SUBMITTED VIA ONLINE PORTAL

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Dr. Mitchell Levine, M.D., M.Sc., FRCPC, FACP, FISPE
Chair, Patented Medicine Prices Review Board
333 Laurier Avenue West, Suite 1400
Ottawa, Ontario K1P 1C1

Subject: Patented Medicine Prices Review Board (PMPRB) Revised Draft Guidelines

Dear Dr. Levine:

On behalf of EMD Serono Canada ("EMD Serono"), I write to provide input to the Consultation on the revised PMPRB Draft Guidelines 2020 (the "Draft Guidelines").

EMD Serono, the Canadian biopharmaceutical business of Merck KGaA, Darmstadt, Germany, is committed to ensure patients in Canada will benefit from innovative products in oncology, neurology, fertility and endocrinology. Our pipeline includes novel investigational therapies in neurology, oncology and immuno-oncology. In Canada, we support research through clinical trials in multiple sclerosis (MS) and oncology. EMD Serono has its headquarters located in Mississauga, Ontario and employs more than 100 people across Canada.

EMD Serono is a member of Innovative Medicines Canada (IMC) and fully supports its submission to the Consultation. In this letter, I articulate our further concerns about the new methodology for price regulation specified in the Draft Guidelines.

Our key concerns are outlined as follows:

1. The methodology for assessing therapeutic benefit is both improper and unclear;
2. The economic factors used to reduce prices are arbitrary and will limit patient access to innovative medicines in Canada; and
3. Pharmacoeconomic factors and calculation of Maximum Rebated Price (MRP) continue to introduce significant uncertainty for manufacturers.

Importantly, the revised Draft Guidelines represent an improvement over the previous version from November 2019; we appreciate the consideration and effort by the PMPRB to update the Guidelines based on stakeholder feedback. We note that in their current state, aspects of the revised Draft Guidelines continue to be a concern. These concerns put patient access to medical innovations at risk.

We submit that there is an opportunity to further improve the Draft Guidelines by eliminating aspects that create significant uncertainty for manufacturers or devalue medical innovations.

We respectfully urge the PMPRB to further revise the Draft Guidelines and engage in bilateral working groups with industry. This approach will lessen the impact to industry and establish Guidelines that create a more favourable environment for patient access to medical innovations.

1. The methodology for assessing therapeutic benefit is both improper and unclear.

a. Therapeutic benefit should be assessed by clinical experts using clear methodology

While the re-introduction of therapeutic benefit assessment [via Therapeutic Criteria Levels (TCL)] to the pricing analysis is a laudable revision to the November 2019 iteration of the Draft Guidelines, the revised Draft Guidelines indicate that this assessment will be conducted by PMPRB staff rather than clinical experts.

We submit that the level of therapeutic improvement, appropriate comparators, and relevant indications for patented products should be assessed by clinical experts who have the scientific expertise to determine such parameters and are independent of PMPRB staff. As such, we recommend the Human Drug Advisory Panel (HDAP) expert committee which currently assesses therapeutic benefit must continue to have a primary role in the therapeutic assessment of patented medicines, rather than PMPRB staff.

b. QALYs are an inappropriate metric to assess therapeutic benefit

In addition, the Draft Guidelines specify that the Quality-Adjusted Life Year (QALY) will be used to determine therapeutic benefit. QALYs are used in the economic evaluations to assess the health benefit of medical interventions. Specifically, QALYs are generally thought to be inconsistent with the general public's valuing of health outcomes, they largely discriminate based on age and disability and are arguably not "patient-centric".[1] QALYs are subjective and not appropriate to determine the level of therapeutic improvement of an intervention. This determination should be based solely on the evidence demonstrated through clinical trials and not, as the PMPRB proposes, an arbitrary measure of health benefit such as the QALY.

Overall, the assessment of therapeutic benefit requires further input from stakeholders and feedback from technical working groups prior to implementation.

2. The economic factors to reduce prices are arbitrary and will limit patient access to innovative medicines in Canada.

For Category I patented medicines, the Draft Guidelines specify the use of economic factors to implement price reductions based on annual cost or market size. The PMPRB's approach introduces revenue limits on innovative medicines with the possible application of flawed assumptions that will penalize manufacturers and limit competition.

a. **It is unclear how the PMPRB will account for market share in its calculation of estimated revenue and market size.** The PMPRB's approach to estimate market size and classify a drug as Category I is based on "(i) an estimate filed under the Regulations or (ii) actual revenue filed under the Regulations."[2] The PMPRB methodology to determine estimated market size is unclear in its assumption of market share for a given product in a specific indication. Interpreted on its face, this means that the PMPRB methodology may include flawed assumptions about relevant market share for each product. If the PMPRB intends to assume 100% market share in its calculation of estimated market size, this assumption is clearly flawed in many instances: in fact, for most indications there are multiple therapeutic options and the market will be shared amongst them. However, the Draft Guidelines are not clear about that market reality. The PMPRB's methodology may therefore lead to an irrational result, such that two manufacturers for products with the same indication would each be assumed to have 100% market share for their respective products – when the actual market would realistically be divided between them.

