CADTH

CADTH REIMBURSEMENT REVIEW

# Clinician Input

**zanubrutinib (Brukinsa)**

BeiGene, Ltd.

**Indication:** For the treatment of patients with Waldenström's macroglobulinemia (WM).

**May 14, 2021**

# CADTH Reimbursement Review
# Clinician Group Input Template

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|---|---|
| **CADTH Project Number** | PC0248-000 **Due: May 14, 2021** |
| **Generic Drug Name (Brand Name)** | Zanubrutinib (Brand: Brukinsa); Manufacturer: BeiGene, Ltd. |
| **Indication** | **For the treatment of patients with Waldenström's macroglobulinemia (WM)**<br><br>**Manufacturer Requested Reimbursement Criteria[1]:** For the treatment of patients with Waldenström's macroglobulinemia (WM) |
| **Name of the Clinician Group** | **Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee** |
| **Author of the Submission** | **Dr. Tom Kouroukis, Dr. Pierre Villeneuve** |
| **Contact information** | Name: Dr. Tom Kouroukis<br>Title: Provincial Head – Complex Malignant Hematology (OH-CCO)<br>Email: [redacted]<br>Phone: |

## 1. About Your Clinician Group

Please describe the purpose of your organization. Include a link to your website (if applicable).

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

## 2. Information Gathering

Please describe how you gathered the information included in the submission.

Discussed jointly via email.

## 3. Current treatments

### 3.1. Describe the current treatment paradigm for the disease

*Focus on the Canadian context.*

*Please include drug and non-drug treatments.*

*Drugs without Health Canada approval for use in the management of the indication of interest may be relevant if they are routinely used in Canadian clinical practice. Are such treatments supported by clinical practice guidelines?*

*Treatments available through special access programs are relevant.*

*Do current treatments modify the underlying disease mechanism? Target symptoms?*

***Response:***

First line therapy include bendamustine-rituximab (BR), ibrutinib-rituximab (private pay). Alternatively, chlorambucil for palliative use.

Relapsed disease include BR retreatment or ibrutinib (private pay) or other rituximab-chemo combination, or palliative chlorambucil.

## 4. Treatment goals

### 4.1. What are the most important goals that an ideal treatment would address?

*Examples: Prolong life, delay disease progression, improve lung function, prevent the need for organ transplant, prevent infection or transmission of disease, reduce loss of cognition, reduce the severity of symptoms, minimize adverse effects, improve health-related quality of life, increase the ability to maintain employment, maintain independence, reduce burden on caregivers.*

***Response:***

Prolong life, delay disease progression, improve health-related quality of life, prevent end-organ effects related to hyperviscosity

## 5. Treatment gaps (unmet needs)

### 5.1. Considering the treatment goals in Section 4, please describe goals (needs) that are not being met by currently available treatments.

*Examples:*

- *Not all patients respond to available treatments*
- *Patients become refractory to current treatment options*
- *No treatments are available to reverse the course of disease*
- *No treatments are available to address key outcomes*
- *Treatments are needed that are better tolerated*
- *Treatment are needed to improve compliance*
- *Formulations are needed to improve convenience*

***Response:***

Current available treatments are not curative. Patients become refractory with limited treatment options. Also, some patients are unable to tolerate ibrutinib because of toxicities

**5.2. Which patients have the greatest unmet need for an intervention such as the drug under review?**

*Would these patients be considered a subpopulation or niche population?*

*Describe characteristics of this patient population.*

*Would the drug under review address the unmet need in this patient population?*

***Response:***

Most patients have good response to frontline BR and remain relapse-free for a few years. The greatest unmet need is in patients with relapsed disease.

## 6. Place in therapy

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

*Is there a mechanism of action that would complement other available treatments, and would it be added to other treatments?*

*Is the drug under review the first treatment approved that will address the underlying disease process rather than being a symptomatic management therapy?*

*Would the drug under review be used as a first-line treatment, in combination with other treatments, or as a later (or last) line of treatment?*

*Is the drug under review expected to cause a shift in the current treatment paradigm?*

***Response:***

Zanubrutinib may be used in first-line or relapsed WM.

**6.2. Please indicate whether or not it would be appropriate to recommend that patients try other treatments before initiating treatment with the drug under review. Please provide a rationale from your perspective.**

*If so, please describe which treatments should be tried, in what order, and include a brief rationale.*

***Response:***

There's no evidence to suggest zanubrutinib should be sequenced in any specific manner as the ASPEN study enrolled newly diagnosed and previously treated patients. There is no evidence that zanubrutinib should be given in patients who either fail or are intolerant to ibrutinib.

**6.3. How would this drug affect the sequencing of therapies for the target condition?**

*If appropriate for this condition, please indicate which treatments would be given after the therapy has failed and specify whether this is a significant departure from the sequence employed in current practice.*

*Would there be opportunity to treat patients with this same drug in a subsequent line of therapy? If so, according to what parameters?*

***Response:***

No known sequencing with zanubrutinib.

