CADTH

pan-Canadian Oncology Drug Review Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation (Sponsor)

Acalabrutinib (Calquence) for Chronic Lymphocytic Leukemia (previously untreated)

January 8, 2021

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	CALQUENCE® (acalabrutinib) Previously Untreated CLL (pCODR 10210)
Eligible Stakeholder Role	Manufacturer
Organization Providing Feedback	AstraZeneca Canada Inc.

** CADTH may contact this person if comments require clarification. Contact information will not be included in any public posting of this document by CADTH.*

3.1 Comments on the Initial Recommendation

a) Please indicate if the stakeholder agrees, agrees in part, or disagrees with the initial recommendation:

☒ Agrees ☐ Agrees in part ☐ Disagrees

AstraZeneca (AZ) supports the pERC Initial Recommendation for reimbursement of acalabrutinib (ACA) monotherapy for adult patients with previously untreated CLL for whom a fludarabine-based regimen is inappropriate, based on the available clinical evidence.

Clinical Benefit
As highlighted by pERC, Patient Groups, and Clinicians, because CLL is considered a chronic and incurable disease, a continued need exists for treatment options that offer disease control while reducing toxicity and improving on tolerability, to provide patients with options that best meet their individual needs and preferences.

AZ agrees with pERC and the CGP that there is a net clinical benefit with the use of ACA with or without obinutuzumab (OBI) in previously untreated CLL patients when compared with the combination of chlorambucil and obinutuzumab (CLB-OBI). AZ also agrees with pERC, the CGP, and Clinicians that ibrutinib (IBR) is the most appropriate comparator in this patient population. The summary of Clinician Input highlighted that Clinicians would use ACA in all patients they would consider treatment with IBR, including patients with high-risk cytogenetics (TP53 aberrations including del17p, and unmutated IGHV) regardless of age and fitness level.

Patient-Based Values
AZ acknowledges that, based on the available clinical evidence, ACA as a monotherapy best aligns with patient values. ACA as a monotherapy showed a statistically significant and clinically meaningful improvement in PFS vs CLB-OBI, coupled with less toxicity compared with ACA-OBI and CLB-OBI, aligning to the patient value of improved disease control with less toxicity. AZ agrees with pERC, the CGP, Patient Groups, and Clinicians that, as an oral treatment option, ACA offers a more convenient administration for a primarily elderly patient population compared with treatment regimens that require intravenous infusions.

AZ agrees with pERC that ACA would provide another treatment option vs IBR, with the potential to have a lower AE profile compared with IBR. Along this line, Patient Groups identified that "ACA was reported to be a less toxic alternative to IBR for many patients." Similarly, in addition to considering ACA for all patients they would consider IBR for, Clinicians would consider ACA instead of IBR in older patients who are at risk for cardiovascular events such as atrial fibrillation and hypertension.

Economic Evaluation

AZ agrees with pERC and the EGP that IBR is the most appropriate comparator, and further agrees with the EGP reanalysis that ACA monotherapy is dominant when compared to IBR.

With respect to the willingness-to-pay (WTP) threshold of $50,000 per QALY articulated by the EGP and pERC, AZ believes that this is problematic. As part of a retrospective analysis of pCODR recommendations from 2011 to 2017, Skedgel et al (2018) investigated whether there was "an implicit maximum willingness-to-pay or cost-utility threshold in pCODR recommendations".[1] This maximum threshold was approximately $140,000 per QALY, which is significantly higher than the threshold referenced by pERC and the EGP. Specific to CLL, a WTP threshold of $50,000 per QALY has not been consistently applied to the nine final recommendations from 2012 to 2020. As such, AZ believes that the conversion from an implied threshold of $140,000 per QALY to an explicit threshold of $50,000 per QALY is not equitable to patients, as this represents a marked shift compared with drugs that are now on the market. Compounding this threshold issue are the PMPRB guidelines, which specifically use different value thresholds. AZ believes that there should be a formal consultation process that highlights the patient experience, to evaluate this new threshold, and that until such a consultation process is conducted, the historically relevant thresholds ($100,000 to $140,000 per QALY) should be adhered too.

Adoptions Feasibility

Given pERC's recommendation to fund the ACA as monotherapy based on the available data, and the questions regarding population size and treatment uptake, AZ acknowledges the budget impact analysis requires additional revisions. AZ looks forward to working with pCPA and jurisdictions to discuss a budget impact model that reflects the regional nuances of funding and use of CLL treatments across Canada.

References

1. Skedgel, C., Wranik, D., & Hu, M. (2018, April). The Relative Importance of Clinical, Economic, Patient Values and Feasibility Criteria in Cancer Drug Reimbursement in Canada: A Revealed Preferences Analysis of Recommendations of the Pan-Canadian Oncology Drug Review 2011–2017. PharmacoEconomics, 36(4), 467-475. https://doi.org/10.1007/s40273-018-0610-0

b) Please provide editorial feedback on the initial recommendation to aid in clarity. Is the initial recommendation or are the components of the recommendation (e.g., clinical and economic evidence) clearly worded? Is the intent clear? Are the reasons clear?

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity

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3.2 Comments Related to Eligible Stakeholder Provided Information

Notwithstanding the feedback provided in part a) above, please indicate if the stakeholder would support this initial recommendation proceeding to final recommendation ("early conversion"), which would occur two business days after the end of the feedback deadline date.

☒ Support conversion to final recommendation.

