CADTH

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

Sonidegib (Odomzo) for Basal Cell Carcinoma

April 29, 2021

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	Odomzo (sonidegib) for the treatment of adult patients with histologically confirmed laBCC that is not amenable to radiation therapy or curative surgery
Eligible Stakeholder Role	Sponsor and manufacturer
Organization Providing Feedback	Sun Pharma 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

Sun Pharma Canada acknowledges the following statements in the initial recommendation:

- "pERC agreed with the Clinical Guidance Panel (CGP), the registered clinicians, and the patient groups that there is a need for effective treatment options for patients with laBCC".
- "Overall, pERC agreed that sonidegib is reasonably safe with no unexpected or unmanageable toxicities, and that its safety profile is consistent with other Hedgehog (Hh) inhibitors".
- "The committee agreed with the Clinical Guidance Panel (CGP) that laBCC commonly develops in the elderly population, which increases the potential for treatment toxicity due to the presence of significant comorbid illnesses and can lead to significant morbidity in patients".
- "pERC concluded that sonidegib aligned with patient values of delaying progression, causing potentially less scarring or disfigurement, oral option, manageable side effect profile, and no apparent detriment in quality of life. However, pERC noted that the impact of sonidegib on patient outcomes and quality of life compared with vismodegib is uncertain".
- "pERC concluded that the comparative efficacy of sonidegib to vismodegib was unknown".

The unmet need, as stated by pERC, is for additional options for patients, which need only demonstrate efficacy and safety, not necessarily superiority, or even equivalence, to existing options. However, the CGP reports the following:

"Based on clinical experience and response data from the ERIVANCE and BOLT trials, sonidegib is expected to be at least as efficacious as vismodegib. Sonidegib may also provide an alternative toxicity profile that may be suitable for some patients when vismodegib is not well tolerated. Overall, due to longer-term data and clinical experience with vismodegib, vismodegib would still be the preferred treatment in this patient population and sonidegib would be used as an alternative option". (Table 3, *CADTH Clinical Guidance Panel Response to Provincial Advisory Group Implementation Questions*).

It is Sun Pharma Canada's position that the efficacy of sonidegib is supported by the trial results which met with the trial's own definition of clinical benefit, the experience of patients who provided

feedback to CADTH's invitation, and the desire of contributing clinicians to make sonidegib available to patients who need it.

In addition to the rarity of laBCC, at the time of the design of the BOLT trial vismodegib was not licensed or available, explaining the absence of an active comparator arm. The BOLT study design called for predefined efficacy against specified target lesions in the absence of a comparator, similar to ERIVANCE, which was the basis of pCODR's positive recommendation for vismodegib. While broadly similar, in that it was a single-arm trial conducted in a relatively small population, there are notable differences between BOLT and ERIVANCE, and ERIVANCE would no longer be acceptable to the FDA because its response methodology is understood to be inappropriate for LaBCC lesions. Current trials conducted in laBCC utilize BOLT's more rigorous definitions of response.

All 42 months of the BOLT Study were centrally reviewed, whereas only the first 12 months of ERIVANCE provide centrally reviewed results, an important distinction given the innate potential for bias in investigator-assessed outcomes. The lengthy centrally reviewed results provide additional confidence in the 26.1 mDOR demonstrated by sonidegib, compared with 9.8 months mDOR seen in ERIVANCE.

In addition, the BOLT Study contained meaningful quality of life data using validated questionnaires developed by the European Organization for Research and Treatment of Cancer (EORTC), including the Quality of Life Questionnaire C30 (QLQ-C30) and the Head and Neck Cancer Module 35 (H&N35). Questionnaires were completed at baseline, weeks 9 and 17 and Q8W thereafter during year 1, and Q12W after the first year. The omission of such data was considered a shortcoming of the vismodegib submission. The quality of life questionnaires demonstrated that 80% or more of patients felt that their QoL had either improved or was maintained over the course of therapy, which is consistent with the 92% disease control rate.

The company agrees that the single-arm registration trials of the two hedgehog pathway inhibitors do not permit indirect comparisons adequate to establish that one is superior to the other. In acknowledgement of this uncertainty, the company is prepared to offer an additional 10% discount to the list price, effective immediately, as the starting point for negotiations with the pCPA, to ensure that sonidegib can be made available in a sustainable manner and can deliver substantial cost-savings of at least 19% to cancer agencies and drug plans. The cost-savings acknowledged in EGP's review of the budget impact analysis can be guaranteed by Sun Pharma Canada.

In summary:

- All stakeholders acknowledge a need for new treatments;
- The efficacy and safety of sonidegib do not appear to be in doubt in the CGP report;
- The place in therapy for sonidegib is clearly spelled out;
- And the provision of sonidegib is assured to be cost-saving to plans and cancer agencies.

We applaud pERC's consistent application of context-dependent decision making, and their unwavering prioritization of unmet medical need. We would only argue that there remains an unmet need for additional, effective treatment options in this comparatively rare disease. Sun Pharma Canada is entirely confident that the reimbursement of sonidegib will enhance population health while offering important savings to drug plans and cancer agencies.

Sun Pharma Canada hopes that pERC and the provincial advisory group take advantage of this opportunity to provide an effective, safe and cost-saving therapeutic option.

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

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