

August 4, 2020

Dr. Mitchell Levine, Chairperson
Patented Medicine Prices Review Board (PMPRB)
Box L40 | Standard Life Centre
333 Laurier Avenue West, Suite 1400
Ottawa, Ontario, K1P 1C1

RE: PMPRB 2020 Draft Guideline Consultation

Dear Dr. Levine:

On behalf of BIOTECCanada members, this submission is in response to the Patented Medicine Prices Review Board's (PMPRB) request for written comments to the revised draft PMPRB Guidelines issued on June 19, 2020 (the Guidelines).

These changes come at a critical time for Canada and Canadian patients. Aside from the reality of both the short term and longer-term impact of the COVID 19 pandemic, the nature of how healthcare solutions are discovered and ultimately accessed is undergoing unprecedented levels of change. Rapidly emerging technologies such as stem cell, gene and cell therapies, immuno-oncology therapeutics, CRISPR editing and new vaccines stand to dramatically improve treatment and even provide cures for health challenges, including rare diseases. Importantly, Canadian scientists, researchers and early stage companies are playing important roles in advancing global research and development including the development of new data constructs, clinical trial design and artificial intelligence.

Medicines are an important element of the healthcare system's overall ability to provide healthcare solutions to Canadian patients. As a result of significant advancements in science, including the availability of transformative curative therapies, new medicines and biotechnologies are being brought forward for patients that are significantly changing how healthcare is delivered. Importantly, these new innovations are allowing many Canadians to live longer and more productive lives. Moreover, many of the new therapies are delivering significant savings to other parts of the healthcare system by reducing and even eliminating expensive traditional healthcare treatments including transplants and lengthy hospital stays. Correspondingly, governments recognize that medicines are a vital cornerstone within the healthcare system to help create solutions that offer expanded treatment and home care options.

The Canadian regulatory and policy environment has a vital role to play in ensuring the knowledge base supporting clinical care and patient outcomes are aligned with international practices and opportunities. As the world calls upon the industry to deliver solutions for the current pandemic crisis, public expectations for improved innovative therapies for oncology, rare disease and autoimmune disorders also continue to grow. Globally, and in Canada, the industry has developed extensive research capacity aimed at meeting these demands.

.../2

Throughout the recent consultation period, the industry has highlighted the serious gaps in details relating to the implementation of the Guidelines. PMPRB staff have stated that in those cases where clarity is not established on how the new regulations will be applied to products, they will undertake decision making on a case-by-case basis. This approach creates a significant vulnerability for the Canadian system of access. Not being able to have a transparent and value-based decision process for new products entering the Canadian market, places this country at a distinct disadvantage compared to other jurisdictions. New product launches will be focused on markets where this certainty is provided and product value and price are evaluated collectively to help ensure the best use of therapies is serving patients who can truly benefit.

While the PMPRB has made some adjustments to the draft Guidelines since the last version, these changes fail to address the more fundamental and concerning questions stakeholders have raised throughout the consultation period. The price of a drug is but one element when evaluating a cost to the healthcare system. Focusing narrowly on price as the primary threshold in evaluating a new medicine negates the broader value a medicine brings to the entire system of care. The proposed policy modernization demonstrates PMPRB has diverted significantly from its risk-based approach and instead focuses on limiting access to the most innovative and breakthrough treatments or the medicines that are most successful in treating patients.

The high level of business uncertainty resulting from these reforms will leave Canada out of step internationally with the potential for far-reaching negative real-world impacts on the Canadian biotechnology industry. Furthermore, there is risk Canada's standard of clinical practice will be diminished as research and investment are directed to markets where regulations supporting access to new therapies exist. Clinical practice requires certainty in access to new therapies in order for patients to benefit from new treatments. This is particularly relevant as we look towards medicines of the future addressing the vast unmet needs of patients with rare diseases, the pipeline of oncology therapies and vaccines, and in many cases potential cures for currently debilitating or terminal illnesses. These advancements build on an established foundation and bring with them a need for evaluation of capturing real world patient outcomes.

The engagement of multinational pharmaceutical and biotechnology companies is a critical component of the Canadian biotech ecosystem. While this is clearly not the purview of the PMPRB, the implications for investment in Canada are a significant concern to the pre-commercial early stage company members of BIOTECanada. There is no question that the market uncertainty being created will negatively impact investment and business decisions of the multinational companies in Canada.

As evidenced by the document attached, there remain outstanding and critical issues related to how the regulations will be applied to new products attempting to enter the Canadian system of care. These issues have been identified throughout the consultation periods and remain as potential barriers to entry, particularly for Canadian patients who need access to rare disease therapies, biologics and new transformative therapeutics anticipated for improved patient care.

