table 2: Conflict of Interest Declaration for Clinician 2

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	X ($0)			
none	X ($0)			
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4
Name: Martha L Louzada

Position: hematology Consultant
Date: 30 -04-2024

☒ **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.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
BMS	x			
Janssen	x			
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 5

Name: Dr. Darrell White
Position: Hematologist, Dalhousie University and QEII Health Sciences Centre
Date: 30-04-2024

☒ 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.

Table 5: Conflict of Interest Declaration for Clinician 5

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
BMS		X		
Janssen			X	

Declaration for Clinician 6

Name: Dr. Rami Kotb
Position: Hematologist, Oncologist, Cancer Care Manitoba
Date: 30-04-2024
☒ 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.

Table 6: Conflict of Interest Declaration for Clinician 6

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
BMS, Amgen, JNJ		X		
Takeda	X			
Sanofi, Merck				X
Karyopharm				X

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 7

Name: Dr. Nichole La ferriere
Position: Hematologist
Date: 30-04-2024

☒ 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.

Table 7: Conflict of Interest Declaration for Clinician 7

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Abbvie	x			
Alexion	x			
Amgen	x			
Astellas	x			
Astra Zeneca	x			
Bayer Oncology	x			
Beigen Pharma	X			
Jansen	x			
Pfizer	x			
Sanofi	x			
Sobi	x			

Declaration for Clinician 8

Name: Dr. Kevin Song
Position: Hematologist, Vancouver General Hospital
Date: 30-04-2024

☒ 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.

Table 8: Conflict of Interest Declaration for Clinician 8

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Bristol Myers Squibb		X		
Janssen		X		
Amgen		X		

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 9

Name: Jesse Shustik
Position: Medical Oncologist, BC Cancer – Surrey Centre
Date: 30-04-2024

☒ **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.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Janssen		x		
Sanofi		x		
Pfizer	x			
BMS	x			
Forus	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 10

Name: Bethany E. Monteith
Position: Hematologist, Kingston Health Sciences Center
Date: 30-04-2024

☒ **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.

Table 10: Conflict of Interest Declaration for Clinician 10

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Janssen				x
Honoraria				x
Sanofi				x
Pfizer				x

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 11

Name: Dr. Donna Reece

Position: Chief Medical Officer, CMRG

Date: 08-09-2023

☒ 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.

Table 11: Conflict of Interest Declaration for Clinician 11

Company	Check appropriate dollar range*

	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
BMS/ Celgene			X	
Janssen			X	
Amgen			X	
Sanofi	X			
GSK	X			
Takeda	X			

Declaration for Clinician 11

Name: Dr. Hira Mian
Position: Assistant Professor
Date: 30-04-2024

☒ 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.

Table 11: Conflict of Interest Declaration for Clinician 11

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Takeda, Jansen, BMS, Sanofi, Amgen, GSK (advisory board fees)		X		
Jansen Research Funding				X
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 12

Name: Dr. Victor Zepeda

Position: Hematologist, Oncologist

Date: 30-04-2023

☒ 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.

Table 12: Conflict of Interest Declaration for Clinician 12

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Janssen		X		
BMS	X			
Takeda	X			
Amgen	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 13

Name	Alissa Visram
Position	*Physician, The Ottawa Hospital*
Date	20/03/2025

X	**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**
Janssen	X	☐	☐	☐
Pfizer	X	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Declaration for Clinician 14

Name: Dr. Alfredo de la Torre

Position: Hematologist

Date: 30-04-2024

☒ 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.

Table 14: Conflict of Interest Declaration for Clinician 14

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Nothing to declare				

* Place an X in the appropriate dollar range cells for each company.