Recommendation does not require reconsideration by pERC.

☐ Do not support conversion to final recommendation.

Recommendation should be reconsidered by pERC.

If the eligible stakeholder does not support conversion to a final recommendation, please provide feedback on any issues not adequately addressed in the initial recommendation based on any information provided by the stakeholder during the review.

Please note that new evidence will be not considered at this part of the review process, however, it may be eligible for a resubmission.

Additionally, if the eligible stakeholder supports early conversion to a final recommendation; however, the stakeholder has included substantive comments that requires further interpretation of the evidence, the criteria for early conversion will be deemed to have not been met and the initial recommendation will be returned to pERC for further deliberation and reconsideration at the next possible pERC meeting.

Page Number	Section Title	Paragraph, Line Number	Comments related to Stakeholder Information

Template for Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation

1 About Stakeholder Feedback

CADTH invites eligible stakeholders to provide feedback and comments on the pan-Canadian Oncology Drug Review Expert Review Committee (pERC) initial recommendation.

As part of the CADTH's pan-Canadian Oncology Drug Review (pCODR) process, pERC makes an initial recommendation based on its review of the clinical benefit, patient values, economic evaluation and adoption feasibility for a drug. The initial recommendation is then posted for feedback from eligible stakeholders. All eligible stakeholders have 10 business days within which to provide their feedback on the initial recommendation. It should be noted that the initial recommendation may or may not change following a review of the feedback from stakeholders.

CADTH welcomes comments and feedback from all eligible stakeholders with the expectation that even the most critical feedback be delivered respectfully and with civility.

A. Application of Early Conversion

The stakeholder feedback document poses two key questions:

1. **Does the stakeholder agree, agree in part, or disagree with the initial recommendation?**

   All eligible stakeholders are requested to indicate whether they agree, agree in part, or disagree with the initial recommendation, and to provide a rationale for their response. Please note that if a stakeholder agrees, agrees in part or disagrees with the initial recommendation, they can still support the recommendation proceeding to a final recommendation (i.e. early conversion).

2. **Does the stakeholder support the recommendation proceeding to a final recommendation ("early conversion")?**

   An efficient review process is one of the key guiding principles for CADTH's pCODR process. If all eligible stakeholders support the initial recommendation proceeding to a final recommendation and that the criteria for early conversion as set out in the *Procedures for the CADTH Pan-Canadian Oncology Drug Review* are met, the final recommendation will be posted on the CADTH website two business days after the end of the feedback deadline date. This is called an "early conversion" of an initial recommendation to a final recommendation.

   For stakeholders who support early conversion, please note that if there are substantive comments on any of the key quadrants of the deliberative framework (e.g., differences in the interpretation of the evidence), the criteria for early conversion will be deemed to have **not** been met and the initial recommendation will be returned to pERC for further deliberation and reconsideration at the next possible pERC meeting. Please note that if any one of the eligible stakeholders does not support the initial recommendation proceeding to a final recommendation, pERC will review all feedback and comments received at a subsequent pERC meeting and reconsider the initial recommendation.

B. Guidance on Scope of Feedback for Early Conversion

Information that is within scope of feedback for early conversion includes the identification of errors in the reporting or a lack of clarity in the information provided in the review documents. Based on the feedback received, pERC will consider revising the recommendation document, as appropriate and to provide clarity.

If a lack of clarity is noted, please provide suggestions to improve the clarity of the information in the initial recommendation. If the feedback can be addressed editorially this will done by the CADTH staff, in consultation with pERC, and may not require reconsideration at a subsequent pERC meeting.

The final recommendation will be made available to the participating federal, provincial and territorial ministries of health and provincial cancer agencies for their use in guiding their funding decisions and will also be made publicly available once it has been finalized.

2 Instructions for Providing Feedback

- The following stakeholders are eligible to submit feedback on the initial recommendation:
    - The sponsor and/or the manufacturer of the drug under review;
    - Patient groups who have provided input on the drug submission;
    - Registered clinician(s) who have provided input on the drug submission; and
    - CADTH's Provincial Advisory Group (PAG)
- Feedback or comments must be based on the evidence that was considered by pERC in making the initial recommendation. No new evidence will be considered at this part of the review process.
- The template for providing stakeholder is located in section 3 of this document.
- The template must be completed in English. The stakeholder should complete those sections of the template where they have substantive comments and should not feel obligated to complete every section, if that section does not apply.
- Feedback on the initial recommendation should not exceed three pages in length, using a minimum 11-point font on 8 ½″ by 11″ paper. If comments submitted exceed three pages, only the first three pages of feedback will be provided to the pERC for their consideration.
- Feedback should be presented clearly and succinctly in point form, whenever possible. The issue(s) should be clearly stated and specific reference must be made to the section of the recommendation document under discussion (i.e., page number, section title, and paragraph). Opinions from experts and testimonials should not be provided. Comments should be restricted to the content of the initial recommendation, and should not contain any language that could be considered disrespectful, inflammatory or could be found to violate applicable defamation law.
- References may be provided separately; however, these cannot be related to new evidence.
- CADTH is committed to providing an open and transparent cancer drug review process and to the need to be accountable for its recommendations to patients and the public. Submitted feedback must be disclosable and will be posted on the CADTH website.
- The template must be filed with CADTH as a Microsoft Word document by the posted deadline.
- If you have any questions about the feedback process, please e-mail requests@cadth.ca