The economic, social and healthcare crisis resulting from the emergence of COVID-19 underscores how important this industry will be in not only solving for the current crisis but also preparing for a similar virus event in the future and rebuilding the economy. Narrowly focused healthcare policy which chooses to ignore the broader benefits and these objectives risks undermining Canada's competitiveness as a destination for innovation, investment and talent at this critical time.

Sincerely,

A handwritten signature in blue ink, appearing to read 'Andrew Casey', with a long, sweeping underline.

Andrew Casey
President and CEO

Enclosure: BIOTECanada Submission to PMPRB 2020 Draft Guidelines Consultation

Attachment: BIOTECanada Submission to PMPRB 2020 Draft Guidelines Consultation August 4, 2020

Despite significant feedback submitted by a cross-section of stakeholders during PMPRB's first round of consultations, BIOTECanada remains concerned by the volume of issues left unaddressed in these draft Guidelines. It is strongly recommended the PMPRB review its approach in order to eliminate the uncertainty, complexity and regulatory burden that result from the reformed Guideline package proposed. This should be done in consultation with patentees through Technical Working Groups, to ensure the Guidelines are operational, fair and offer the predictability needed to ensure Canada remains a priority destination for new medicines.

The recent Federal Court judicial review of the Patented Medicines Regulations provides the PMPRB and the Government with an opportunity to revisit and even remove the economic factors from the regulations. The Federal Court determined the requirement to report rebates exceeds the scope of the regulation-making power in the *Patent Act*. The MRP ceilings and PEP concepts as well as patentee's ability to comply have been heavily based on PMPRB's expectation that average transaction prices would include third-party and payer rebates. This fundamental change requires time to pause, and reconsider the approach to ensure revisions made to the Guidelines address the judicial review decision and ensure ceilings are reflective of the prices regulated by PMPRB. Importantly, this should require an additional opportunity for stakeholder consideration and input in order for the PMPRB to meet its obligation to consult with patentees and other stakeholders. Given the judicial review was clear the jurisdiction of the PMPRB should not go beyond the factory gate price based on the *Patent Act*, the PMPRB should recommend to the Government of Canada that the economic factors be removed from the Patented Medicines Regulations. Should appropriate actions not be taken, there will be a significant and long-lasting impact on the health of the Canadian pharmaceutical market.

As stated above, the regulation of "beyond the factory gate" rebated prices is now unviable in light of the recent Federal Court decision. Nevertheless, if PMPRB was able to proceed with the MRP ceiling price as proposed in the June 2020 draft of the Guidelines, BIOTECanada has the following additional concerns regarding the proposed implementation, namely:

- Maximum Rebated Price
 - Impact on New Transformative Medicines and Drugs for Rare Diseases
 - Confidentiality Concerns Remain
 - Pharmacoeconomic Value Inappropriate for Setting Maximum Excessive Price Ceilings
 - Absence of Fairness in Proposed Derivation of MRP
 - Market Size Factor Raises Fundamental Concerns
- Additional concerns
 - Broad and Excessive Discretion of PMPRB Staff
 - Inappropriate application of international price comparison tests
 - Non-Excessive Price (NEAP) Should Not be Used
 - Unidirectional Classification of Products is Problematic
 - Operational Considerations

Maximum Rebated Price

Impact on New Transformative Medicines and Drugs for Rare Diseases

As Canadian governments look to provide access to healthcare for Canadian patients especially during a pandemic, emerging innovative biologic treatments, vaccines and therapies will play an important role in helping governments realize these objectives.

The punitive approach and unpredictability posed by the Guidelines will impact access to innovative breakthrough therapies including medicines such as first-in-class drugs and medicines for rare diseases, as a very high proportion of these drugs are likely to be designated as Category I “high priority” medicines. In the latest 2019 data published by PMPRB on drugs for rare diseases, Canada is in fact already right at the median of OECD countries on prices for rare diseases.¹ Despite this favorable global position, PMPRB is taking extraordinary steps to further reduce the prices of first-in-class drugs for rare diseases. The Guidelines offer no consideration for the unique challenges associated with bringing drugs for rare conditions to the market. Canada is unique in that unlike most other jurisdictions in the world, Canada does not have a regulatory framework for rare diseases (CADTH, INESSS, Health Canada nor PMPRB have rare disease processes or frameworks). As such, Health Technology Assessments performed by CADTH in Canada that the PMPRB intends to use do not fairly evaluate rare disease medicines. Rare disease medicines, by definition, are studied in very few patients (i.e. small sample size) where it is often unethical to perform randomized clinical trials. This reality of rare disease medicine often translates into high level uncertainty with pharmacoeconomic analyses. Of note, pharmacoeconomic analyses provide a range of possible outcomes depending on the inputs used and assumptions made and are only one of many factors that go into pharmaceutical decision-making process with other important elements. At present, Canada does not have the necessary tools required to effectively and fairly evaluate these medicines that currently do not exist in Canada. Accordingly, the proposed PMPRB rules in these Guidelines will limit transformative medicines and drugs for rare diseases from entering Canada by putting in place price controls far greater than other countries.

