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INNOVATIVE MEDICINES CANADA | MÉDICAMENTS NOVATEURS CANADA

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Dr. Brian O'Rourke
President and CEO
Canadian Agency for Drugs and Technologies in Health
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Ottawa, ON, K1S 5S8

By electronic email: briano@cadth.ca

Re: Revising CADTH Common Drug Review Recommendations in the CADTH Therapeutic Review Process

Dear Dr. O'Rourke,

On behalf of Innovative Medicines Canada and BIOTECanada, thank you for the opportunity to provide you with joint feedback on the consultation arising from *CDR Update – Issue 124* with respect to CDR Recommendations and the Therapeutic Review process.

The industry appreciates the measures CADTH is taking to review drugs for individual therapeutic indications from a lifecycle perspective and the role therapeutic reviews play in this area. We also appreciate the need for enhanced efficiencies within current CADTH drug review processes and that this proposal is an attempt to improve efficiencies regarding the implementation of Therapeutic Reviews. However, we have concerns regarding potential implications of Therapeutic Reviews (TRs) superseding recommendations under CADTH's well-established Common Drug Review (CDR) process, as described in the CADTH consultation document.[1]

Specifically, our members have identified a number of concerns with the proposed changes, as follows:

1. **CDR and pCODR drug review procedures are substantively distinct from CADTH's framework for Therapeutic Reviews. The two review streams and their final outputs (i.e. recommendations) should not be considered interchangeable.**

Although the therapeutic review framework provides multiple written feedback opportunities from the stakeholders, there are major differences in how reviews are initiated and their subsequent scope from one process to the other. CDR reviews are typically for single technologies only and are initiated through a

[1] *We appreciate that TRs have not been conducted in oncology, however, the CADTH consultation document suggests that the proposed approach would not preclude this policy from also being applied to oncology drugs in the future.*

manufacturer submission under a clearly identified process and scope, including advance stakeholder public notification.

The topic selection process for Therapeutic Reviews is largely informed or driven by jurisdictions, with no input opportunities for external stakeholders.

Therapeutic reviews often carry the risk of overgeneralizing groups of technologies and diminish the unique nature and benefits of individual technologies. In many cases, the class-comparison methodology does not provide the specificity required to inform decision making on individual technologies.

CADTH should develop a recommendation framework specific to therapeutic reviews with tangible examples of implementation guidance. TR comparison methodologies and an associated TR recommendation framework should allow for recognition of the unique benefits of different technologies for different patients.

At present, there are several notable differences between the CDR procedure in comparison to the TR framework or process. The respective processes require different models to address certain clinical or economic questions, linked to the context and research questions in each review. The body of evidence could be different at any given point in time. Feedback opportunities are different and may address important evidentiary or implementation issues. Although the recommendations are issued by the same expert committee, each process generates recommendations which are different in both their construction and potential application.

The following table summarizes several key differences and highlights the need for a careful review of both processes to ensure appropriateness and consistency of intent and high-quality review in line with stakeholder needs.

Table 1: Key Differences between the CDR Process and the Therapeutic Review Framework

Process Element	Common Drug Review	Therapeutic Review
Manufacturer initiates drug submission	Yes	No
Provinces can request advice / review	Yes	Yes
Topic selection predictable and transparent	Yes	No
Transparent recommendation framework • Expert committee is guided by a transparent set of recommendation options	Yes	No (no recommendation framework specific to

that has been validated through extensive stakeholder consultation		therapeutic reviews available)
Subject of clinical comparison is the subject of expert committee recommendation • Expert recommendations directly relate to the clinical comparisons made as part of the analysis	Yes	Maybe
Process to validate how patient and manufacturer input has been considered by the review	No	No
Patient engagement	Yes	Yes
Typically, less than 8 months to complete review	Yes	No
Appeal opportunity	No	No
Off-label reviews • Recommendations include indications not approved by Health Canada and thus face implementation challenges	No	Yes
Health Economics Model and Analysis	Yes (developed and submitted by the manufacturer; cost-utility analysis in most cases)	Yes (developed by CADTH; NMA[2] based cost-minimization analysis commonly used)

[2] *Network meta-analysis*

Opportunity to redact sensitive information • Enables the submission of complete information that may impact review quality	Yes	No

2. **Policy proposal would effectively replace the Request for Advice process that already includes appropriate mechanisms for stakeholder engagement. The TR framework does not have comparable input mechanisms. This shift would require the addition of new process elements such as check-point meetings and an effective appeal mechanism.**

Removing the use of the CDR Request for Advice procedure in the context of TRs would result in comparatively less useful information for all parties and a relatively less robust review process overall.

It is important to note that the Request of Advice process includes a clear step where the issues of interest and/or research questions from the CDR participating public drug plans are clearly stated. This context and opportunity to identify which elements of the review are of most interest to jurisdictions is critical. This has consequences for the presentation of most relevant evidence, in addition to any implementation or other practical considerations.

The current CDR Request for Advice process results in a report or a revised recommendation that includes meaningful details. Within this report, the explanation of how the results of a Therapeutic Review impact specific existing Expert Committee recommendations is important – this impact cannot simply be assumed and made automatic as context is often relevant for all stakeholders.

