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THE CANADIAN FORUM FOR RARE DISEASE INNOVATORS

RESPONSE

To the Pan-Canadian National Formulary Discussion Paper

Canadian Agency for Drugs and Technologies in Health (CADTH)

February 25, 2021

1. As part of developing a framework, the panel recommended 6 guiding principles and accompanying definitions that would shape the overall system for a potential pan-Canadian formulary. Please refer to Table 1 in the discussion paper.
Do you agree with the proposed principles and definitions? Please provide the reason(s) and suggested changes, if any.

While RAREi has no major objections to the principles outlined by the panel, it would propose adding at least one that would require national formulary managers to administer the list in a way that supports continued treatment innovation and the introduction of new technologies on an ongoing basis. This will ensure that Canada will be able to maintain a globally competitive stance in terms of providing patients with timely access to the latest scientifically advanced treatment options to improve outcomes, reduce health system utilization, improve productivity and meet their quality of life expectations and needs. It will also align with the broader national policy objective of supporting a globally competitive innovation economy and a viable and productive biomanufacturing and life sciences strategy in this country.

RAREi also notes that the chosen principles were developed in the context of health funding transfers and inter-jurisdictional relations, as opposed to addressing an evaluation framework. For this reason, the panel should review and consider adapting the principles developed and followed by the pan-Canadian Oncology Drug Review and later, largely adopted by the pan-Canadian Pharmaceutical Alliance. These principles were developed in the context of a review program for health technologies which, fundamentally, is the core function of the advisory panel as well. Notably, these guiding principles also will be helpful in responding to many of the "out of scope" issues noted in the discussion paper. They include:

1. *Governance* - A review process with governance structures that are fair, objective, transparent and accountable to patients, payers, the public and innovators

2. *Representation* – A review process that is multidisciplinary, cross-jurisdictional and collaborative in nature with appropriate representation from diverse stakeholders and linked to other key national initiatives

3. *Efficient and Effective* – A review process that is cost-efficient, effective and streamlined (i.e. reduced duplication) to support timely decision-making

4. *Evaluation* – A review process with capacity for data capture and ongoing evaluation (decision monitoring / performance measurement) to support continuous process improvements. In addition, capacity for health outcomes and economic impact analysis to support decision-making and planning

5. *Health System Focus* - Medications are evaluated within a review process and decision making framework that are consistent with those used for medicines for other diseases

6. *Evidence-based* - A review process with capacity for rigorous and consistent evidence-based clinical and pharmacoeconomic reviews to support evidence-based decision-making

7. *Excellence* - A review process that reflects an ongoing commitment to excellence through incorporation of best practices in a spirit of continuous quality improvement

8. *Ethical Framework* - A review process that includes an ethical framework which balances the need for timely and quality therapies with broader societal values

2. The panel recommended a 3-stage approach to creating a potential pan-Canadian formulary. Stage 1 is developing a process to create a proposed sample list of commonly prescribed drugs and related products. The proposed sample list is a starting point and is meant to be a proof of concept for the process. Part of the process involved comparing the listing status of each drug on existing public drug plan formularies and identifying gaps in access. The proposed principles were also applied when discussing each drug. A predefined assessment criteria was used by the panel to determine if a drug or related product should be included, flagged for additional expert consultation, or excluded from the proposed sample list. Please refer to Table 2 in the discussion paper for more information on the proposed assessment criteria.
Do you agree with the proposed assessment criteria? Please provide the reason(s) and suggested changes, if any.

Once again, there is little to criticize conceptually in the proposed assessment criteria adopted by the panel. However, it appears to be an exercise without much point. According to a 2017 Patented Medicine Prices Review Board report examining alignment among public formularies, there is already a high degree of concordance (at least 80%) among public drug plan formularies in Canada, and that alignment is even higher when one considers the most utilized products.[1] Those findings beg the question of what problem the panel is being asked to solve.

If the intention is to ensure that every medication coverage plan offers a minimum range of effective medicines, then it would appear that objective has been met already since public plans across the country offer a similarly broad range of treatments, and private plans almost always cover a more extensive list of medicines than are reimbursed publicly.

