Biogen's Written Submission Regarding the Patented Medicines Price Review Board's 2020 Draft Guidelines

On behalf of Biogen Canada, we are pleased to submit our feedback on the Patented Medicine Prices Review Board's (PMPRB) June 2020 Draft Guidelines (Draft Guidelines), published on June 19, 2020.

This submission is supplementary to our submission to the November 2019 Draft Guidelines (2019 Draft Guidelines) consultation as well as those of our industry associations, BIOTECanada and RAREi.

We acknowledge that the PMPRB made significant changes to Draft Guidelines in response to feedback received during the 2019 Draft Guidelines consultation, in particular, the new Maximum List Price (MLP) calculation for grandfathered and line extension products, and the reintroduction of "degree of innovation" into price controls.
However, Biogen submits that the Draft Guidelines still do not encourage equitable and fast access to innovative products for all Canadians nor do they encourage research investments and first mover advantage for innovative launches in Canada, especially as it pertains to breakthrough innovations and rare diseases.

In our previous submission, Biogen outlined three fundamental areas of concern: the pharmacoeconomic value assessment, the market size adjustment methodology and compromised confidentiality. We will not repeat them here. These fundamental concerns have not been addressed in the Draft Guidelines. While we acknowledge that the thresholds have been amended, they continue to be arbitrary and unsupported by evidence.

We recommend that the Draft Guidelines need to:

1. Embody a value-based approach to pricing regulation
2. Incentivize rare disease and breakthrough therapies
3. Include a change management strategy for successful implementation

Value-Based Pricing

Biogen supports value-based pricing that encompasses broad and holistic considerations of value to Canadians and their health care system. True value to Canadians goes beyond price and includes patient outcomes, savings and improvements of quality of life, productivity and socioeconomic cost, medical and research investments, patient support programs, compassionate access programs and more, most of which are excluded from the narrow R&D investment allowable for PMPRB filings.

The Draft Guidelines attempt to introduce a value lens by importing the findings of Health Technology Assessment (HTA) agencies into the PMPRB's mandate of price regulation.

Biogen disagrees with this approach because:

1. HTAs are not intended for price controls and the role of cost-utility analysis (CUA) in pricing regulation is controversial and untested
2. HTAs become now, in effect, mandatory

3. HTAs are being used inappropriately in markets for which they were not designed; their application to PMPRB decisions is not afforded the principles of procedural and administrative fairness expected of a quasi-judicial body, and
4. HTA agencies often produce inconsistent analyses

The Canadian Agency for Drugs and Technologies in Health (CADTH) and the Institut National D'excellence en Santé et en Services Sociaux (INESSS) do not produce consistent CUAs. As agencies, they focus on different perspectives for pharmacoeconomic analyses that can produce vastly different CUA results. Economic evaluations submitted to INESSS, for instance, need to include indirect societal costs (*e.g.*, productivity losses) because its perspective is societal and broader than that of CADTH, which sets the health system perspective as base case.

CUAs submitted by manufacturers and re-analyzed by HTA agencies on the same product/indication often result in highly variable incremental cost effectiveness ratios. For example, analysis of 27 files with published incremental cost utility ratios (ICURs) in the pan Canadian Oncology Drug Review (pCODR) database suggested that the mean difference between manufacturer submitted ICURs and pCODR estimates was 128%. The difference was as high as 718% when estimating the high-end ranges of the ICURs in the model.[1]

Notwithstanding these inconsistencies, the Draft Guidelines, in effect, mandate patentees to make HTA submissions by applying an automatic 50% reduction to a product's MLP in the absence of CUA. The decision to submit to an HTA agency and undertake the associated administrative burden and costs should be a business decision, based on the patient population, made by the manufacturer and not mandated by a pricing regulator.

In addition to compelling HTA submissions, the Draft Guidelines inappropriately expand the application of CUAs to drug prices overall, including for private payors. However, CADTH and INESSS are public agencies designed to conduct HTAs for public payors; their assessments are driven by public interests that differ from those of employers and private drug insurers.

Since the PMPRB established a new relationship between itself and HTA agencies, it is now imperative that its process for determining, and using, CUAs be subject to review and appeal. As a quasi-judicial body, if the PMPRB intends to rely on the findings of HTA agencies, the rights of procedural and administrative fairness expected of the PMPRB must also be extended to the assessment conducted by HTA agencies.

Biogen values the role of HTA agencies but disagrees with their mandatory use and extension beyond public payors. In many EU countries, pricing and HTA processes remain independent to ensure impartial data review and assessment of social impact. We recommend that the PMPRB re-evaluate its relationship with HTA agencies and broaden its definition of value. At minimum, if the PMPRB maintains the role of HTAs in pricing regulation, it should adopt the approach of INESS for greater alignment with holistic, value-based pricing.

