CADTH

ELCADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

ELRANATAMAB (Elrexfio)

(Pfizer Canada ULC)

Indication: For the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 3 prior lines of therapy including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

May 16, 2024

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0315-000-000
Brand name (generic)	ELREXFIO (elranatamab)
Indication(s)	Relapsed or refractory multiple myeloma
Organization	Myeloma Canada
Contact information	Name: Aidan Robertson – [redacted]

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

Myeloma Canada is pleased that pERC has decided to recommend elranatamab for reimbursement (with conditions) and agrees with the approval recommendations given the concerns noted in the review. However, we do not agree with the conditionality of the price reduction at the recommended 72%, we think this will be too high and may limit patient access. Regardless, we were glad to note that this is a comparatively lower required price reduction than for other recently reviewed treatments in myeloma (teclistamab, cilta-cel). Access to this novel therapy will be another critical step towards meeting the growing need for effective myeloma treatment options in the fourth line setting and beyond.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐

Yes, it appears our feedback has been considered in the decision and is accurately described.

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

The reasons for the recommendation are generally clear. The areas that require clarification are largely where this recommendation differs from the recommendation for teclistamab. Especially considering when asked if the reimbursement criteria for elranatamab should be aligned with that of teclistamab, *"The clinical experts indicated that it would be reasonable for the two drugs to have similar reimbursement criteria if they are recommended for reimbursement by pERC" (pg12)*. A point with which Myeloma Canada strongly agrees.

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

We feel clarification is needed regarding why the 'feasibility of adoption' issues articulated in the recommendation depart from those issued for teclistamab, as we are concerned these discrepancies may unduly impact price negotiations.

For example, both "7. *The organizational feasibility of jurisdictions having specialized treatment centres with the infrastructure and resources required to administer elranatamab and manage adverse events must be addressed*." (Table 1; pg6), and the following point in Table 2: "*There are additional costs associated with the requirement of tocilizumab for CRS, which impact drug program budgets (acute care)." (pg13)* are not included in the teclistamab recommendation, yet CRS and ICANS are side-effects occurring at very similar rates for both drugs.

On page 5, in row 7 of Table 1; the recommendation states: "*The product monograph recommends monitoring patients for CRS and neurologic toxicity, including ICANS, and states that elranatamab should be administered by a healthcare professional with appropriate medical support to manage these severe reactions."* As seen below, the Canadian product monographs for both elranatamab and teclistamab, on their respective 4th pages, in the 'SERIOUS WARNINGS AND PREAUTIONS BOX' each list Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) and recommend '*monitoring patients'.*

	Elranatamab (p4)	Teclistamab (p4)
ICANS	*"Neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) and serious and life-threatening reactions, can occur with Elrexfio**. Monitor patients for signs and symptoms of neurologic toxicity, including ICANS, during treatment.** The onset of ICANS may be concurrent with CRS, following resolution of CRS, or in the absence of CRS. Withhold Elrexfio until the neurologic toxicity resolves or permanently discontinue based on severity."*	"*Serious or life-threatening neurologic toxicities, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), can occur following treatment with Tecvayli. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS. **Monitor patients for signs or symptoms of neurologic toxicity, including ICANS, during treatment**. Withhold Tecvayli until neurologic toxicity resolves or permanently discontinue based on severity."*

There is considerable clinical evidence of similar experiences with ICANS between elranatamab and teclistamab (low incidence, low severity), and the product monograph's requirement that elranatamab be "*administered by a healthcare professional with appropriate medical support to manage these severe reactions",* can be seen as equivalent to the teclistamab monograph's requirement to remain within 48 hours of a specialized treatment centre. As well, both recommendations concur that following the step-up dosing period, it would in most cases, be safe to administer *both* treatments in an outpatient setting (Table 2; pg13).

Therefore, it remains unclear why pERC perceived the implementation issues for both drugs differently, particularly why elranatamab raised notably more concerns.

In the spirit of transparency, we ask that either:

A) the Final Recommendation provides a brief explanation as to why infrastructure, resource issues etc. related to management of ICANS and CRS were of significantly greater concern for elranatamab, than for teclistamab, and include reference to the clinical evidence pERC relied on to make this determination.
OR
B) The recommendation(s) for teclistamab and/or elranatamab are modified to bring them into alignment.

