CADTH

CADTH REIMBURSEMENT REVIEW

# Stakeholder Feedback on Draft Recommendation

**zanubrutinib (Brukinsa)**

(BeiGene Canada ULC)

**Indication:** For the treatment of adult patients with chronic lymphocytic leukemia (CLL).

**August 18, 2023**

CADTH

# CADTH Reimbursement Review
# Feedback on Draft Recommendation

| Stakeholder information | |
|---|---|
| CADTH project number | PC0310-000 |
| Brand name (generic) | Zanubrutinib (Brukinsa) |
| Indication(s) | For the treatment of adult patients with chronic lymphocytic leukemia (CLL) |
| Organization | Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee |
| Contact information[a] | Name: Dr. Tom Kouroukis |

| Stakeholder agreement with the draft recommendation | | |
|---|---|---|
| **1. Does the stakeholder agree with the committee's recommendation.** | Yes | ☒ |
| | No | ☐ |
| Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.<br><br>The Heme DAC agrees with the committee's recommendation that the use of zanubrutinib should be available for all patients irrespective of genetic risk status. | | |

| 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 | ☒ |
| OH-CCO provided a secretariat function to the group. | | |
| **2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?** | 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:<br>• Dr. Tom Kouroukis<br>• Dr. Selay Lam | | |

CADTH

# CADTH Reimbursement Review

# Feedback on Draft Recommendation

| Stakeholder information | |
|---|---|
| CADTH project number | PC0310 |
| Name of the drug and Indication(s) | Zanubrutinib for chronic lymphocytic leukemia (CLL) |
| Organization Providing Feedback | PAG |

## 1. Recommendation revisions

Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.

| | | |
|---|---|---|
| **Request for Reconsideration** | **Major revisions:** A change in recommendation **category** or patient **population** is requested | ☐ |
| | **Minor revisions:** A change in reimbursement **conditions** is requested | ☐ |
| **No Request for Reconsideration** | **Editorial revisions:** Clarifications in recommendation **text** are requested | x |
| | **No requested revisions** | ☐ |

## 2. Change in recommendation category or conditions

Complete this section if major or minor revisions are requested

Please identify the specific text from the recommendation and provide a rationale for requesting a change in recommendation.

## 3. Clarity of the recommendation

Complete this section if editorial revisions are requested for the following elements

### a) Recommendation rationale

Please provide details regarding the information that requires clarification.

### b) Reimbursement conditions and related reasons

Please provide details regarding the information that requires clarification.

### 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.

A rapid algorithm is needed (PAG lead Amanda H- NFLD)

Under Considerations for initiation of therapy (p.9): can there be a statement either from pERC or from the clinical expert indicating that SLL is treated the same way as CLL and so it may be clinically reasonable to extend to SLL? (Note: the ibrutinib recommendations for CLL from 2015 and 2016 include both CLL and SLL in the eligibility, but the acalabrutinib recommendations for CLL from 2020 only state CLL. Jurisdictions have aligned eligibility criteria for BTKi for CLL, and it would be useful to specify that it may be clinically reasonable to extend zanubrutinib eligibility to SLL.)

Under Considerations for initiation of therapy in Table 2, in the 3rd paragraph: please confirm that pERC is agreeing with expert to extend to all patients (high risk or not) or disagreeing.

Under Considerations for initiation of therapy, in the 3rd paragraph: Some jurisdictions fund ibrutinib/acalabrutinib for high risk CLL only. This statement would be problematic given some jurisdictions may have to expand eligibility criteria and could result in misalignment of eligibility between various BTKi's for CLL. Can this be entire statement be replaced with - pERC acknowledges that 'funding access across jurisdictions is variable for BTK inhibitors.' In the setting wherein a BTK inhibitor is publicly funded for previously untreated CLL patients without high-risk features or who could not receive IV therapy, zanubrutinib would be a reasonable option.

Under Economic Evidence – Treatment cost (p. 20): please include the cost per 28-days.

# 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.<br>2. |
| **2. Please specify other implementation questions or issues that should be addressed by CADTH** |
| 1.<br>2. |
| **3. Please specify questions or issues that should be addressed by CAPCA. (oncology only)** |
| 1.<br>2. |
| **Support strategy** |

CADTH

# CADTH Reimbursement Review
# Feedback on Draft Recommendation

| Stakeholder information | |
|---|---|
| CADTH project number | PC0310-000 |
| Brand name (generic) | Brukinsa (Zanubrutinib) |
| Indication(s) | For the treatment of adult patients with chronic lymphocytic leukemia (CLL |
| Organization | Lymphoma Canada (with input and assistance from CLL Canada) |
| Contact information[a] | Name: Antonella Rizza, CEO; [redacted] |

| 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 agree with the committee's recommendation. Given the variability of CLL and the need for multiple lines of treatment, CLL patients have expressed that it is important to them to have a choice of treatments that will be best tolerated and best suited to their personal clinical history. Overall the patients we surveyed that did have experience with Zanubrutinib found it was more effective in controlling their disease with fewer side effects than previous lines of therapy. Zanubrutinib has addressed patient preferences with respect to choice and fewer side effects as well as longer progression free survival.

| 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.