**6.4. Which patients would be best suited for treatment with the drug under review?**

*Which patients are most likely to respond to treatment with the drug under review?*

*Which patients are most in need of an intervention?*

*Would this differ based on any disease characteristics (e.g., presence or absence of certain symptoms, stage of disease)?*

***Response:***

Patients with symptomatic relapse/refractory WM.

**6.5. How would patients best suited for treatment with the drug under review be identified?**

*Examples*: *Clinician examination or judgement, laboratory tests (specify), diagnostic tools (specify)*

*Is the condition challenging to diagnose in routine clinical practice?*

*Are there any issues related to diagnosis? (e.g., tests may not be widely available, tests may be available at a cost, uncertainty in testing, unclear whether a scale is accurate or the scale may be subjective, variability in expert opinion.)*

*Is it likely that misdiagnosis occurs in clinical practice (e.g., underdiagnosis)?*

*Should patients who are pre-symptomatic be treated considering the mechanism of action of the drug under review?*

***Response:***

As per usual diagnostic work-up for WM.

**6.6. Which patients would be least suitable for treatment with the drug under review?**

***Response:***

Patients with prior BTK inhibitor exposure were excluded from the ASPEN study.

**6.7. Is it possible to identify those patients who are most likely to exhibit a response to treatment with the drug under review?**

*If so, how would these patients be identified?*

***Response:***

No since study did not identify subgroup of patients that were likely to derive greater benefit from zanubrutinib.

**6.8. What outcomes are used to determine whether a patient is responding to treatment in clinical practice?**

*Are the outcomes used in clinical practice aligned with the outcomes typically used in clinical trials?*

***Response:***

Response rate based on blood count and IgM level. Imaging as per current practice.

**6.9. What would be considered a clinically meaningful response to treatment?**

*Examples:*

- *Reduction in the frequency or severity of symptoms (provide specifics regarding changes in frequency, severity, and so forth)*
- *Attainment of major motor milestones*
- *Ability to perform activities of daily living*
- *Improvement in symptoms*
- *Stabilization (no deterioration) of symptoms*

*Consider the magnitude of the response to treatment. Is this likely to vary across physicians?*

***Response:***

At least a partial response or better to treatment with zanubrutinib and prevent end-organ effect.

**6.10. How often should treatment response be assessed?**

***Response:***

As per usual clinical practice, e.g., every 1-3 months.

**6.11. What factors should be considered when deciding to discontinue treatment?**

*Examples:*

- *Disease progression (specify; e.g., loss of lower limb mobility)*
- *Certain adverse events occur (specify type, frequency, and severity)*
- *Additional treatment becomes necessary (specify)*

***Response:***

Lack of response, progression, or treatment-related toxicities.

**6.12. What settings are appropriate for treatment with the drug under review?**

*Examples: Community setting, hospital (outpatient clinic), specialty clinic*

***Response:***

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| Community setting – zanubrutinib is an oral take home cancer drug |
| **6.13. For non-oncology drugs, is a specialist required to diagnose, treat, and monitor patients who might receive the drug under review?** |
| *If so, which specialties would be relevant?*<br>***Response:***<br>NA |
| **7. Additional information** |
| **7.1. Is there any additional information you feel is pertinent to this review?** |
| ***Response:***<br>NA |

## 8. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

   OH-CCO provided secretariat support to the DAC in completing this input.

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

   No.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for <u>each clinician</u> that contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

**Declaration for Clinician 1**

| **Clinician Information** |
|---|

| | |
|---|---|
| **Name** | *Dr. Tom Kouroukis* |
| **Position** | *Provincial Head – Complex Malignant Hematology (OH-CCO)* |
| **Date** | *22 April 2021* |
| ☒ | **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**

| **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* | ☐ | ☐ | ☐ | ☐ |

**Declaration for Clinician 2**

| **Clinician Information** | |
|---|---|
| **Name** | *Dr. Pierre Villeneuve* |
| **Position** | *Hematologist/oncologist* |
| **Date** | *6 May 2021* |
| ☒ | **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**

| **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* | ☐ | ☐ | ☐ | ☐ |

**Declaration for Clinician 3**

| **Clinician 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 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 | | | | |
|---|---|---|---|---|
| **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* | ☐ | ☐ | ☐ | ☐ |

**Declaration for Clinician 4**

| Clinician 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 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 | | | | |
|---|---|---|---|---|
| **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* | ☐ | ☐ | ☐ | ☐ |

**Declaration for Clinician 5**

| Clinician 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 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 | | | | |
|---|---|---|---|---|
| **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* | ☐ | ☐ | ☐ | ☐ |