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

We acknowledge the pERC felt the current evidence was insufficient to support reimbursement of elranatamab in patients previously treated with BCMA targeted therapies, nor biweekly dosing in patients achieving a certain level of response. Yet we feel giving physicians the ability to treat patients in these (currently) smaller cohorts with elranatamab, will help generate the real-world data necessary to better understand its efficacy in these contexts. As pERC noted on page 6 there is a *"gap in the available comparative evidence for this population [patients with prior exposure to BCMA-directed therapy]".* Similarly, we hope that if additional *supporting* evidence on biweekly dosing becomes available, the pERC's position on these issues will be amended— in which case we would feel it necessary for the price reduction conditions to be recalculated based on both the reduction in healthcare resource utilization costs, and potential improvement in quality of life for patients.

CONDITION 1.4: "*No prior exposure to BCMA-directed therapy*" (page 4)
It is unclear to us why this condition was included for elranatamab, but not teclistamab.
Both the *MajesTEC (teclistamab)* and *MagnetisMM (elranatamab)* trials presented results from a small number of patients previously treated with BCMA targeted therapies. We recognize there is limited insight to be gained from direct comparison between trials, but the published results of two pooled analyses do not appear meaningfully different enough for us to understand the pERC's decision in favour of teclistamab. Especially considering the very small sample sizes in both trials, the clinical experts' advice to include patients with prior BCMA exposure (pg11), and the persistent, critical need for better treatment options in the 4th line+ relapsed/refractory myeloma setting.

Elranatamab	Teclistamab
86 patients included, mFU of 10.3 months (0.3−32.3) *"ORR was **45.3%** (95% CI 34.6−56.5), with complete response or better achieved in **17.4%**. ORR for patients with prior BCMA-directed ADC and CAR-T cells was **41.4%** (95% 28.6−55.1) and **52.8%** (95% 35.5−69.6), respectively. Median duration of response was not reached…"*	38 patients included, mFU of 6.9 months (0.7–8.7) *"ORR was **40%** (95% CI 21–61). 5 pts (**20%**) achieved a complete response or better. The ORR (95% CI) was **38%** (15–65) in ADC-exposed pts and **45%** (17–77) in CAR-T–exposed pts respectively. Median duration of response was not reached."*
Manier S et al., P870: Efficacy and Safety Of Elranatamab In Patients With Relapsed/Refractory Multiple Myeloma And Prior B-Cell Maturation Antigen (Bcma)-Directed Therapies: A Pooled Analysis From Magnetismm Studies. Hemasphere.	Touzeau, C. et al., Efficacy and safety of teclistamab (tec), a B-cell maturation antigen (BCMA) x CD3 bispecific antibody, in patients (pts) with relapsed/refractory multiple myeloma (RRMM) after exposure to other BCMA-targeted

2023 Aug 8; https://doi.org/10.1097%2F01.HS9.0000970384.26808.c7 .	agents. *JCO* **40**, 8013-8013(2022). DOI:10.1200/JCO.2022.40.16_suppl.8013

For Canadian patients with prior exposure to BCMA targeted therapies, treatment options are *extremely limited,* considering many of the newest treatments for mm available (or accessible through clinical trials) in Canada are BCMA targeted (idecel, cilta-cel, blenrep, teclistamab, elranatamab, linvoseltamab, etc…), and they are primarily approved for use in later lines of therapy (fourth line+). Similarly, patients who have received BCMA directed therapy (likely on their 4th line or beyond), patients are increasingly less likely to qualify for clinical trials as need for a new treatment often aligns with a decline in health, and prior BCMA directed therapy may also be a criterion of exclusion. Excluding these patients from access to new treatments like elranatamab and teclistamab means they will have next to zero options— funded or otherwise.
As well, conditions such as these, when implemented by provincial and territorial drug plans increase complexity for patients and may cause difficulties and delays in accessing treatment. For example, a patient receives funding for cilta-cel, the T-cell collection is completed, but the patient becomes ill, or their myeloma progresses to the point they are unable to receive their infusion. Though there would be a paper record of them 'receiving' a BCMA-directed therapy, they would still clinically qualify for elranatamab as per the listed conditions.