If, on the other hand, the hope is to create one common list that all plans must offer, then much more fundamental questions arise about who pays, how such a program would be administered and how existing programs would be affected. The concepts of equality (same) and equity (fairness) need to be considered carefully, especially in the context of rare disorders where it is especially critical for a range of clinical options and tools to be made available in order to treat some of the most complicated and challenging medical conditions. In any case, a broader national discussion that takes into account many of the "out of scope" issues for this exercise is required in order for it to remain a principles-guided exercise.

In addition to policy-design challenges, the proposals raise administrative and resource issues. Already, the Canadian public medication review and approval process is duplicative, lengthy and often backlogged.[2] It relies on a large number of expert reviewers who are kept quite busy with the workload currently facing them. Diverting that expertise to undertake the additional assessments required by this national formulary development exercise seems counter-productive to the ongoing effort to increase the efficiency of the existing processes.

Anything that would add steps or extend the timelines associated with the current review process would be viewed as highly problematic by RAREi members.

[1] PMPRB, *Alignment Among Public Formularies in Canada, Part 1: General Overview*, October 2017: http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1327&lang=en.
[2] Innovative Medicines Canada, Explaining Public Reimbursement Delays for New Medicines for Canadian Patients, July 30, 2020: http://innovativemedicines.ca/resource/explaining-public-reimbursement-delays-new-medicines-canadian-patients.

In the context of rare disease treatments specifically, RAREi encourages the panel to consider starting from the first article of the United Nations resolution on rare diseases adopted by the General Assembly on December 16, 2021. It calls upon all member states to strengthen their respective health systems, notably in terms of primary health care, in order "to provide universal access to a wide range of healthcare services that are safe, of quality, accessible, available and affordable, timely, and clinically and financially integrated, which will help to empower persons living with a rare disease in addressing their physical and mental health needs to realize their human rights, including their right to the highest attainable standard of physical and mental health, to enhance health equity and equality, end discrimination and stigma, eliminate gaps in coverage and create a more inclusive society."[3]

3. Related products (devices that assist with the delivery or administration of drugs and/or are necessary for the optimal use of drugs), primarily those for patients with diabetes, were assessed by the panel for inclusion on the proposed sample list. The panel felt strongly that the inclusion of related products on a potential pan-Canadian formulary should be explored because this could help improve patient access and could potentially improve adherence with drug treatment. In many cases, these related products are covered through different programs within the health system, which makes accessing coverage difficult for patients. As such, a potential pan-Canadian formulary could be an opportunity to streamline the process, provide simplified access, and ultimately help patients access these types of products. The panel noted the importance of having standard criteria to help determine which related products should be eligible for inclusion on the potential pan-Canadian formulary. This standardization will be particularly important when assessing new or emerging technologies that could be numerous and costly and might impact sustainability.
a. Do you have suggestion(s) on a definition and/or criteria to determine the eligibility of related products that could be included on a potential pan-Canadian formulary? Please provide details.
b. Should related products be listed in the same list for drugs and have the same evaluation criteria applied to them (see Table 3 in the discussion paper)? Please provide the reason(s). Note that this question pertains only to evaluation of related products; there will be an opportunity to comment on the proposed criteria for evaluation of new drugs in question 6.

RAREi members support the notion that devices that assist with the delivery or administration of medicines and/or are necessary for the optimal use of medications should be included as covered benefits within medication coverage programs.

In particular, members are keenly aware of the lack of clear budgets and defined assessment processes related to companion diagnostics. These important clinical tools, which are relied upon to aid in selecting or excluding specific patients for treatment with a given medication based on the patient's biological characteristics that determine responders and non-responders to the therapy, are increasingly vital to effective treatment in a range of therapeutic circumstances. However, they are often not funded and in most jurisdictions there is no obvious mechanism to facilitate consideration of them.

If this exercise was being undertaken in the context of informing a health system formulary consultation, we would agree that other related products that are directly associated with a given medication should also be included as benefits at the same time as the relevant product is listed on the formulary.

[3] United Nations *Resolution 76/132 - Addressing the challenges of persons living with a rare disease and their families.* Adopted by the General Assembly on December 16, 2021: https://www.rarediseasesinternational.org/wp-content/uploads/2022/01/Final-UN-Text-UN-Resolution-on-Persons-Living-with-a-Rare-Disease-and-their-Families.pdf.

