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Dr. Mitchell Levine
Chair, Patented Medicine Prices Review Board (PMPRB)
333 Laurier Avenue West, Suite 1400
Ottawa ON, K1P 1C1

RE: Revised PMPRB Draft Guidelines Consultation

Dear Dr. Levine,

Thank you for the opportunity to provide input into the revised PMPRB Draft Guidelines Consultation. Over the past several years, AstraZeneca Canada (AstraZeneca) has been actively participating in consultations regarding the reform of the PMPRB, including through our industry associations, Innovative Medicines Canada and BIOTECanada.

AstraZeneca currently employs more than 875 Canadians involved in research, development and commercialization of innovative medicines across our main therapeutic areas of cardiovascular, renal and metabolic diseases; oncology; and respiratory and immunology illnesses. In 2019, AstraZeneca invested more than CAD $145 million in Canadian health sciences research in our core therapy areas.

Our company is now entering an exciting new period of research, innovation and unprecedented scientific advances to improve patient outcomes. At the moment, more than 80 percent of our existing pipeline is focussed on precision medicines – innovative therapies that target an individual's unique genetic makeup. As we enter the era of precision medicines, there will be greater certainty around treatment outcomes as we are better able to predict which patients will respond to a given therapy. This will lead to improved health outcomes for patients and significant long-term savings for payers and health systems. Breakthrough scientific innovation leveraging AI and other forms of technologies now permits patient outcomes like never before, and the work we have before us means making sure that our health care policies can keep pace with the science.

AstraZeneca is also very much involved in the fight against COVID-19. We have partnered with the University of Oxford on the development of a new COVID-19 vaccine and are actively collaborating with a number of countries and multilateral organizations worldwide to make the potential vaccine widely accessible around the world, and at no profit during the pandemic.[1]

[1] https://www.astrazeneca.com/media-centre/articles/2020/astrazeneca-takes-next-steps-towards-broad-and-equitable-access-to-oxford-universitys-potential-covid-19-vaccine.html

Moreover, we are currently investigating two of our existing medicines for their potential use as treatments for COVID-19.[2]

However, much of this ground-breaking innovation, which we are hoping to bring to Canada, is being significantly challenged by the federal drug pricing controls. It is now undeniable that the reforms have already reduced Canadians' access to medicines, even before the new pricing system has become fully operational. Over the past two years Canada has seen a dramatic drop in the number of new medicines marketed in this country, whereas medicine launches in other jurisdictions have increased over the same period of time.[3]

AstraZeneca has also been faced with difficult decisions about whether to delay product launches as a result of the new pricing system. The new rules as they are currently written will impact as many as 10 of our pipeline medicines and vaccines, as well as new indications under development for our existing products, some of which are combinations with other developers. Our medicines will be affected by one or more of the many proposed changes, ranging from the country comparisons to how the new economic factors (e.g., high cost, market size, pharmacoeconomics) will be applied. The majority of our experimental medicines are pioneering treatments that have been or are expected to be granted priority review status by Health Canada. Ultimately, the PMPRB changes are adding another potentially insurmountable barrier on top of an already complicated, costly and uncertain commercialization pathway that will prevent access to many Canadians who need these important medicines.

This is a particularly troubling development in the context of the ongoing COVID-19 pandemic. The PMPRB continues to experiment with novel and uncertain approaches to price regulation at a time when new research, innovation, medicines and vaccines are needed the most. The latest PMPRB Annual Report also confirms that prices of patented medicines in Canada are on the decline and have remained consistently lower than the median in the seven comparator countries. [4] This calls into question the need to adopt pricing measures as stringent as those proposed in the latest version of the Guidelines.

A summary of our concerns is set out below, each of which is developed in more detail in the attached **AstraZeneca Position on the 2020 PMPRB Draft Guidelines**:

1. There is continued uncertainty about how the new pricing system will work in practice, particularly with respect to the proposed economic factors.

[2] https://www.astrazeneca.com/media-centre/articles/2020/investigating-an-existing-medicine-as-a-potential-treatment-for-covid-19.html
[3] https://lifesciencesontario.ca/news/canada-may-be-losing-its-status-as-a-top-global-destination-for-new-medicine-launches/
[4] 2018 PMPRB Annual Report: https://www.canada.ca/en/patented-medicine-prices-review/services/reports-studies/annual-report-2018.html

2. The new PMPRB Guidelines have added additional and unnecessary layers of complexity to an already unworkable system.
3. Innovation continues to be penalized at a time when pushing the boundaries of science has never been more critical.
4. The application of the economic factors present major challenges for commercialization.
5. The maximum rebated price concept needs to be revisited in light of the recent Federal Court ruling on confidential rebates.
6. The use of pharmacoeconomics to establish price ceilings is inappropriate and remains an ongoing concern.
7. The pharmacoeconomic price (PEP) is not truly confidential.
8. The market size adjustments go far beyond the PMPRB's mandate to protect consumers from excessive prices and represent *de facto* revenue control.
9. The new Therapeutic Criteria Levels introduce many methodological problems and implementation challenges.
10. Excessive discretion is provided to PMRPB staff regarding evaluations and decisions that may be beyond the scope of their expertise.
11. The continued use of the domestic Therapeutic Class Comparison (dTCC) test that includes generic products, is punitive to innovators.
12. The PMPRB's excessive discretion on the timing and extent of reassessments introduces significant uncertainty and volatility.
13. The decision to retain the median international price (MIP) to set the maximum list price (MLP) for new patented medicines will cause further product launch delays in Canada.
14. A number of key operational questions remain and should be the subject of this consultation, such as sources of international prices, application of the Non-Excessive Average Price, etc.