The proposed changes would result in the elimination of these meaningful points of reference for all parties, including key issues such as the past record of submissions in the given therapeutic area, the comparison of past Expert Committee recommendations (which themselves may have taken different formats over time due to process changes within CDR), and a compendium of relevant patient and stakeholder input on the record. We suggest that appropriate mechanisms should be put in place to ensure these opportunities are not lost in the revised TR process.

Without appropriate safeguards in the TR framework and process outline, the policy changes could remove important opportunities for interaction between reviewers and manufacturers. If moving to this model, CADTH would need to add other process elements to the Therapeutic Review process including a mechanism for more meaningful engagement during the review to address issues that tend to arise with TRs, including a check-point meeting opportunity for the affected manufacturers during the review process and after an initial or draft TR recommendation is available.

3. **The revised process may have significant implications for the pan-Canadian Pharmaceutical Alliance (pCPA) process and existing Product Listing Agreements (PLAs).**

This proposal would appear to inevitably impact current and future drug listing negotiations, but the nature of how the various procedures would fit together is unclear. There are outstanding questions from our perspective as to the intended impact of Therapeutic Review recommendations and revised Expert

Committee recommendations, including from a jurisdiction implementation standpoint. Existing agreements may include unique terms on pricing or other criteria tied to place in therapy which may not be addressed by either the Therapeutic Review or previous Expert Committee recommendation.

Greater elaboration and clarity is required on the application of the revised process recommendations to the evolving pharmaceutical negotiation and reimbursement landscape. In particular, a transparent and predictable recommendation framework specific to therapeutic reviews is required to help all stakeholders understand the key considerations from a recommendation as well as down-stream implementation perspective. This would have to include clear guidance and explicit determinations by the expert committee on any revisions to previous recommendations.

Implementing this in a fair and consistent way that usefully informs pCPA negotiations would be much more difficult and complex than currently envisioned. It will not be as simple as one review 'superseding' another and suggest that a clear framework be developed and consulted on in advance of any implementation of this proposal. Superseding an existing agreement between the manufacturer and the payer with the results of a TR will be procedurally unfair to the manufacturer who negotiated in good faith and could result in reduced market access, without the opportunity for the manufacturer to engage or appeal the new decision.

4. **Need for more direct engagement with external stakeholders (i.e. industry, patient groups, clinical experts etc.) through the entire course of a therapeutic review, from initiation to the final recommendation stage.**

Both the CDR process and the TR framework would be enhanced if opportunities for direct engagement were incorporated into the process through a check-point meeting similar to the pCODR process. Furthermore, there is no clear process or mechanism to validate how patient and manufacturer input has actually been considered within the review.

Further clarity is needed to understand the impact this proposal will have on the mechanism of Request for Reconsideration where a specific Therapeutic Review recommendations would supersede existing CDR recommendations. The proposed process is a departure from the current Request for Reconsideration mechanism which is the only opportunity CADTH provides in the absence of an appeal mechanism. Requests for Reconsideration are important and legitimate opportunities for manufacturers to make arguments on procedural fairness in the application of the CDR procedure.

Although CADTH provides an opportunity to stakeholders to comment on draft recommendations, this is not the same as the opportunities for fling a reconsideration request through the CDR process. Any changes to Expert Committee recommendations should always include meaningful opportunities for stakeholder feedback, especially from patients and clinicians impacted by potential changes, to ensure the implications of any changes are identified and assessed appropriately.

5. **The process should ensure that the right research questions are being addressed and any comparisons between therapies are fully appropriate.**

It is critical that the analysis make appropriate "apples-to-apples" comparisons, that all the necessary data are available, and the process allows for the introduction of emerging evidence from a variety of sources. Depending on the specific research or policy question of interest, manufacturers may be aware of newer

information beyond traditional Randomized-Controlled Trials (RCT) data previously submitted for either marketing authorization or HTA purposes.

6. **The proposed manufacturer feedback period is insufficient.**

Given the importance of reviewing draft Therapeutic Review recommendations, procedural fairness would suggest that a much more reasonable feedback window is warranted. Ten business days represents a substantial and unreasonable burden on manufacturers to assess and respond to draft recommendations and, in some cases, hundreds of pages of analysis. We would recommend that CADTH consider extending the feedback period for all therapeutic reviews to thirty (30) business days.

7. **Greater clarity on the application of Therapeutic Reviews to past CDEC/CEDAC reviews is needed.**

The language in the consultation document around the replacement of existing CDEC and CEDAC recommendations would benefit from further clarification from CADTH (see point #1, and footnote #1 in the CADTH consultation document).

CADTH should confirm that no previous Therapeutic Reviews would be applied retroactively to revise previous CDR recommendations.

We appreciate your careful consideration of our comments. We recognize that there may be other points of context or direction received by CADTH from its member jurisdictions related to these changes. As such, we would appreciate the opportunity to meet with your staff to elaborate on our comments on a more direct basis prior to any revised procedures being finalized.

Sincerely,

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BIOTECanada

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