The reasons for the recommendations are clearly stated. However, perhaps to further clarify Reimbursement Condition #1 the following additional wording could be considered as follows: 1.3 – or for whom another BTKi treatment has unacceptable toxicity. Patients suffering from the side effects of another BTKi are at times switched to Zanubrutinib, as described in the survey data we have compiled from patients and have found it to be more easily tolerated. This additional information may clarify this.

| | | |
|---|---|---|
| **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.

Reimbursement condition 3-3.1 precludes patients from accessing Zanubrutinib if they have had prior progression on a BTK inhibitor. We are in contact with a patient in Quebec City whose CLL has been controlled by Zanubrutinib for the past 8 months despite having had his CLL progress on both Ibrutinib (first line) and Venetoclax (second line).

Patients who relapse on a BTKi and on Venetoclax have very few treatment options, other than a clinical trial or perhaps a stem cell transplant, with all the risks involved in the latter. There is an important unmet need for treatment of double refractory CLL patients. For these patients being able to be treated on Zanubrutinib can help bridge them to a clinical trial for example. We would recommend updating reimbursement condition 3.1 to allow for the possibility of reimbursement of Zanubrutinib for double refractory patients to enable them to access another line of therapy in a clinical trial.

| **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** | *Antonella Rizza* |
| **Position** | *CEO* |
| **Date** | *August 17, 2023* |
| ☒ | 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.<br><br>Yes this feedback was completed in collaboration with CLL Canada. | | |
| **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.<br><br>Yes, CLL Canada assisted in promotion of the original survey created by Lymphoma Canada | | |

| 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* | ☐ | ☐ | ☐ | ☒ |
| *Astra Zeneca* | ☐ | ☐ | ☐ | ☒ |
| *Janssen* | ☐ | ☐ | ☐ | ☒ |

| A. Collaborating Patient Group Information | |
|---|---|
| **Name** | *Raymond Vles* |
| **Position** | *Board Chair* |
| **Date** | *August 17, 2023* |
| ☒ | 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. |

**1. 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** |
| *Biegene* | ☐ | ☐ | ☒ | ☐ |
| *Astra Zeneca* | ☐ | ☒ | ☐ | ☐ |
| | ☐ | ☐ | ☐ | ☐ |

CADTH

# CADTH Reimbursement Review
# Feedback on Draft Recommendation

| Stakeholder information | |
|---|---|
| CADTH project number | PC0310 |
| Brand name (generic) | BRUKINSA (zanubrutinib) |
| Indication(s) | For the treatment of adult patients with chronic lymphocytic leukemia (CLL) |
| Organization | BeiGene Canada ULC |
| Contact information[a] | [redacted] |

| Stakeholder agreement with the draft recommendation | | |
|---|---|---|
| **1. Does the stakeholder agree with the committee's recommendation.** | Yes | ☒ |
| | No | ☐ |
| The sponsor (BeiGene Canada ULC [BeiGene]) agrees with the committee's recommendation to reimburse with conditions. BeiGene is pleased that the value of BRUKINSA has been recognized by CADTH and that Canadian patients with chronic lymphocytic leukemia (CLL) will be able to benefit from the clinical effectiveness and safety of BRUKINSA.<br><br>BeiGene looks forward to collaborating with pCPA and jurisdictions to provide access to BRUKINSA for patients with CLL in a timely manner in order to realize the substantial savings for public drug programs. | | |
| **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 | ☐ |
| BeiGene appreciates that the committee recognized the need for more treatment options with improved tolerability for patients with CLL compared to existing chemoimmunotherapy and other Bruton tyrosine kinase inhibitor (BTKi) options. Further, the committee acknowledges the clinical benefits of BRUKINSA for both treatment-naïve (TN) and relapsed or refractory (R/R) patients. | | |
| **Clarity of the draft recommendation** | | |
| **3. Are the reasons for the recommendation clearly stated?** | Yes | ☒ |
| | No | ☐ |
| The reasons for the recommendation are clearly stated in referring to the strength of the submitted clinical trial evidence, input received by CADTH from patient groups and clinician groups, and the economic advantage of BRUKINSA over other BTKi options. | | |
| **4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?** | Yes | ☒ |
| | No | ☐ |
| CADTH clearly described the implementation issues raised by the drug programs and provided clear guidance around prescribing and dosing of BRUKINSA, in addition to recommending the avoidance of placing too many restrictions on the use of BRUKINSA due to potential benefits over earlier BTK inhibitors. | | |
| **5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?** | Yes | ☒ |
| | No | ☐ |
| CADTH clearly stated the conditions and rationale for the conditions in reimbursing BRUKINSA in the treatment of patients with CLL. | | |

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