4. Stage 2 involves scaling the process to add drugs and select related products for other health conditions to the proposed sample list. The proposed approach would follow the review steps described for stage 1 — considering the listing status from existing federal, provincial, and territorial formularies; utilization data; availability of generic or biosimilar for the drug molecule; information about safe use in pregnant and lactating women; and references summarizing available drugs and use in Canada. These considerations would be supplemented with literature reviews of pharmacotherapeutic areas that have been shown to improve health outcomes in people made vulnerable by systemic inequities (if available). Assessment would include reviewing the totality of the information.
The panel recommends that the proposed principles (e.g., universal and integrated) be applied. As part of the refinement, the panel suggests that products listed under specialized programs (e.g., cancer and special drug programs) be included. This is because product listing and eligibility, among other aspects, may differ across the country and a gap could inadvertently be created. The panel also suggests that therapeutic areas could be prioritized based on national health priorities. Further details can be found in the Stage 2: Expanding to Other Therapeutic Areas section of the discussion paper.
a. Do you support the proposed approach to expand to other therapeutic areas? Please provide the reason(s).
b. Should the remaining therapeutic areas be prioritized based on national health priorities? Please provide the reason(s).

Question 4a pre-supposes support for the creation of a national formulary in the first place and, as stated above, the objective of the exercise is unclear, which makes it challenging to comment effectively on individual process elements. It is difficult to assess the value of doing so without understanding the ultimate aim of the project and its potential impact on access to medicines in Canada.

On a general note, RAREi has consistently called for equitable coverage for rare disease treatments for Canadians, and for each component of the current medication review and approval process to be customized in ways that meet the needs of rare disease patients. That requirement also applies in the context of formulary design.

It is clear that the traditional population-based approach to identifying a range of potential medications to be prescribed to treat a given condition by placing them on general list of benefits for a broad range of possible prescribers to consider is not a practical model to meet the needs of rare disease patients.

The nature of rare disease treatment demands a more personalized approach that takes into account the specific medical needs of each patient and permits treating clinicians, who often have highly specialized expertise, extensive leeway in finding ways to address their patients' needs most effectively. Any national formulary would need to be adapted to ensure that the appropriate level of flexibility is offered for potential rare disease treatments to be made available to those in need.

Beyond those considerations for rare disease treatments, RAREi has no feedback to offer regarding the sequence of additions to three therapeutic classes already evaluated by the panel, or how additional classes should be prioritized.

5. The panel explored alternative approaches to the first-in, first-out process for reviewing new products and indications for inclusion on a potential pan-Canadian formulary (see the Selecting New Products to be Considered on a Potential Pan-Canadian Formulary section of the discussion paper). The following options were explored:

- **Option #1:** A prioritization model could be developed to align with Health Canada's priority reviews. This would allow for a predictable process for identifying products that represent a significant therapeutic advancement. Although this approach could support a seamless integration between regulatory and health technology assessment (HTA) processes, it does not address the inability to control when a submission is initiated.
- **Option #2:** A clear and transparent scoring system that would prioritize new drug submissions could be created and applied (e.g., new innovative products that address unmet needs of a population could score higher and be prioritized on a review agenda).
- **Option #3:** Opportunities to work together at an international level to review and prioritize products collectively could be explored. There have been international collaborations in several areas of regulatory and HTA processes. This could potentially save on resources and accelerate access for Canadians and international partners.

The panel encourages strong engagement and collaboration with all key stakeholders (e.g., patients, clinicians, industry, government, and HTA bodies) through all steps in the process and recommends the use of a transparent process.

a. Which option could be adopted as an alternative to a first-in, first-out submission review process? Please provide the reason(s) for your choice.

b. What criteria could be used to identify priority products?

RAREi believes that the current first-in, first-out approach to undertaking reviews of new medications / indications by regulators (Health Canada) and evaluators (CADTH, INESSS, etc.) should also be adopted by formulary designers and policymakers. That approach is necessary in order to permit innovators, which are managing within a complex global environment, to make an informed decision about whether to launch of new medicine in Canada based on a set of clear expectations regarding when a public funding review will be taken up and how long it should take to be completed.