For Condition 1.4 (exclusion of prior BCMA patients), we would appreciate if the Final Recommendation either:

A) Details how pERC's analyses of the data for elranatamab and teclistamab in patients *with* prior exposure to BCMA targeted therapies, illuminated the meaningfully inferior efficacy of elranatamab in this population, and supported the decision to include this additional condition only for elranatamab, (with reference to the evidence used).
   OR
B) Modifies the recommendation(s) for elranatamab and/or teclistamab to align them**.**

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

Appendix 1. Conflict of Interest Declarations for Patient 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.

A. Patient Group Information	
Name	*Aidan Robertson*
Position	*Advisor, Health Policy and Advocacy*
Date	*15-05-2024*
☒	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
Abbvie	☐	☒	☒	☒
AstraZeneca	☐	☐	☒	☐
Apotex	☐	☐	☐	☒
Amgen	☐	☐	☐	☒
The Binding Site	☐	☐	☐	☒
BMS	☐	☐	☐	☒
FORUS Therapeutics	☐	☒	☐	☒

GSK	☐	☐	☐	☒
IMC	☐	☒	☐	☒
JAMP	☐	☐	☒	☐
Janssen	☐	☐	☐	☒
Merck	☐	☐	☒	☐
Pfizer	☐	☐	☐	☒
Rapid Novor	☐	☐	☐	☒
Roche	☐	☐	☒	☐
Sanofi	☐	☐	☐	☒
Sebia Diagnostics	☐	☐	☒	☐
Takeda	☐	☐	☒	☐

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: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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

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

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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

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

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0315-000
Brand name (generic)	Elrexfio (elranatamab)
Indication(s)	For the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.
Organization	The Leukemia & Lymphoma Society of Canada (LLSC)
Contact information[a]	Name: Colleen McMillan, Advocacy Lead - [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
We agree that there is a currently unmet need within this patient population for accessible and effective treatment options, beyond third line, that delay disease progression, prolong survival, improve quality of life, and have manageable side-effects. elranatamab could be an effective and more accessible treatment option that may delay disease progression and prolong survival in patients. elranatamab could be more accessible compared to the relevant comparator CAR-T cell therapy.		

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	☐
The LLSC did not submit input regarding this review, however, we fully support the input submitted by Myeloma Canada on behalf of patients and caregivers.		

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.		

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

Appendix 1. Conflict of Interest Declarations for Patient 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.

A. Patient Group Information	
Name	*Colleen McMillan*
Position	*Advocacy Lead*
Date	*15-05-2024*
☒	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**
Pfizer Canada	☐	☐	☐	☒
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0315
Brand name (generic)	Elrexfio (elranatamab)
Indication(s)	For the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.
Organization	OH (CCO) Hematology 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. Patients with plasma cell leukemia, amyloid related to myeloma, controlled CNS disease should be eligible for elranatamab despite being excluded from the trial. Despite lack of evidence, there should be an allowance for elranatamab after CAR-T cell therapy or following other anti-BCMA therapies.		

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐
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.		

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

Appendix 1. Conflict of Interest Declarations for Patient 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.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

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

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

D. New or Updated Conflict of Interest Declaration

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

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

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 a secretariat function to the group.		
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. Pierre Villeneuve		

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	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0315-000
Brand name (generic)	Elranatamab
Indication(s)	Relapsed or refractory multiple myeloma
Organization	The Canadian Myeloma Research Group
Contact information[a]	Name: Donna E Reece, MD

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

Bispecific and CAR-T cell therapies are presently positioned to address the unmet need in the "triple-class exposed/refractory" myeloma patients. Like the recently endorsed products cilta-cel and bispecific monoclonal antibody teclistamab, the latest data for elranatamab are expected to be better than any currently utilized—or publicly funded--regimens for "triple-class refractory" patients.

Currently, it would be used in sequence after the other lines of therapy described in the available information from CADTH.

As elranatamab will be used late in the lines of myeloma treatment, i.e. after failure of multiple agents, it is not expected to impact the sequencing of agents earlier in the disease course or lead to a major change in the upstream treatment algorithms. We believe elranatamab will provide an additional, more readily accessible T-cell redirecting therapy to patients refractory to the most commonly used agents, given that it represents an "off the shelf" treatment.

