MEMORANDUM TO: Megan Ashlee Bowes
Vice-President, Corporate Strategy and Services, CADTH

FROM: Diane McArthur
Chair, Procedural Review Panel

Date: February 1, 2023

RE: Procedural Review of tafasitamab (Minjuvi™)

Dear Ms. Bowes,

I am writing on behalf of the Procedural Review Panel (Panel) regarding the results of our recent review of procedures followed by the CADTH in its review of tafasitamab (Minjuvi™). This is the third Panel review to determine if any errors were made by CADTH with respect to its adherence to the procedures as outlined in the *Procedures for CADTH Reimbursement Reviews* (September 2022 version) and is not related to other content or to the scientific validity of the analyses leading to the conclusions in the final recommendation.

The Panel was very impressed by the quality and thoughtfulness of the materials presented by Incyte Biosciences Canada (Incyte) and CADTH and the new issues raised for consideration. However, as in previous reviews, there were issues raised that related to consistency with previous drug reviews' level of evidence. The Panel maintains its previous finding that there is no technical breach of the Procedures and that these arguments fall under the rubric of content and/or scientific issues. This issue is one that could be removed from debate with a clearer statement in the Procedures document relevant to consistency with previous reviews, which the Panel hopes is imminent.

Incyte raised three other issues for the Panel to consider. First, that the recommendation of the CADTH/pERC report aligns with a conclusion of "Reimburse with Conditions" and does not align with "Do Not Reimburse;" second, that CADTH did not adhere to its conflict of interest (COI) guidelines; and third, that there were two issues relating to clinical expertise a) convening of the review panel did not meet the guidelines because it did not include sufficient clinical experts; and b) that an audio recording error meant that not all the evidence presented by one expert during a reconsideration meeting between Incyte and CADTH was provided to pERC. On each of these issues, the Panel does not find that the Procedures were breached, as discussed below.

Panel meeting with Incyte and CADTH

The Panel was convened on January 12, 2023 to hear presentations from Incyte and the CADTH Drug Review Team with respect to the CADTH/pERC final recommendation

for tafasitamab (Minjuvi™). In preparation for the meeting, the Panel reviewed the following materials:

1. Meeting agenda
2. Procedural Review Application submitted by Incyte
3. Slide Decks prepared by Incyte and CADTH
4. Procedures for CADTH Reimbursement Reviews (September 2022 version)

The Panel reconvened on January 23, 2023 to review the following materials requested in follow-up to the January 12, 2023 meeting:

1. January 17, 2023 Memo from [redacted], Incyte Biosciences Canada
2. CADTH Response documentation on COI and Reimburse with Conditions, Table 20 of the Procedures.

Panel Deliberations

In addition to the issue of consistency discussed above, the Panel's findings on the three remaining issues are set out below.

1. CADTH/pERC Conclusion

> With respect to the issue that the conclusions reached by CADTH/pERC in the review of tafasitamab (Minjuvi™) fit more closely with a "Reimburse with Conditions" recommendation than a "Do not Reimburse" recommendation as described in the Procedures, the Panel does not agree. The Panel reviewed the wording of the CADTH/pERC final recommendation report, with particular attention to the sections "Rationale for the Recommendation" and "Discussion Points." The Panel concluded that the CADTH/pERC statements regarding the clinical benefit and the safety of tafasitamab (Minjuvi™) in combination with lenalidomide, the ability of this treatment to meet patient needs, and the comparison of this treatment to other available treatments for this patient population, did not satisfy the relevant "Reimburse with recommendations" criterion[1], and did not conflict with the "Do not Reimburse" criterion.[2] Therefore, the Panel finds no breach of the Procedures in this regard.

2. Conflict of Interest

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[1] "The drug under review demonstrates clinical benefit, with a greater degree of uncertainty and an acceptable balance between benefits and harms in a therapeutic area with significant unmet clinical need. In such cases, if the cost or cost-effectiveness relative to one or more appropriate comparators is unacceptable, a condition may include a reduced price."

[2] "The drug under review does not demonstrate comparable clinical benefit relative to one or more appropriate comparators. "

Incyte argued that one of the pERC members had a conflict of interest that was undeclared in that the member had participated in the development of a methodology for assessing real world evidence that was not used in the analysis of tafasitamab (Minjuvi™), and that this presented a COI. COI is a very complex and nuanced area, and the Panel is not qualified to make a determination of whether or not a COI exists in this particular situation. Because COI is so nuanced, the best practice is to ensure CADTH expert committee members are informed of their obligations and canvassed at the outset of every meeting to declare if they believe a real or perceived conflict exists.

The Panel requested and received details regarding the canvassing of pERC members for COI, and records to confirm COI canvassing at the pERC meetings relevant to this specific concern. The Panel is satisfied that pERC members were canvassed regularly, and that in previous meetings the member in question was consistent in their declaration. The Panel encourages CADTH to continually educate its expert committee members on their responsibilities and best practices in COI.

3. Clinical Expertise

a) The first issue that Incyte argued was that the review of tafasitamab (Minjuvi™) was flawed in that it did not have sufficient experts providing advice, citing the clinical diversity of the INESSS subcommittee that advises its main decision-making arm. The Panel finds that pERC, with its mandate to “make recommendations regarding the reimbursement and the optimal use of oncology pharmaceutical products to publicly funded drug programs and cancer agencies in the federal, provincial and territorial ministries of health in Canada that participate in the program”, includes oncologists, hematologists and cancer patients from various provinces as standing members, and receives clinical input from at least one additional clinical expert during its assessment of each submission. Furthermore, pERC, unlike the expert committee convened to advise INESSS, has the benefit of being the recommendation-making body.

b) The second issue raised was that because there was a recording error affecting part of the presentation of a clinical expert during the first ten minutes of the Request for Reconsideration meeting between Incyte and CADTH, important information was not subsequently conveyed to pERC. The Panel heard from CADTH that in response to the recording issue, the meeting was extended by ten minutes to compensate. In addition, Incyte was responsible for documenting the data presented at the meeting. Both of these measures should have been sufficient to allow Incyte opportunity to raise information it felt critical to the process even though the clinical expert they retained was unable to remain for the additional time. The Panel did not find the recording error to be a breach of the Procedures.

Once again, I would like to thank my fellow Panel members Jonah Dupuis and Dr. Anthony Fields for the open, respectful, and frank debate on the issues raised in this Review. Their willingness to challenge all aspects of the process and their clinical and professional experiences dealing with both patients and clinicians has been exceedingly helpful in rounding out our discussions. With respect to the presenters, the Panel is unanimous in their gratitude for the high quality and professionalism of both the materials and the discussion.

Sincerely,

Diane McArthur,
Chair, Procedural Review Panel

c Jonah Dupuis
Dr. A.L.A. (Tony) Fields