Pharmacoeconomic Value Inappropriate for Setting Maximum Excessive Price Ceilings

BIOTECCanada members strongly oppose the application of pharmacoeconomic (PE) value assessment to set ceiling prices. The introduction of the Pharmacoeconomic Price (PEP) and ongoing price reassessment for Category I medicines, as conceived in the draft Guidelines, are extremely problematic and therefore cause unacceptable uncertainty for future medicines impacting their availability in Canada.

There is no opportunity for patentees to present evidence to refute the application of inappropriate methods and/or assumptions in any Cost Utility Analysis (CUA) prepared by a Canadian HTA agency that would be used to establish the PEP/MRP. There is no independent expert arbitrator that can be consulted when a manufacturer and CADTH/INESSS disagree regarding the clinical applicability of specific modeling assumptions, even though assessments conducted by these agencies would now carry legal weight with PMPRB under the new proposed Guidelines.

¹ PMPRB Research Webinar June 23, 2020. Insights on Spending on Expensive Drugs for Rare Disease. PMPRB.

Second, the industry has serious concerns with the rule that requires an automatic 50% reduction for drugs that do not have a pharmacoeconomic assessment. This proposed approach unfairly penalizes medicines that do not have a CUA reanalyzed by publicly-funded institution and forces patentees to either file public HTA submissions for drugs even if no public reimbursement is intended (i.e. private payers) or for which clinical evidence is limited (phase 2 trials or the absence of quality of life data). Moreover, this proposed approach will penalize medicines that do not have a CUA reanalyzed by publicly-funded institution and could potentially contribute to delays or absence of regulatory filings to Health Canada for any drugs not meant or ready for public reimbursement.

Third, drugs for rare diseases will be at a greater disadvantage due to high incremental cost-effectiveness ratios (ICERs) from CADTH reanalysis, coupled with potentially being further pushed down to lower Therapeutic Criteria Level (TCL), as explained in the previous section on Drugs for Rare Diseases.

Absence of Fairness in Proposed Derivation of MRP

The re-introduction of therapeutic value is important. However, the addition of determining the TCL alongside the PEP or median domestic Therapeutic Class Comparison (dTCC) is punitive and brings even more uncertainty when a patentee is considering whether to launch new products into Canada or not. Based on historical trends, most new products will fall into what is now defined as Level 4 (83% of historic drugs have been Level 4, 12% have been Level 3 and the remaining 5% was Level 1 and 2 combined). Significant uncertainty in the TCLs exists for all medicines but in particular for drugs for rare diseases. This is due, in part, to a lack of recognition of the value of satisfying an unmet need within all four of the TCLs. Specifically, drugs for rare diseases may be at a greater disadvantage due to high ICERs from CADTH reanalysis coupled with potentially being pushed down to a lower TCLs due to the PMPRB-assessed level of data quality. The proposed floors are arbitrary and are inappropriate as an instrument for price regulation. When used, Human Drug Advisory Panel (HDAP) should have disease area experts participating on the panel to ensure that the decision that is issued is reasonable and aligned with current practices.

Market Size Factor Raises Fundamental Concerns

BIOTECanada members are opposed to the application of market size to adjust the net price ceiling of Category I products. Using this approach for pricing purposes would not be grounded in an evidence-based rationale. The current framing of the market size adjustment is as a revenue control tool (i.e., method of reducing the revenue realized by a patentee), not a price evaluation tool (i.e., method of assessing excessive pricing). The MRP and market size-related price reductions of up to 65% create an unfavorable and uncertain market for new medicine launches in Canada. For example, even if a new medicine is cost saving (less expensive than all the comparators) the market size-related price reduction could be as much as 35%. Effectively, the Guidelines penalize treatments that offer a cure or life-changing benefits in a market with a high unmet need. Mandated reductions of this magnitude and scale create difficulties for patentees looking to launch first-in-class products. Furthermore, it also imposes great penalties to launch alternative treatment options, even if they bring improvements over standard of care, and even if these new treatments are priced less than the existing alternatives.

