CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

zanubrutinib (Brukinsa MCL)

(BeiGene Canada ULC)

Indication: Mantle cell lymphoma (MCL)

April 14, 2022

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0267
Brand name (generic)	Brukinsa (Zanubrutinib)
Indication(s)	For the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy
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	☒
Patients who are intolerant to ibrutinib but otherwise responding should be offered a swift to an alternative BTK inhibitor, such as zanubrutinib. If these patients cannot tolerate any BTK inhibitor then there are no additional treatment options and the outcomes will be poor.		

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	☐
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
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 assistance 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 • Dr. Guilliame Richard-Carpentier		

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0267
Name of the drug and Indication(s)	Zanubrutinib for MCL
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
None.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
In the Economic Evidence section, treatment cost row, PAG is requesting to include the cost per 28 days.
b) Reimbursement conditions and related reasons
None.
c) Implementation guidance
None.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0267-000
Brand name (generic)	Zanubrutinib (Brukinsa)
Indication(s)	For the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.
Organization	Lymphoma Canada
Contact information[a]	Name: Kaitlyn Beyfuss-Laski

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 Mantle Cell Lymphoma is an aggressive lymphoma subtype that has very limited treatment options in the relapsed setting. With patient's succumbing to the difficult symptoms of their lymphoma, patients are in need of treatment options that will result in improved disease outcomes and limited overall impact (i.e. side effects, access difficulties, etc.). pERC had stated that Zanubrutinib addressed only one of the following patients needs, specifically related to treatment access only (oral treatment): Patients expressed a need for faster remission and longer survival, disease and symptom control, quality of life improvement, fewer side effects, and ease, simplicity, and access of treatment administration. We do not agree with this statement and both patients and the organization feel that Zanubrutinib addresses more than just ease of access being an oral therapy:

- Zanubrutinib is associated with less toxicity (i.e. atrial fibrillation) as stated in the report compared to Ibrutinib. Thus, patients may see improved quality of life with fewer side effects from treatment.
- A pooled analysis of the two clinical studies (BGB-3111-AU-003 and BGB-3111-206) in relapsed mantle cell lymphoma patients revealed important survival data to which the pERC report indicated survival data was not available. After a median follow-up time of 24.7-24.9 months, PFS and OS were 25.8 and 38.2 months, showing an efficacious treatment in this patient population that addresses patients need for longer survival[1].

  [1]Zhou, K. et al. (2021). Zanubrutinib monotherapy in relapsed/refractory mantle cell lymphoma: a pooled analysis of two clinical trials. *Journal of Hematology & Oncology*, 14 (167).

- Being an oral therapy, it fully aligns with patient's values, allowing for improved quality of life in terms of treatment administration and access.

Further, patients that progress on Ibrutinib or must stop Ibrutinib due to toxicity, another treatment option is required. However, with no other standard of care therapies in this setting, patients have limited options, either palliative care options or clinical trials (extremely limited trials and sites in Canada). Zanubrutinib addresses this need, provided a less toxic effective treatment option for patients.

Expert committee consideration of the stakeholder input

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

pERC did highlight important points from the report, however one of the biggest highlights is the lack of standard of care treatment options in the relapsed/refractory setting. Patients are in need of more treatment options, and patients dually noted that they desire to have to have a choice in treatment selection and would also prefer an oral rather than intravenous option. Zanubrutinib is a treatment that addresses these patients needs.

It is also important for pERC to understand the complex profile of symptoms and treatment side effects that patients have to manage. Therefore, providing a treatment option with a reduced toxicity profile is needed, and Zanubrutinib addresses this need.

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 further expansion into the discussion points is required.

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

For the discussion point 2 on page 4, the uncertainty described by pERC related to the ORR between studies is thought to be a result of different geographic locations and age groups; this is reflective however of having a mixed population receiving treatment which is more characteristic of the general public that would receive treatment outside of the clinical setting.

For discussion point 3 on page 4, we would like to highlight that this is not a negative against the therapy, and is in fact why mantle cell lymphoma patients, who have extremely limited treatment options in the relapsed/refractory setting require multiple treatment options, especially an option that has an improved toxicity profile against the comparator in other subtypes.

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

It did not seem that cost-effectively of therapy was clearly described and analyzed based on this report. Further information should be provided for evaluation including its comparative pricing to existing therapies available.

[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.
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- 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	*Kaitlyn Beyfuss-Laski*
Position	*National Scientific Director*
Date	*04-04-2022*
☒	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	☐
n/a		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
n/a		

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**
Beigene	☐	☐	☐	☒
Janssen	☐	☐	☐	☒
AstraZeneca	☐	☐	☐	☒