Recommendations:

- the PMPRB broaden its consideration of value to embody a more holistic approach of what matters to Canadians

[1] Yin et al. "Analysis of Differences in Incremental Cost-Effectiveness Ratio Estimates from Manufacturers and the pan-Canadian Oncology Drug Review Economic Guidance Panel" (2015) <http://cc-arcc.ca/wp-content/uploads/2015/01/136-Yin-Sunday.pdf>

- the PMPRB re-evaluate its intended relationship with HTA agencies and remove the automatic MLP reduction to products without a CUA
- CUAs generated by INESSS be considered with equal or greater weight to CUAs generated by CADTH, or in the alternative CADTH aligns to the more holistic approach of INESSS
- the process by which CUAs are determined and used by the PMPRB be subject to review and appeal

Incentives for Rare Disease and Breakthrough Products

Biogen is deeply concerned that the Draft Guidelines do not include a specific approach that encourages the investment in and introduction of breakthrough therapies for Canadians. The PMPRB states: *"[t]he revisions to the MRP approach in the June 2020 Draft Guidelines no longer distinguish between medicines for rare and non-rare conditions. Instead, a full exemption from the MRP has been made for all medicines which would otherwise qualify as Category I because of their annual treatment costs if their annual revenues is below $12M. This measure, coupled with the higher Pharmacoeconomic Value (PV) thresholds and capped price reductions for medicines based on their Therapeutic Criteria Level (TCL), go a long way to address concerns raised by certain stakeholders about unfair treatment of medicines for rare diseases under the new regime."*[2]

We submit that while the focused rare disease framework outlined in the 2019 Draft Guidelines was problematic, it, nonetheless, provided critical recognition by the PMPRB of the unique consideration for rare disease products and the profound vulnerability and unmet needs of rare disease patients. By effacing this recognition in the Draft Guidelines, the PMPRB has misunderstood and misrepresented the value of rare disease medicines to Canadians.

Drug regulators and HTA agencies across the world are increasingly addressing the societal demand for quicker access to new medications by introducing alternative and accelerated review pathways for breakthrough drugs in diseases with high unmet need. Health Canada has an accelerated review mechanism available under certain circumstances. INESSS introduced an HTA approach for the evaluation of innovative medicines (including rare disease products) that allows for special considerations to be given to the evidence submitted.

The PMPRB's alternative strategies to protect rare disease products are not rationally connected to the commercial realities of bringing rare disease products to market. We acknowledge that the first $12M in sales are exempt from an Maximum Rebated Price (MRP), however, products with annual sales exceeding $12M are subject to the compounding reductions of the MRP and the market size adjustment that can exceed the price floors set out in the Therapeutic Criteria Level (TCL) MRP calculation. This approach, in general, is tantamount to regulating industry profits and will have a disproportional impact on the investment in rare disease treatments with smaller patient populations and high unmet needs, while not taking in consideration the value that innovations bring to patients' lives.

While the re-introduction of levels of improvement, or TCL, is a step in the right direction, the Draft Guidelines do not clearly define what quality of evidence is acceptable for each category.

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[2] Patented Medicine Prices Review Board, *Backgrounder on June 2020 Draft Guidelines: Explanation of Changes from November 2019 Draft Guidelines* (June 19, 2020) at 15 online: Government of Canada <https://www.canada.ca/content/dam/pmprb-cepmb/documents/consultations/draft-guidelines/2020/PMPRB-Backgrounder2020-en.pdf>

The definitions contained in the Draft Guidelines create significant risk that breakthrough therapies will be classified as Level IV due to poor quality evidence.

An alternative can be seen in the INESSS approach to rare disease products. INESSS will consider unmet health needs when evaluating clinical data submissions and the uncertainties that may exist due to the nature of the disease states involved. For instance, under exceptional circumstances, when it is not possible to conduct a randomized controlled trial, other types of studies with a weaker level of evidence may be acceptable. Further, in certain circumstances, INESSS will employ the concept of a *promise of value*, which includes criteria for clinical monitoring to collect real world data to later be utilized to confirm therapeutic value. This ensures that access to breakthrough therapies is equitable and not limited or delayed.

Biogen believes that the 'acceptable quality' level of evidence for rare disease products should be consistent with the size of the disease population, and strongly recommends that the definitions in the TCL framework be revised accordingly. We agree that rare diseases therapies need to be supported by robust clinical development programs, however the size of the disease population should be taken in consideration when assessing quality of evidence.

Equally problematic in the TCL framework is the PMPRB's exclusive delegation of this classification to PMPRB staff who are neither impartial nor clinically trained. Therapeutic value can only reasonably be assigned for breakthrough therapies after a dedicated effort has been made to understand: the therapeutic area, the reasonable types of data submission for this area, the patient experience, clinical expertise, and should also include post-marketing data and real-world evidence. We submit that the Human Drug Advisory Panel (HDAP) be reconstituted as an arms-length, unbiased evaluator with a mandate of assessing therapeutic value.