However, there is one provision in the current draft that the concerns the CMRG physicians. There is increasing information supporting re-treatment with BCMA-targeting agents at the time of further relapse. Such data has been available for CAR-T and teclistamab previously, and now has been presented for enranatamab as its trials have matured. Specifically, Nootka AK, et al presented an oral abstract at ASCO 2023 (abstract 8008) summarizing the results of enranatamab in in a pooled analysis of 87 patients with prior BCMA exposure treated on clinical trials, including 64 who participated in cohort B of the pivotal MagnetisMM-03 study. This group had received a median of 7 prior regimens, primarily an ADC (n=59) or CAR-T cell therapy (n=36), and 62.1% were considered refractory to the BCMA agent. The overall response rate was 46% and median duration of response 17.1 months. The median PFS was 5.5 months (3.9 months after ADC and 10.0 months after CAR-T) while the median overall survival was 12.1 months for all subgroups studied.(final slide presentation available).

Therefore, the specific wording for eligibility for elranatamab--based on prior exposure to an alterative BCMA-targeted agent at relapse--is of considerable concern to Canadian hematologists. Belantamab mafodotin, the BCMA-directed antibody drug conjugate (ADC), has been the only "modern" immunotherapeutic available to date for our Canadian triple-class exposed patients in the absence of CAR-T and bispecific antibody accessibility. Although the target is the same, the mechanism of action of belantamab differs from that of the bispecifics and CAR-T cell therapy. The point has been raised previously that there is a strong precedent for repeating drugs that act on the same target but work differently (examples include the different PIs (target = the proteasome) and different IMiDs (targets = ikaros and aiolos) in myeloma. As mentioned in previous documents assessing the role of BCMA bispecific antibodies in relapsed/refractory myeloma, there are settings in which a previously exposed patient is likely to retain sensitivity to another BCMA agent—such as when an ADC has been stopped due to ocular toxicity—and these patients should not be automatically excluded from elranatamab. Prior CAR-T represents another setting, since myeloma progression is likely due to failure of CAR-T cell persistence rather than BCMA antigenic change/loss.

Moreover, it is noted that the CADTH recommendation for the BCMA-directed bispecific antibody teclistamab does NOT specifically exclude prior BCMA exposure in order for a patient to be considered for treatment. Given the similarity in these 2 agents in terms of target and mechanism of action, as well as the emerging and consistent data on use of a second BCMA agent, Canadian hematologists feel strongly that there should be consistency in the definitions of the eligible population with these 2 bispecific antibodies and that both BITEs should **not** automatically disallow those with prior BCMA exposure in the eligibility criteria.

. 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.		

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

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
1. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
3. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)* *IN ADDITION TO DECLARATIONS PROVIDED AT THE OUTSET THE FOLLOWING WERE UPDATED*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. Donna Reece*
Position	*Chief Medical Officer, CMRG*
Date	*16-05-2024*

☒	**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
BMS/ Celgene	☐	☐	☒	☐
Janssen	☐	☐	☒	☐
Amgen	☐	☐	☒	☐
Sanofi	☒	☐	☐	☐
GSK	☒	☐	☒	☐
Takeda	☒	☐	☐	☐

New or Updated Declaration for Clinician 2

Name	*Dr. Hira Mian*
Position	*Assistant Professor, Hamilton*
Date	*16-05-2024*
☒	**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
BMS	☐	☒	☐	☐
Janssen	☐	☐	☐	☒
Amgen	☐	☒	☐	☐
Sanofi	☐	☒	☐	☐
GSK	☐	☒	☐	☐
Takeda	☐	☒	☐	☐

New or Updated Declaration for Clinician 3

Name	*Dr. Sindu Kanjeekal*
Position	*Hematologist/Oncologist, Windsor*
Date	*16-05-2024*

☒	**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
Nothing to Declare	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Dr. Anthony Reiman*
Position	*Professor, Department of Oncology, Saint John Regional Hospital*
Date	*16-05-2024*
☒	**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
Nothing to Declare	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Dr. Sita Bhella*
Position	*Hematologist/Oncologist, Toronto*
Date	*16-05-2024*
☒	**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
Gilead	☒	☐	☐	☐
Novartis	☒	☐	☐	☐
Sanofi	☒	☐	☐	☐
Amgen	☒	☐	☐	☐
BMS	☒	☐	☐	☐

