CADTH

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

Isatuximab (Sarclisa) for Multiple Myeloma

April 1, 2021

CADTH

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	Isatuximab (Sarclisa)
Eligible Stakeholder Role	Patient group
Organization Providing Feedback	Myeloma Canada

** 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

Myeloma Canada (MC) agrees with the initial pERC recommendation. We believe the benefits of this new medication for myeloma patients offer a significant improvement in the indicated population. The recommendation offers a very effective treatment for those patients who may not be eligible for the daratumumab triplet combination because of being refractory to either bortezomib or lenalidomide.

Additional comments:
MC is pleased that pERC is suggesting that patients currently on Pd who meet the eligibility criteria could have Isa added to their regimen. MC is also pleased to see that sequencing considerations are being proposed. This is confirmed by the recommendation that for patients currently on Kd or PVd who qualify based in the ICARIA eligibility that IsaPd could be considered if progression or intolerance to Kd or PVd.

Of greater significance to patients is the recommendations that IsaPd can be used in patients who have relapsed with bortezomib or lenalidomide who therefore are not eligible for a daratumumab triplet. Those patients would now have access to a CD38 which is a prerequisite for CAR-T treatments and for many clinical trials with BYTEs or other treatments under investigation, offering a much richer option to additional therapies.

MC praises pERC and the CGP for the very thorough review and pragmatic approach to their recommendations provided in the "Sequencing and priority of treatments." Treatment sequencing is very important to patients as they all know they will relapse at some point. Hence having a "game plan" is critical for their well-being (both physical and emotional). pERC and the CGP recognized that clinical evidence is not available to address all possible situations. However, they did make recommendations that are flexible and offer solutions that are so essential from a patient's perspective. We hope that the provinces will adopt these recommendations.

Additionally, the recommendation document is clear, uses simple language and is easily understood by a nonclinical and health economic person.

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
4	Summary	Para 5 line 10	The sentence" … included information on 4 patients who had direct … should read:…. Included information on 6 patients who had direct… Page 11 para # 2 line 9 … correctly refers to 6 patients having direct experience with the IsaPd combination as per our submission.
12	Economic evaluation	Para 4 lines 1-3	Is pERC suggesting that IsaPd would never be considered cost effective at the $50,000 per QALY threshold given to reach this level the price of Isa would need to be discounted by 98% and 50% reduction for Pom achieved. It is very challenging to expect a manufacturer to reduce its price by such a large amount (98%) while they do not have any influence on the combination drug (Pom) as they are two different manufacturers. This sentence is very discouraging, as it seems to indicate an extremely slim chance to the conclusion of a successful pCPA negotiation.
4 & 5 & 12	Summary and Economic evaluation	Para 5, last line Numerous places on page 12	MC request clarity on the use of the $50,000 cost effectiveness per QALY threshold. We note that pERC uses the $50,000 per QALY as a benchmark threshold more and more often. In fact, in a previous HTA evaluation for DRd in newly diagnosed patients who are not eligible for autologous stem cell transplant (final recommendations published on March 5, 2020, pages 6 and 12) pERC seems to refer to $100,000 per QALY as being an acceptable threshold. Additionally, in the PMPRB guidelines to be implemented on July 1, 2021 the acceptable threshold for cancer drugs is suggested at $150,000 per QALY. Should there be more consistency on the acceptable QALY threshold and why is there difference between pERC and PMPRB thresholds? We have done a cursory review of recent recommendations of oncology drugs and have found many of them to refer to a $50,000 cost per QALY. Can you provide more details as to why a $50,000 per QALY threshold is now used for oncology drugs?

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
12	Summary and economic evaluation	Para 1, line 6	This next comment comes from an observation looking at the daratumumab in combination with lenalidomide and dexamethasone recommendation issued on October 5, 2017, in comparison to the one being reviewed here. MC finds it puzzling that the ICERs for DRd and IsaPd are so different: $594,144 per QALY and $1,555,947 per QALY respectively given that the price of these two combinations do not differ greatly and their respective efficacy is in the same ballpark. The magnitude of difference of about $1,000,000 which seems very high. Accepting we cannot make a direct comparison between these two therapies; from a patient perspective, we would assume the QALYs to be closer. Can CADTH provide insights on why that is?

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