We would ask the panel to appreciate that bringing a new medicine to Canada requires investments of multiple millions of dollars to support years of development and testing. It also involves the dedication of myriad human resources, logistical supports , marketing efforts, and a not insignificant outlay to cover submission fees at Health Canada, CADTH and INESSS. The current medication review and approvals patchwork system in Canada already challenges innovators with several layers of uncertainty, (such as the PMPRB changes, both in terms of how comparator countries are applied and the economic factors, a range of national and provincial HTA reviews and the pan-Canadian Pharmaceutical Alliance (pCPA) negotiations maze). Within this already challenging process, some level of regulatory and government decision-making certainty is necessary. With those considerations in mind, RAREi believes that innovator expectations can only be met effectively with a first-in-first out review system.

If the issue driving this desire to implement a prioritization scheme is about limited resources for review, then it must be managed as a resourcing issue, which could be addressed effectively in other ways (i.e., efficiency reviews, more funding, etc.), rather than by subjecting new products to more bureaucracy and additional reviews that could well lead to an arbitrary, resource-intensive, time-consuming and ultimately controversial determinations.

That said, there are already ways to prioritize certain products for faster reviews without changing the overall target timeframes for evaluation and decision-making. One good example is Health Canada's priority review system which operates in a manner that gives enhanced attention to important new therapies without affecting the efficiency of the review process for non-priority products. There are also clear examples at other levels of the current medication review and approval processes where prioritization occurs organically. For example, when a pCPA Letter of Intent is finalized just days or weeks after receiving a positive CADTH clinical recommendation. RAREi believes more efforts of that nature should be applied in the context of rare diseases treatments in order to streamline the existing process and speed up access for people living with rare disorders to fully realize the benefits and improved outcomes for those living with rare disease given they already face a five-year wait on average for a correct diagnosis.

6. To guide the evaluation of new drugs and new indications for a potential pan-Canadian formulary, the panel considered the following proposed criteria:

- alignment with patient and societal values
- clinical benefit
- feasibility of adoption into health systems
- value for money

The panel proposed 2 additional criteria — equitable access and additional considerations or long-term thinking — to enhance the deliberative process. The proposed criteria are linked with the guiding principles and provide the basis for decision-making with respect to the selection and evaluation of drugs for a potential pan-Canadian formulary. Please refer to Table 3 in the discussion paper for details on the proposed evaluation criteria for new products.

Do you agree with the proposed evaluation criteria and the considerations for new products? Please provide the reason(s) and suggested changes, if any.

Broadly speaking, RAREi supports the concept of deliberative frameworks and the criteria they rely on to guide the development of formulary recommendations and decision-making. That said, the current processes used by CADTH and INESSS have significant gaps and inconsistencies that we believe must be remedied before they are adopted by a pan-Canadian formulary design initiative.

As a starting point, RAREi recommends incorporating concepts such as the "rule of rescue," ethical considerations and societal values, such as the need for an innovative life sciences and pharmaceutical sector in Canada. In addition, the deliberative process should be open, transparent and available for external reviews to ensure accountability for reasonableness.

7. The panel also provided recommendations on a deliberative process for using the proposed criteria and applying them in practice. Of particular interest, they explored ways to structure the deliberative process so that evidence from multiple disciplines and perspectives could be weighted. The panel proposed that evaluating and selecting products for a potential pan-Canadian formulary should involve an expert committee. Please see the Deliberative Process section in the discussion paper for details.

Should the deliberative process include weighting of the evidence or a score for each criterion? If yes, how should weight be distributed among the proposed criteria?

While multi-criteria decision analysis (MCDA) has some utility, it should be used as a tool, not a rule, given that it could in some cases lead to inequitable outcomes. An evidence weighting system needs to account for specific therapeutic contexts, such as ensuring access to rare disease treatments. If the panel proposes an MCDA approach, then further stakeholder dialogue involving methodological expertise would be required.

8. Current Canadian drug review processes generally focus on assessment of new products. There is a desire to ramp up formulary modernization strategies (e.g., reassessments, therapeutic reviews) and to re-evaluate existing listed products with emerging new evidence on a regular cycle (e.g., every 3 years to 5 years). This would likely increase the workload of stakeholders throughout the health system (e.g., clinicians, patients and patient groups, researchers, industry, regulators, and plan administrators).
What measures could be put in place to ensure operational sustainability, with limited resources and time, including the ability of stakeholders to participate meaningfully in multiple processes (e.g., should there be a prioritization system for listed products to be re-evaluated or other criteria to determine eligibility for reassessment or therapeutic review)?