New or Updated Declaration for Clinician 6	
Name	*Dr. Guido Lancman*
Position	*Hematologist/Oncologist, Toronto*
Date	*16-05-2024*
☒	**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
Janssen	☐	☐	☒	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 7	
Name	*Dr. Ibraheem Othman*
Position	*Hematologist/Oncologist, Regina*
Date	*16-05-2024*
☒	**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
Nothing to Declare	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 8	
Name	*Dr. Darrell White*
Position	*Hematologist, Dalhousie University and QEII Health Sciences Centre*
Date	*16-05-2024*
☒	**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**
BMS	☐	☒	☐	☐
Janssen	☐	☐	☒	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 9	
Name	*Dr. Kevin Song*
Position	*Hematologist/Oncologist, Vancouver*
Date	*16-05-2024*
☒	**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**
BMS	☐	☒	☐	☐
Janssen	☐	☒	☐	☐
Amgen	☐	☒	☐	☐

New or Updated Declaration for Clinician 10	
Name	*Dr. Christopher Venner*
Position	*Hematologist/Oncologist, Vancouver Centre*
Date	*16-05-2024*

☒	**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
Celgene/BMS	☒	☐	☐	☐
Takeda	☒	☐	☐	☐
Janssen	☒	☐	☐	☐
Amgen	☒	☐	☐	☐
Sanofi	☒	☐	☐	☐
GSK	☒	☐	☐	☐

New or Updated Declaration for Clinician 11

Name	*Dr. Jean Roy*
Position	*Hematologist/Oncologist, Montreal*
Date	*16-05-2024*
☒	**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
Nothing to Declare	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 12

Name	*Dr. Julie Stakiw*
Position	*Oncologist, Saskatoon*
Date	*16-05-2024*

☒	**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
Sanofi	☒	☐	☐	☐
Janssen	☒	☐	☐	☐
BMS	☒	☐	☐	☐
Forus	☒	☐	☐	☐
Pfizer	☒	☐	☐	☐
Beigene	☒	☐	☐	☐

New or Updated Declaration for Clinician 13	
Name	*Dr. Alfredo de la Torre*
Position	*Hematologist/Oncologist, Halifax*
Date	*16-05-2024*
☒	**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
Nothing to Declare	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 14	
Name	*Dr. Bethany E. Monteith*
Position	*Hematologist, Kingston Health Sciences Center*
Date	*16-05-2024*

☒	**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
Forus	☒	☐	☐	☐
Sanofi	☒	☐	☐	☐
Pfizer	☒	☐	☐	☐

New or Updated Declaration for Clinician 15	
Name	*Dr. Arleigh McCurdy*
Position	*Hematologist/Oncologist, Ottawa*
Date	*16-05-2024*
☒	**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
Janssen	☐	☒	☐	☐
Sanofi	☒	☐	☐	☐
GSK	☒	☐	☐	☐
Pfizer	☒	☐	☐	☐
Forus	☒	☐	☐	☐
Amgen	☒	☐	☐	☐

New or Updated Declaration for Clinician 16	
Name	*Dr. Suzanne Trudel*
Position	*Hematologist/Oncologist, Toronto*
Date	*16-05-2024*
☒	**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**
Sanofi	☒	☐	☐	☐
BMS	☐	☐	☒	☐
Add or remove rows as required	☐	☐	☐	☐

Canada's Drug and Health Technology Agency

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0315
Name of the drug and Indication(s)	elranatamab for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 3 prior lines of therapy including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.
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. - PAG suggested changing the last statement in the second discussion point (page 5): (e.g., CAR-T cell therapy or antibody-drug conjugate such as belantamab)

Version: 1.0
Publication Date: TBC
Report Length: 3 Pages

Single

Technology

- PAG suggested clarifying the last statement in the eighth discussion point (page 6): "The patient groups and the clinical experts expressed that patients who are resistant or intolerant to a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody should be eligible to receive elranatamab..." to emphasize that this is the opinion of the patient groups and clinical experts, but not of pERC.

b) Reimbursement conditions and related reasons

Please provide details regarding the information that requires clarification.

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.