   Of particular concern, the PMPRB's current approach to estimate revenue may encourage monopolies by disincentivizing future competition: while the first product to be launched for an

indication would appropriately have the 100% market share calculation applied to its estimated revenue, subsequent competitor products would be inappropriately subjected to the same 100% market share assumption. Based on these assumptions, the subsequent product may be classified as a Category I medicine based on an inflated estimate of market size, with the potential for associated revenue limitations specified in the Draft Guidelines. The potential to be classified as a Category I medicine would disproportionately penalize the new competitor. This approach is a disincentive for manufacturers to launch future innovative and competitive products, which would otherwise reasonably and efficiently split the market across products. The PMPRB's approach may therefore dissuade further launches by limiting revenue for subsequent products and effectively inhibit the development of truly competitive markets. Competition is one way to achieve lower prices across the market, thus the PMPRB's approach is counterproductive to their overall objective. To avoid potential overestimates of revenue, products should be classified by the PMPRB as Category I medicines based only on actual net revenue, not estimates of market size.

b. **The PMPRB may overestimate market size by assuming 100% medication adherence.** The PMPRB's approach to categorize a new medicine as Category I based on calculated annual cost or estimated market size assumes 100% of the patients will take 100% of their medicine, 100% of the time. In developed countries, approximately 50% of patients with chronic illnesses will not take their medicine as prescribed.[3] The Draft Guidelines mandate significant price reductions for drugs that are classified as Category I; as such, the potential for a new drug to be classified as Category I is a disincentive for manufacturers, particularly if that classification is based on an inflated market estimate that is not remotely reflective of the actual market for the drug. To avoid this, we suggest that the PMPRB should not classify a medicine as Category I based on estimated revenue or market size, but rather based on actual net revenue reported by the patentee.

c. **Medicines may be re-assessed upwards based on a larger market size yet there is no mechanism to re-assess medicines downwards as revenue diminishes.** The Draft Guidelines include a mechanism to reassess patented medicines based on increases in market size. First, this approach penalizes manufacturers for making medical innovations and clinical benefit available to a larger number of patients. Second, this approach does not reflect the life cycle of medicines, which typically involves the introduction of other innovative products to the market, and a corresponding reduction in revenue for the existing product as its utilization decreases. The Draft Guidelines do not include a mechanism to reflect that dynamic. As a result, the PMPRB will arbitrarily penalize products subject to greater future competition by applying price reductions based on initial market size adjustment even as the actual utilization of the product diminishes over its life cycle.

3. Pharmacoeconomic factors and calculation of MRP continue to introduce significant uncertainty.

The Draft Guidelines seek to use pharmacoeconomic factors to regulate price ceilings for high-value and innovative products. We submit that this approach is highly inappropriate. It simplistically reduces multiple indications, and often vast pharmacoeconomic ranges, to a single point estimate that is then applied broadly to regulate price across Canadian public and private markets. Importantly, there are generally large discrepancies between pharmacoeconomic outputs submitted by manufacturers compared to those calculated by CADTH. Pharmacoeconomic model outputs vary widely according to the inputs and specific assumptions made by the user. The Draft Guidelines fail to take into consideration model uncertainty. For any pharmacoeconomic model the outputs are subjective and highly variable, and while informative/instructive, models cannot reliably or accurately predict future

pharmacoeconomic value. The inclusion of pharmacoeconomic factors to regulate price is highly flawed and disregards the inherent uncertainty that is fundamental to any pharmacoeconomic model.

Furthermore, the Draft Guidelines specify the calculation of MRP using factors that were recently deemed by the Federal Court to be beyond the PMPRB's jurisdiction.[4] Given that the Draft Guidelines link the new economic factors (pharmacoeconomic value, market size, and GDP/GDP-per-capita) to the calculation of MRP, a fundamental reconsideration of the approaches specified by the Draft Guidelines should be undertaken. The PMPRB should convene technical working groups with patentees to address such issues in order to further revise the Guidelines and be consistent with regulatory tools that are within the mandate of the PMPRB.

Conclusion

The PMPRB is intended to protect Canadian consumers by ensuring that the prices of patented medicines sold in Canada are not excessive. The Guidelines should be directed to establish reasonable ceiling prices rather than the arbitrary limitation of revenue, which essentially imposes a tax on innovation. If the Draft Guidelines are implemented in their current state, with the associated uncertainty and arbitrary limits on revenue based on inaccurate assumptions, EMD Serono's ability to launch products in Canada on a priority basis will be severely challenged. This will negatively impact patient access to innovative medicines.

Our ask is simple: We strongly yet respectfully urge the PMPRB to seek input through technical working groups to further revise the Guidelines. This approach will help mitigate the issues and unintended consequences outlined above in this correspondence, by IMC, by patient groups, and by other stakeholders throughout the PMPRB consultation period.

An appropriate balance is required between improving the affordability of medicines, ensuring timely patient access to medicines, and creating a world-class innovative life sciences environment in Canada. The implementation of the Draft Guidelines in their current form will not achieve that balance.

Sincerely,

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