CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

tafasitamab (Minjuvi)

(Incyte Biosciences Canada Corporation)

Indication: Diffuse large B-cell lymphoma (DLBCL)

May 19, 2022

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0266-000
Brand name (generic)	Minjuvi (Tafasitamab)
Indication(s)	In combination with lenalidomide for the treatment of adult patients with relapsed or refractory DLBCL not otherwise specified, including DLBCL arising from low grade lymphoma, who are not eligible for ASCT.
Organization	Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Contact information[a]	Name: Dr. Tom Kouroukis

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒
Current treatment options for R/R DLBCL remain limited. Recently Pola-BR has been made available but additional options would be beneficial for patients including lenalidomide as an oral component to 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	☐

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

[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	☒
Ontario Health provided secretariat function to the DAC.		
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: • Dr. Tom Kouroukis		

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0266-000
Brand name (generic)	Tafasitamab
Indication(s)	In combination with lenalidome in patients with relapsed, refractory diffuse large B cell lymphoma ineligible for autologous stem cell transplant
Organization	Lymphoma Canada
Contact information[a]	Name: Dr. Ghazaleh Shoja E Razavi

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.

We disagree that there is a high degree of uncertainty regarding the magnitude of clinical benefit directly attributable to tafasitamab plus lenalidomide. It is stated in the draft recommendation that "Although 57.5% (95% CI: 45.9%, 68.5%) of patients from the L-MIND study showed an objective response, there was a high degree of uncertainty regarding the magnitude of clinical benefit directly attributable to tafasitamab plus lenalidomide due to the non-randomized, non-comparative, open-label study design and the small sample size. It should be added that objective response is not the only endpoint to focus while discussing the efficacy of any treatment modality in an aggressive, and potentially fatal disease such as diffuse large B cell lymphoma. Responses with short duration such as few months, although acceptable in selected cases, usually need a backup including but not limited to auto-transplant or CAR T cell therapy."

As reported in the L-MIND study and the extension follow up, the median duration of response was 43.9 months (95% confidence interval [95% CI]: 26.1-not reached), the median overall survival was 33.5 months (95% CI: 18.3-not reached) and the median progression-free survival was 11.6 months (95% CI: 6.3-45.7). This demonstrates a reasonable outcome in relevant time to event analyses in a significant number of patients that typically would have a dismal clinical outcome and limited survival. It is important to note that there are few treatment options for this patient population. The other available combination with a positive CADTH recommendation is polatuzumab in combination with bendamustine and rituximab.

The draft recommendation also highlights uncertainty in the trial outcomes due to the non-randomized design and absence of a comparator arm: "there was a high degree of uncertainty regarding the magnitude of clinical benefit directly attributable to tafasitamab plus lenalidomide due to the non-randomized, non-comparative, open-label study design and the small sample size. Further, due to the absence of a comparator arm, the potential clinical benefit of tafasitamab plus lenalidomide compared to other relevant treatment comparators was unknown. Health-related quality of life (HRQoL) was also not assessed in the L-MIND study".
It is not realistic to expect a randomized phase III trial in this setting using this regimen given the available data at this time. Confirmatory phase III testing is being performed in a different setting. There is no longer any opportunity to study this regimen in this setting against a control given the consistently poor outcomes reported with "standard therapy" regimens in.DLBCL. The comparison

with the RE-MIND data provides a reasonable benchmark for standard of care therapy in DLBCL (lenalidomide was compared against standard chemotherapy as published in Czuczman Clin Cancer Res 2017). This large retrospective dataset served as a comparison to L-MINE study where DLBCL patients were 1:1 matched with patients receiving lenalidomide as single agent. With 490 patients enrolled in this study, the overall response rate, complete response and progression free survival have been in favor of the tafasitamab-lenalidomide combination with ORR of 67.1% (95% CI: 55.4–77.5) for the L-MIND cohort versus 34.2% (95% CI: 23.7–46.0) for the RE-MIND cohort (odds ratio 3.89; 95% CI: 1.90–8.14; p < 0.0001). The CR rate was 39.5% (95% CI: 28.4–51.4) in the L-MIND cohort and 13.2% (95% CI: 6.5–22.9) in the RE-MIND cohort. A significant difference in OS favored the L-MIND cohort (HR = 0.499; 95% CI: 0.317–0.785). ORR and CR outcomes in the RE-MIND cohort were similar to other published literature for LEN monotherapy in R/R DLBCL. Although lenalidomide is not available as a funded agent in DLBCL in Canada, the data from this comparison is informative as the outcome of the control LEN population is similar to other therapies typically used in Canada in this setting. This retrospective comparison also provides data supporting the impressive efficacy improvement using the doublet of tafasitamab-lenalidomide versus lenalidomide monotherapy.