- In Table 2, under Considerations for initiation of therapy, PAG suggested adding: "pERC acknowledged that clinical experts thought it would be reasonable to consider patients previously treated with BCMA-targeted therapy (e.g., CAR-T cell therapy), eligible for elranatamab; **however**, pERC also noted...". PAG also suggested adding the condition from Table 1 on the exclusion of prior BCMA-directed therapy at the end of this paragraph.
- In Table 2, under Considerations for initiation of therapy, PAG suggested modifying the second paragraph for the question "Are three prior lines of therapy...?" as follows: "pERC acknowledged the clinical experts' opinion that patients who are resistant to PIs, an immunomodulatory agent, and an anti-CD38 antibody (i.e., all 3), or intolerant to any of them and resistant to the others should be eligible to receive elranatamab, regardless of what line of therapy it is in. However, pERC noted that there is no evidence reviewed [...] on the last therapy."
- In Table 2, under Generalizability, PAG suggested modifying paragraph 2 for the question "At the time of funding, should patients receiving alternative therapies...?" as follows: "Although the option to switch could be provided, pERC agreed with the clinical experts that physicians usually would keep the patient on effective treatments until they no longer work. Patients can also be switched to another drug if the existing treatment stops working."

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. Please update the algorithm (rapid algorithm)

2.
2. Please specify other implementation questions or issues that should be addressed by CADTH
1. 2.
Support strategy
3. Do you have any preferences or suggestions on how CADTH should address these issues?
May include implementation advice panel, evidence review, provisional algorithm (oncology), etc.

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0315-000
Brand name (generic)	ELREXFIO (elranatamab)
Indication(s)	For the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.
Organization	Pfizer Canada ULC
Contact information[a]	[redacted]

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

Pfizer Canada ULC (Pfizer) agrees with and welcomes the recommendation to reimburse ELREXFIO (elranatamab) for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 3 prior lines of therapy including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy. However, Pfizer would ask the CDEC to kindly consider revising the final portion of the recommendation, "and without prior exposure to B cell maturation antigen (BCMA)-directed therapy", for the following reasons:

- The exclusion of patients with prior BCMA exposure does not reflect the feedback provided by the clinical experts consulted by CADTH nor by clinician groups who provided input for the review.
    - Clinical experts consulted by CADTH noted that "although the results for Cohort B (patients with prior BCMA-directed treatments) were not as promising as Cohort A (patients with no prior BCMA-directed treatments), patients with previous BCMA-directed therapy should be eligible for elranatamab" Table 2, page 11 of the draft recommendation.
    - Input provided by the Canadian Myeloma Research Group (CMRG), which was signed by 26 physicians, was supportive of reimbursement of elranatamab for patients with prior BCMA exposure: "Given that prior anti-BCMA exposure does not preclude responsiveness to subsequent anti-BCMA therapy, CMRG would suggest that patients with prior anti-BCMA therapy who did not progress during it (i.e., non-refractory to anti-BCMA therapy) be allowed access to elranatamab" page 10 of the draft recommendation.
- The statement that there is limited evidence to support that patients previously treated with BCMA-targeted therapy does not accurately reflect the evidence from the pivotal trial

(MagnetisMM-3[1]), which demonstrated that the overall response rate (ORR) in Cohort B was greater than the pre-specified alternative hypothesis.
    - The sample size for Cohort A and Cohort B was calculated to provide adequate power for testing the statistical hypotheses regarding the primary endpoint of ORR independently in the two cohorts using a two-stage design based on exact binomial distribution.[1] A total of 120 participants enrolled and treated in Cohort A provided approximately 98% power to reject the null hypothesis (ORR by blinded independent central review [BICR] of 30%) when the alternative hypothesis that ORR by BICR of 48% is true, with a 1-sided significance level of 0.025.[1] Similarly, a total of 60 participants enrolled and treated in Cohort B provided approximately 95% power to reject the null hypothesis when the alternative hypothesis is true, with a 1-sided significance level of 0.025.[1]
- Based on results from MagnetisMM-3[1] and pooled analyses of MagnetisMM studies[2], elranatamab is efficacious in patients with relapsed/refractory multiple myeloma (RRMM) and prior exposure of BCMA-directed therapy (ADC and/or CAR-T). In pooled analyses, the ORR was 46.0% in patients with any prior anti-BCMA therapy, 42.4% in patients with prior ADC treatment, and 52.8% in patients with prior CAR-T treatment.[2] For patients who achieved an objective response (n=40), the median time to response was 1.7 months.[2] These results demonstrate that elranatamab is effective for patients with RRMM and prior exposure with BCMA-directed therapy, particularly post-CAR-T.
- In pooled analyses of MagnetisMM-3 trials, the patient population with prior exposure to BCMA-directed therapy was heavily pre-treated, with a median (range) of 7.0 (3, 19) prior lines of therapy.[2] In this patient population, 85.1% of patients were penta-drug exposed, and 55.2% were penta-drug refractory.[2] It is therefore reasonable that fewer patients would achieve ORR in Cohort B compared to Cohort A, and this was reflected in the respective pre-specified alternative hypotheses in MangetisMM-3.[1]
- The exclusion of patients with prior BCMA exposure is inconsistent with feedback from the clinical experts consulted by CADTH that it would be reasonable for the reimbursement criteria for elranatamab to be aligned with that of teclistamab. In the reimbursement recommendation for teclistamab, pERC noted that "there is limited evidence for using teclistamab in patients previously treated with BCMA-targeted therapy". However, this patient population was not excluded from the reimbursement recommendation.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐

The recommendation reflects that the committee considered the patient and clinician input that there are unmet needs for RRMM patients for new effective treatments that are tolerable and target a different mechanistic pathway, and that elranatamab represents a treatment option for patients who are refractory to other standard of care treatments.

However, the recommendation that elranatamab should not be reimbursed for patients with prior BCMA exposure does not reflect the input provided by the CMRG, nor by the two clinical experts consulted by CADTH during the review, that patients with previous BCMA-directed therapy should be eligible for elranatamab.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☒

	No	☐
The reasons for the recommendation are clearly stated.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒

Pfizer wishes to provide additional clarity with regard to the implementation issue addressed in the following statement in Table 2: "pERC recognized that tocilizumab must be readily available for the treatment of CRS."

Pfizer kindly requests that this statement be revised to "pERC recognized that access to tocilizumab for the treatment of cytokine release syndrome is necessary" to improve alignment of the recommendations for the two bispecific antibodies (teclistamab[3] and elranatamab).

Pfizer also wishes to clarify that monitoring is required the first 2 step-up doses of elranatamab, based on the approved product monograph.[4] A statement in Table 2 suggests that patients starting treatment with elranatamab will receive the first 2 to 3 doses in the hospital; this is not supported by the product monograph, which states[4]:

"Monitoring

- Instruct the patient to remain within proximity of a healthcare facility for 48 hours after each step-up dose.
- Monitor daily for 48 hours for signs and symptoms of CRS after administration of step-up dose 1 or step-up dose 2.
- Alternatively, consider monitoring the patient in hospital for 48 hours after each step-up dose."

Pfizer kindly requests that the statement be revised to clarify that only the first 2 doses require monitoring and may need to be administered in the hospital.

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

The reimbursement conditions are clearly stated and the rationale for the conditions is provided in the recommendation. In some cases, the rationale for the conditions does not reflect clinician input provided for the review.

- The recommendation that elranatamab should not be reimbursed for patients with prior BCMA exposure does not reflect the input provided by the CMRG, nor by the two clinical experts consulted by CADTH during the review, that patients with previous BCMA-directed therapy should be eligible for elranatamab (per comments provided above in response to Question 1).

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

References

1. Pfizer. *Clinical Study Report: An Open-Label, Multicenter, Non-Randomized Phase 2 Study of Elranatamab (PF-06863135) Monotherapy in Participants With Multiple Myeloma Who Are Refractory to at Least One Proteasome Inhibitor, One Immunomodulatory Drug and One Anti-CD38 Antibody (MagnetisMM-3, tables/listings/figure data cut-off: 14Mar2023)*. 2023.
2. Nooka AKea. Efficacy and Safety of Elranatamab in Patients with Relapsed/Refractory Multiple Myeloma (RRMM) and Prior B-cell Maturation Antigen (BCMA)-directed Therapies: A Pooled Analysis from MagnetisMM Studies 2023.
3. CADTH. CADTH Reimbursement Recommendation: Teclistamab (Tecvayli). 2024.
4. Pfizer Canada ULC. ELREXFIO (elranatamab injection). 2023.