Confidentiality Concerns Remain

There are number of areas that raise serious confidentiality concerns in the Guidelines. The utilization of public HTA to determine therapeutic class comparisons, means confidentiality concerns have not been addressed as these can be back calculated in a relatively predictable way. As a result of most products landing at level 4, the ability for a competitor to estimate the PEP via the CADTH recommendation and PVT is a concern. In cases where no pharmacoeconomic assessment is available, the maximum rebated price is fully transparent. Furthermore, the use of cost minimization in the proposed Guidelines leads to a maximum rebated price being equal to the median of dTCC subject to 50% floor allowing a competitor to determine the new price in this specific circumstance.

Additional Concerns

Broad and Excessive Discretion of PMPRB Staff

An additional layer of uncertainty of the proposed Guidelines with Section 94 which is overly broad and provides staff with significant powers and unlimited discretion to upend the review of a patented medicine and each subsequent indication. Contributing to the unfairness and unpredictability issues raised above, Section 94 essentially means that compliance to pre-specified price ceilings may, at any time, be disregarded and superseded by an infinite number of variations of price tests to be arbitrarily determined by PMPRB staff with limited scientific expertise. Permitting Board Staff to discard the Guidelines to impose price tests that are more restrictive than what has been derived through the consultation processes outlined in subsection 96(5) of the *Patent Act* is not aligned with three of the PMPRB's currently held principles; fairness, transparency and predictability.

Inappropriate application of international price comparison tests

PMPRB staff have yet to clearly explain why the new Guidelines have moved from ensuring that list prices of new products are never higher than the highest price from the PMPRB's basket of countries, to list prices being no higher than the median price. The recent adjustment of the PMPRB Draft Guidelines has established that it is reasonable for Grandfathered (i.e, in-market) products to be held to this standard of "excessive". BIOTECanada believes that this approach should correspondingly be expanded to all medicines.

Under the current Guidelines and based on PMPRB data, Canadian prices already fall at the median of the PMPRB7 countries. It has been argued in previous consultations by Health Canada and the PMPRB that the PMPRB7 is not a basket of countries that aligns with Canada economically or from its consumer protection position on patented medicines. The updating of the PMPRB's reference countries to the PMPRB11 was done to address this concern. Given that the existing Guidelines' approach to applying international price comparison tests has been successful in the past and the new basket of countries will have prices that are more in line with the PMPRB's desired price ceiling targets, it is appropriate for in-market Grandfathered, Gap and New medicines to be measured against the highest international price in the PMPRB11.

Non-Excessive Average Price (NEAP) Should Not be Used

In Sections 72(ii) and 74(ii), the proposed Guidelines state that a patented Grandfathered, Line Extension or Gap product's NEAP in a previous period should be one of two "lower of" prices used to set the product's MLP ceiling price. However, the NEAP is clearly a function of the product's previous average price rather than its list price and therefore the NEAP is inappropriate (in an "apples to oranges" sense) to use in setting the MLP. Also, the NEAP is confidential and therefore, if it were to come into play in determining the MLP, PMPRB would be instrumental in betraying this confidentiality. Also, any two-part Guideline that is used to allege whether a price is "excessive" implies that a price that meets either part of the test is in fact "non-excessive" (otherwise each part itself would be an invalid method for determining excessiveness in the first place); for this reason, if the price tests in Sections 72 and 74 are to retain the NEAP part despite the comments above, these tests should each logically be specified as "higher of" the two parts rather than "lower of".

Unidirectional Classification of Products is Problematic

If the reason why a patented medicine was placed in Category I at some point becomes inapplicable (e.g. list price decrease below threshold because the MIP fell or the volume is now below \$50M in sales) then PMPRB should move it to Category II and stop calculating an MRP or MRP[A] for that patented medicine. Failing to implement this recommendation would be an undue regulatory burden on patentees. Also, allowing a product to begin in Category II and later be re-assigned to Category I (based on new information becoming available at that time) while not allowing the reverse to happen (also only if new information becomes available to support such a shift) demonstrates clearly the inequities that exist throughout the proposed Guidelines.

Operational Considerations

The proposed timelines to come into compliance with a new ceiling after being notified (within ~4 months for MLP and within ~10 months for MRP) are not operationally realistic and do not acknowledge the various steps required to implement price adjustments and for those to be properly reflected in the patentee's average transaction price. For example, a change in list price usually necessitates a change in official reimbursement listings and/or contractual obligations which need to be operationalized with enough lead time (often 90 days or more in advance). In addition, only the sales that occur during the portion of the reporting period after these price adjustments are implemented will have an impact on changing the average transaction price rather than having an impact throughout the entire reporting period.