RAREi understands the desire to manage the proposed national formulary in the context of the full life cycles of all the products on the list, and to ensure that the list of benefits remains current with respect to meeting clinical needs. However, care must be taken to avoid directing vital resources away from the already demanding reimbursement review process in Canada.

RAREi members believe that maintaining an efficient and timely HTA review process and ensuring ongoing and regular updates to existing public formularies for new medicines / indications must take precedence over efforts to build or maintain a national formulary and/or to conduct after-market review reassessments and therapeutic class reviews.

Canadian patients already wait longer than those in most comparable nations for access to new treatments. For example, Canada ranks 18th out of 20 Organization for Economic Co-operation and Development countries when considering the time from the first global authorization of a new treatment to public reimbursement for at least 20% of public plan beneficiaries.[4] Given that reality, RAREi recommends that additions to those existing processes should be deferred until efforts to streamline and improve those existing processes are exhausted.

In reality, there are already mechanisms in place within the existing formulary review system that help ensure that the formularies remain relevant and support plan sustainability. Reimbursement policies such as the identification of lowest cost alternatives, mandatory generic substitution and preferential listings for biosimilars already – and in some cases problematically – move patients to less costly versions of specific medicines. In addition, therapeutic class reviews and various reference pricing schemes are used to incent the use of lower cost options within a particular class. At the same time, the system responds organically as clinical practices change. Given all that, it is unclear that dedicating substantial new resources to creating and maintaining a national formulary will be any more effective at keeping the system current or supporting system sustainability.

9. Are there any other comments that you would like to share with us?

The biggest challenge in responding to the discussion paper is the lack of clarity about what problem or objective the exercise is directed at solving.

Given that lack of clarity in terms of how the new formulary would be used, which patients would be served, how it would be governed administered and financed, what impact it might have on existing medication coverage programs in Canada and its place in the broader national pharmaceutical policy proposals currently

[4] Innovative Medicines Canada, Explaining Public Reimbursement Delays for New Medicines for Canadian Patients, July 30, 2020: http://innovativemedicines.ca/resource/explaining-public-reimbursement-delays-new-medicines-canadian-patients.

under development, it is hard to assess the proposal. To be clear, given additional understanding of those questions, RAREi's feedback would likely be quite different.

In light of the many relevant matters that remain unanswered, it appears that the panel's efforts are premature and lacking the necessary context that would allow for a more pragmatic assessment of the necessity and value of pursuing the creation of a new national formulary.

At the same time, the nature of medical care is shifting quickly towards more personalized care models that will demand new ways of thinking regarding what products are made available to which patients. The traditional population-based approach to building and maintaining a list of eligible treatment benefits that are available to a wide range of patients is not a practical model for managing reimbursement of pharmaceutical care in the future, especially within a developed and mature health system such as Canada's. This will require a fundamental rethinking about how we will be able to ensure that the right patient is able to access the treatments that meet their individual clinical needs. With that in mind, it seems counter-productive to invest in building a new national formulary.

This is particularly the case given that most Canadians are well-served by their existing medication coverage. In fact, a national poll conducted by Abacus Data in January 2020 for the Canadian Life and Health Insurance Association found that 83% respondents reported having access to some kind of pharmaceutical coverage, 85% were broadly satisfied with the costs they were required to pay and 84% were satisfied with the range of medicines covered. Among those whose plan required patient cost-sharing, 88% say the co-pay amount was affordable or "affordable enough."[5]

What these data indicate is that there is no broad public demand for a single national formulary in Canada. Where the need exists is among communities, like rare disease patients, whose needs are not being well met by the current coverage system. RAREi believes that rather than pursuing the creation of a national formulary, pharmaceutical policy reform efforts should be focused on addressing coverage gaps. In that context , RAREi members are hopeful that the still-to-be announced national rare disease treatment strategy under development by Health Canada will be organized in such a way as to improve affordable and funded access to treatments for rare disorders.

[5] Abacus Data, *Canadians' views surrounding pharmacare***,** February 27, 2020: https://abacusdata.ca/pharmacare-views-canada.