We agree with the CADTH review statement that “Health-related quality of life (HRQoL) was also not assessed in the L-MIND study.” While the HRQoL can be inferred based on the toxicity data and discontinuation rates for toxicity, this I not a direct measure. HRQoL is typically not evaluated in this type of clinical trial. Patients that have received this treatment in Canada have had the opportunity to provide their experience to CADTH in this process and it would be important to acknowledge their experience which was favourable.

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.

In general, the reasons for the recommended have been clearly stated. However, we disagree with the statement that “when compared with patients enrolled in L-MIND study, the population of Canadian patients with R/R DLBCL who are ineligible for ASCT has a greater proportion of patients with an ECOG PS of 2 or greater, more patients may experience relapse within 6 months of completion of initial therapy (primary refractory and early relapse), and more patients would have failed prior ASCT or have unfavorable cytogenetics, with a higher proportion of non-GCB cell of origin subtype and double or triple hit lymphoma, (who were excluded from the L-MIND trial).”
While it is important to review these data in the context of the entire population of R/R DLBCL, it is expected that criteria will be applied (like the inclusion criteria for the clinical trial) to identify a specific subpopulation that would be appropriate for tafasitamab-lenalidomide treatment. There are a significant number of patients that are ASCT ineligible, with good performance status and absence of high-risk features that would be eligible for treatment with this therapy. These patients may be more likely to be managed in community as opposed to non-academic centers and having a regimen with straightforward administration and lacking a need for hospitalization or expert center management for immune toxicities as may be seen with CAR-T or other novel treatments would be a of significant

value for Canadian clinicians. As these patients are being managed palliatively, it is important to have good options and choices available to Canadian patients.

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

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- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
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  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

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	*Ghazaleh Shoja E Razavi*
Position	*Clinical assistant professor, University of Calgary*
Date	*May 18, 2022*
☒	**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	*Laurie H.Sehn*
Position	*Clinical Professor of Medicine, Division of Medical Oncology, University of British Columbia*
Date	*May 19, 2022*
☒	**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**
InCyte, Honoraria for consulting	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*John Kuruvilla*
Position	*Associate Professor of Medicine, University of Toronto*
Date	*May 19, 2022*
☒	**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				
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InCyte, Honoraria for consulting	☒	☐	☐	☐
Add company name	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0266
Name of the drug and Indication(s)	Tafasitamab for DLBCL
Organization Providing Feedback	PAG

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

2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested
None.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
None.
b) Reimbursement conditions and related reasons
None.
c) Implementation guidance
None.

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0266-000
Brand name (generic)	Minjuvi (Tafasitamab)
Indication(s)	In combination with lenalidomide for the treatment of adult patients with relapsed or refractory DLBCL not otherwise specified, including DLBCL arising from low grade lymphoma, who are not eligible for ASCT
Organization	Lymphoma Canada
Contact information[a]	Name: Antonella Rizza

Stakeholder agreement with the draft recommendation

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

We do not agree with the committee's recommendation for the reason that patients with DLBCL whose cancer has returned or does not respond to treatment and who cannot have an autologous stem cell transplantation have limited treatment options. These patients have an unmet medical need. Tafasitamab in combination with lenalidomide addresses the need for an effective treatment for these patients and aligns with patient values based on the feedback we have received.

Although of limited number, the patients that did provide feedback on their experience with this treatment, were able to source it locally (without travel) and at no cost to them. These same patients indicated that their overall experience with Tafasitamab was very good to excellent with them willing to take the same treatment again 100% of the time if their doctor recommended it was the best treatment option for them.

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 discussion points did highlight that patient feedback was taken into consideration, however, it is worth noting that one of the most important highlights of our report noted the need to address the lack of treatment options for adult patients with relapsed or refractory DLBCL who are not eligible for ASCT.

In pERC's discussion point (bullet 5) about the input from patient groups it was noted that pERC was uncertain whether tafasitamab plus lenalidomide met important patient needs. In terms of the patient preference feedback submitted at the stakeholder input stage, longer remission than current therapies, longer survival than current therapies and controlled disease symptoms were rated as the most important factors regarding a new drug/therapy for DLBCL with a ranking of 96%, 94% and 94% respectively. As it relates to fewer side effects compared to current therapies, patients ranked this as 72%. We feel that Tafasitamab in combination with lenalidomide addresses these patient preferences.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
Yes, the reasons for the negative recommendation are clearly stated. However, for patients in this setting with limited or no treatments options, the unmet need for a new therapy should be prioritized.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒
In the discussion point (bullet 3) pERC noted that the Canadian patient population was limited and that a large proportion of patients normally seen in Canadian practice would not have been eligible for this indication. We feel that the fact that patients were enrolled with a compassionate program is indicative of the fact that there are patients in need of this therapy and clinicians seeing a value in being able to administer it. This is further supported by the number of patients meeting the criteria and participating in the manufacturer's study.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
N/A		

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

Appendix 1. Conflict of Interest Declarations for Patient Groups

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A. Patient Group Information	
Name	*Antonella Rizza*
Position	*CEO*
Date	*May 18, 2022*
☒	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.

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Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