We hope the Government of Canada, including the PMPRB, will revisit its current flawed approach to patented medicines price regulation and consider a more balanced pricing framework – one that supports an innovation-driven healthcare system and ensures that Canadians can continue to have access to the latest life-changing health innovations.

Thank you for considering our submission. If you have any questions, please do not hesitate to contact me.

Yours Sincerely,

Jane Chung
Country President, AstraZeneca Canada

AstraZeneca Position on the 2020 PMPRB Draft Guidelines

At AstraZeneca, we put patients first and follow the science – two of our corporate values – with a vision of building a healthcare system for the future – one that rewards innovation and encourages commercialization of medicines and vaccines that will keep Canadians in the workforce, out of hospital, raising families, and contributing to our nation's post-COVID economic recovery. But as other countries transition to value-based health care, the federal government's approach continues to put short-term cost savings above all other considerations. This short-sighted approach will ultimately cost Canadians dearly in terms of lives lost, poorer quality of life, lost medical research and investments, and increased provincial health system spending.

In this context, the following are important and outstanding issues that the PMPRB must carefully consider before implementing these Guidelines. AstraZeneca hopes that these considerations will inform and contribute to a more balanced and functional pricing framework.

Overarching issues

1. **There is continued uncertainty about how the new pricing system will work in practice, particularly with respect to the proposed economic factors:** While there are some positive developments for medicines already available in Canada, unfortunately much uncertainty remains for new patented medicines that are in development or waiting to be launched. This means that the next generation of cutting-edge therapies – medicines and vaccines that can save lives, cure previously untreatable diseases, and keep Canadians healthy and productive – will continue to face barriers to entry into Canada. Businesses need clear rules to guide their medicine launches and investment decisions, but rather than reducing the uncertainty created with the 2019 Guidelines, the PMPRB has added to it. It has also given itself an unprecedented level of discretion and powers to unilaterally modify price review processes in the future, which will further deter companies away from the Canadian market.

2. **The new PMPRB Guidelines have added additional and unnecessary layers of complexity to an already unworkable system**: Rather than addressing some of the flawed concepts in the 2019 draft Guidelines, in its new approach the PMPRB has added additional layers of complexity to an already unworkable system. The 2020 Guidelines are even more complicated than the PMPRB's initial draft, with new processes, concepts, lack of clarity and even missing information that will further deter companies from bringing new medicines and investments in health research to Canada.

3. **Innovation continues to be penalized at a time when pushing the boundaries of science has never been more critical**: The federal government has set an ambitious goal of

doubling the size of the life sciences sector by 2025 and is now looking to our sector to develop solutions to address COVID-19. It is therefore unfathomable that the PMPRB continues to penalize and target innovation by mandating the highest price reductions for innovative treatments that are most likely to be considered for priority review by Health Canada due to the current unmet need for patients. Creating disincentives for companies to develop and commercialize medicines in Canada – when we need it more than ever before – goes directly against our government's innovation priorities and is not in the best interest of Canadians or our economy.

Substantive issues

4. **The application of the new economic factors present major challenges for commercialization:** The updated Guidelines continue to mandate significant price reductions for innovative therapeutics through the use of economic factors. While the PMPRB has raised its proposed thresholds, the uncertainty related to these thresholds will continue to present challenges for commercialization. Of note:
    - The raised thresholds are not as significant as they might appear, as they will be calculated using the maximum list price and number of units sold, rather than the lower maximum rebated price as previously proposed. The changes therefore do not provide a significant expansion of the thresholds for categorization.
    - While the new thresholds aim to reduce the overall number of new medicines that fall under Category 1, the economic factors will continue to apply to the majority of medicine sales (68% according to the Guidelines backgrounder), which will still have a substantial impact on the Canadian market.
    - Moreover, the majority of AstraZeneca's upcoming pipeline of products, consisting of specialty drugs in the rare diseases and oncology space, will remain in Category 1.
    - Based on the draft Guidelines we cannot predict what would be considered the Maximum Rebated Price (MRP) and consequently if AstraZeneca can support the regulated price in Canada.
    - The new thresholds can be calculated by other jurisdictions and competitors, creating new and much lower Canadian price anchors, threatening Canada's status as a priority country for new medicine launches.
    - Furthermore, the current rules penalize companies that do not seek public reimbursement by forcing them to go through CADTH at the risk of heavily mandated price reductions if they do not. This may result in companies forgoing or delaying launch in Canada.