Establishing a holistic and patient-centered approach to assessing the therapeutic value of breakthrough products is a profoundly important principle for patients suffering from diseases without treatment. We assert that special consideration for these breakthrough treatments for rare or diseases with high unmet need, including an accelerated review track, is essential for health equity.

Recommendations:

- the definitions of each TCL be amended to make special provisions for exceptional circumstance where there is significant unmet need
- the level of evidence considered acceptable by the PMPRB be consistent with the size of the disease population in question
- the responsibility to assign TCLs be removed from staff and that HDAP be reconstituted as an arms-length, unbiased evaluator with a mandate of assigning TCL levels

Change Management

To successfully lead systemic change of the magnitude proposed in the Draft Guidelines, the PMPRB must apply an established change management process. Fundamental change management principles include acknowledging the risks of the change, assigning clear responsibility for building, testing and implementing the change, allowing a monitoring period to test impact of the change, articulating the relationship between the change at issue and other changes, and communicating the return required from the change.

Biogen believes that a mitigation strategy is essential to stabilize the Canadian market and protect patient access. A phased implementation plan with progressively increasing risk and shadow analysis of the impacts of the Draft Guidelines is an example of how to achieve this. Biogen recommends that mitigation corridors (+/- % variance) be applied to current list prices to allow the PMPRB and industry opportunities to test the methodology through rapid-learning cycles.

We acknowledge the PMPRB's commitment to develop and execute an extensive Guideline Monitoring and Evaluation Plan (GMEP) to assess the impact of the Draft Guidelines on prices, access, the economy and PMPRB processes. However, we note this work has not been completed and does not include mitigation measures. We submit that given the magnitude of this disruption, it is crucial to first complete the development of an evaluation framework prior to implementing the Draft Guidelines. The evaluation must begin on the day the Draft Guidelines come into effect and must generate real time data for quality improvement.

We also highlight that stakeholders have not been provided with an explanation of the relationship between changes. In many respects, the Draft Guidelines blur the roles of related agencies, such as CADTH, INESSS and the pCPA. The agencies continue to work in silos and without coordination. For example, the Draft Guidelines treat a cost minimization analysis (CMA) in a similar punitive manner to a submission with no CUA.

This conflicts with CADTH's proposal to allow CMAs under certain circumstances. The mandate and efficacy of the pCPA has also been called into question in light of the price reductions the PMPRB is seeking to obtain as a condition of market entry. Moreover, the recently announced Canadian Drug Agency and National Pharmacare Plan have not been mentioned or connected to the system changes the Draft Guidelines introduce. Health Canada must transparently steward the system to function as one-team with the primary objective of ensuring fast and more equitable access to innovative products for Canadians. Efficiencies will surely be found in the operation of the PMPRB and related agencies as an integrated healthcare and drug ecosystem.

The return required from the change must directly benefit Canadians. The savings generated from the change must be re-invested back into the health care system and to support the integration of the drug regulation and pricing ecosystem to achieve faster access to innovative products. Biogen submits that this change presents a unique opportunity to strengthen the partnership between industry, the PMPRB and the health system. True partnership and bi-directional communication between stakeholders will be essential to the successful implementation of the Draft Guidelines and to ensure that Canadians receive the return required from this change.
To best serve Canadians, the Draft Guidelines must be improved and aligned with the future R&D pipeline, with incentives to concentrate on breakthrough therapies for diseases with high unmet need and high social cost. The methodology of the Draft Guidelines would grossly distort the market dynamics of these products. It is incumbent on the PMPRB to prepare for this change in order to prevent missed access opportunities for Canadians resulting from pricing controls that penalize these products and create disincentives for their launch. Biogen welcomes the opportunity to partner with the PMPRB on this next phase of work.

Recommendations:

- the PMPRB apply an established change management process to support the implementation of the Draft Guidelines including a mitigation strategy

- Health Canada and related government agencies speak with one voice to articulate a comprehensive system integration plan for the PMPRB, HTA agencies, the pCPA, the Canadian Drug Agency and the National Pharmacare Plan
- the PMPRB accelerate the development of the GMEP framework and ensure that it is launched simultaneously with the coming into effect of the Draft Guidelines
- the PMPRB commit to industry and Canadians that savings generated from the change will be re-invested back into the health care system and the drug regulation ecosystem to achieve faster access to innovative products
- a multi-stakeholder working group be struck to position the PMPRB as relevant and aligned with innovation trends, including developing outcomes-based agreements, focused on transformative, breakthrough therapies in diseases with high unmet need

Thank you for the opportunity to participate in this consultation. Biogen looks forward to continued dialogue with the PMPRB.