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

FROM: Diane McArthur
Chair, Procedural Review Panel

Date: December 12 2022

RE: Procedural Review of Cariprazine (Vraylar™)

Dear Ms. Bowes,

I am writing on behalf of the Procedural Review Panel (the Panel) regarding the results of our recent review of procedures followed by CADTH in its review of Cariprazine (Vraylar™). This is the second 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 scientific issues in the final recommendation.

In June, the Panel submitted its first report to CADTH and, although the Panel found no breach of procedures, it recommended that CADTH, in its reimbursement recommendation documents, should be more clear in communicating the reasons for recommendations:

> *This is especially important during reconsiderations, or where recommendations differ from those made on recently reviewed similar products. Including information about how CDEC has considered input specific to the drug in question as part of each report will enhance stakeholder confidence in the review processes[1].*

In response to that recommendation, CADTH committed to updating its Procedures documents and improving the communications documents relating to product reviews. The Panel understands that these efforts are underway and are expected to be completed shortly.

The Panel was again impressed by the quality and thoughtfulness of the materials presented by AbbVie and by CADTH, and as a result had a very vigorous debate before determining that there was no technical breach. However, given that Cariprazine (Vraylar™) presents a very similar situation to that reviewed in June, CDEC and supporting CADTH staff should have been aware of the Panel recommendations by the time of the reconsideration report, and should be reasonably expected to make efforts to implement the intent.

As a result, the Panel is requesting that the CDEC Chair and CADTH staff review the final reimbursement recommendation document and update the contents to more

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[1] Procedural Panel correspondence: *Procedural Review of Inclisiran (Leqvio™)* 13 June 2022

clearly reflect how the additional information provided to the Committee was considered.

Panel meeting with AbbVie and CADTH

The Panel met on Wednesday, November 16, 2022 to hear presentations by the representatives of AbbVie, the manufacturer of Cariprazine (Vraylar™) and the CADTH Drug Review Team. The Panel had previously received and reviewed the following documentation:

1. Meeting agenda
2. Procedural Review Application and Supporting Documentation
3. Slide Decks prepared by AbbVie and CADTH
4. Additional material submitted by AbbVie in November
5. Reimbursement Review Procedures (September 2022 version)

Subsequent to the meeting, the Panel requested and received a copy of the CDEC Agenda for July 27-28, 2022 and Presenter Materials for Cariprazine (Vraylar™) .

Panel Deliberations

AbbVie raised four issues with regard to the Procedural Review Process.

1. Consistency in Drug Reviews

   AbbVie raised issues similar to those previously debated in the June Review, and the Panel again decided by a vote of 2-1 that CDEC's recommendation on Cariprazine (Vraylar™) did not violate the Procedures. However the Panel was struck by the disappointing lack of attention to the written documentation of the key decision-factors particularly given the fact that this product is similar to another that was reviewed within a relatively close period of time with what could, to a lay person appear to be similar evidence - the exact circumstances commented on in our first Report. The Panel understands that improvements to the Procedural document are in process and hopes that these will be posted in the very near future, but also believes the improvements in report writing can be implemented ahead of those changes.

2. Incomplete stakeholder feedback was provided the CDEC

   The Panel finds that, as disclosed by CADTH in the pre-meeting between CADTH and AbbVie, this was an administrative documentation error on the website, and that complete feedback was provided to the CDEC. This is supported by the CDEC agenda and presenter materials provided to the Panel.

3. Consideration of stakeholder feedback was not transparent in the final recommendation

   The Panel reviewed the materials provided to the CDEC for the reconsideration, and despite the poor documentation of the discussion, the CDEC did consider the additional input and as a result there is no technical breach of the Procedures. However, the Panel recommends that CDEC and CADTH staff make every effort in reconsideration reports to acknowledge the feedback and submissions provided by stakeholders in order to ensure that the core value of transparency is more visible and to illustrate that such feedback is indeed weighed in the review process.

4. Deliberative Framework in the procedures document is mandatory not illustrative

   As previously determined, the Panel finds that the list of factors included in the Deliberative Framework is meant to be illustrative and not exhaustive i.e., not mandatory, and as a result again finds no breach.

Finally a few comments on the Panel's hopes for future CDEC recommendations. While we know it is very difficult to translate the outcomes of complex scientific discussions and deliberations into plain language, the Panel believes that explanations need to be procedurally sound and, in particular convey those factors that affect critical decision-points. As stated previously, nowhere is this more important than in the consideration of products that appear similar or appear to have similar evidentiary outcomes and which are reviewed within a relatively close time horizon.

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