5. **The maximum rebated price concept needs to be revisited in light of the recent Federal Court ruling on confidential rebates**: The recent Federal Court ruling, invalidated the section of the *Patented Medicines Regulations* related to the disclosure of confidential rebates and the "new price calculation." As a result, the Board's regulatory oversight of the

ex-factory price is limited and the PMPRB should revisit how the Maximum Rebated Price is calculated and used.

6. **The use of pharmacoeconomics to establish price ceilings is inappropriate and remains an ongoing concern**:
    - The PMPRB itself has acknowledged the significant uncertainty associated with the use of pharmacoeconomic value as part of price regulation: *"Pharmacoeconomic value is now a s.85(1) factor and the Board has a statutory obligation to consider it. However, until such time as there is more developed empirical evidence in Canada on opportunity cost in the public health system, an argument exists for erring in favour of more generous thresholds that are aligned with the higher end of what is seen internationally and that provide greater certainty and predictability for patentees."* Given the lack of empirical evidence on the use of pharmacoeconomic value, the PMPRB should refrain from implementing these factors until an impact of the reforms is measured.
    - The lack of transparency regarding which specific parameters and economic assumptions will be utilized by HTA bodies during their reanalysis exacerbates the uncertainty for developers of medicines.
    - Furthermore, CADTH's assessments are typically substantially different from a manufacturer's best estimated ICER, which creates significant uncertainty regarding the potential maximum rebated price, with no mechanism for the manufacturer to challenge.
    - Finally, the use of our medicines in combination with other molecules could raise a number of challenges that are not contemplated by the Guidelines. For example, it is unclear how individual products in a combination therapy contribute to establishing the PEP. Individual patentees do not always control efforts to secure reimbursement and use of their products in combination, which could lead to unfair and uncertain evaluations of price excessiveness.

7. **The pharmacoeconomic price** (**PEP) is not truly confidential**: While the PMPRB has attempted to address patentees' concerns associated with keeping the PEP confidential, we believe that over a 2-3-year period, competitors will be able to reasonably deduce what that is.

8. **The market size adjustments go far beyond the PMPRB's mandate to protect consumers from excessive prices and represent de facto revenue control**: The size of a given market for a medicine has no bearing on whether that medicine is priced excessively. This provision discourages the commercialization of the medicines with the most potential to help the greatest number of people. The required adjustments could penalize manufacturers that price relatively lower in a therapeutic class, and subsequently receive a high share of a market. These manufacturers will face further price reductions and

uncertainty, while higher priced competitors are not subject to the same requirements. The new rules are also unclear on whether and how they would address downward changes to market size, based on changing market dynamics.

9. **The new Therapeutic Criteria Levels introduce many problems and implementation challenges:** Many Category 1 medicines –which include breakthrough rare disease and oncology medicines – are likely to be assigned a Level IV Therapeutic Criteria (i.e., considered to provide "no or slight improvement") classification, given potential limitations in clinical data at launch due to early approvals. For example, cross-over clinical trial designs are common in oncology and rare diseases and marketing authorizations for many cancer therapies are increasingly being granted by regulators based on phase 2 data. Many companies will be discouraged from introducing potentially life-saving medicines to Canada, given the risk that they will be categorized as Level IV, not recognizing the value they bring to patients. In France, the introduction of ASMR (similar to Therapeutic Criteria Levels) has seen a reduction in product launches in the country. This issue will be particularly challenging for timely access to new cancer therapies and precision medicines, which may show sufficient clinical value to warrant faster access to save lives, while we collect additional evidence. While price floors have been added, companies will not know what therapeutic area and corresponding price floor will apply to their product, until a few years post launch, which further complicates pricing and launch decisions.

10. **Excessive discretion is provided to PMRPB staff regarding evaluations and decisions that may be beyond the scope of their expertise**: Section 94 of the Guidelines provides unparalleled discretion for PMPRB staff to use whatever price tests they feel they need during an investigation: *"Staff may utilize any of the tests described in the Guidelines and modifications or variations of those tests (e.g., MIP instead of HIP or median as opposed to the top of the dTCC) depending what it believes most appropriate to the factual circumstances surrounding the price of the patented medicine under investigation."* It is impossible for companies to plan for rules that can be unilaterally changed or created at any point. PMPRB staff are also afforded wide discretion in determining the therapeutic criteria level of a medicine, which is outside the scope of their expertise. The PMPRB appears to be drifting further and further beyond its mandate. This is a very concerning development and will further complicate companies' commercialization efforts.

11. **The continued use of the median domestic Therapeutic Class Comparison (dTCC) test that includes generic products is punitive to innovators:** The use of therapeutic class tests could massively de-value innovation by forcing medicine prices down to the price of generics. The new rules could also lead to a paradoxical situation where innovators are mandated to sell products for less than their generic counterparts, which will never be subject to greater price reductions based on economic factors. This incentivizes the

generics industry, which does not invest in or conduct research and development, while punishing innovators who take on massive financial risk and dedicate many years and billions of dollars to create new treatments. To mitigate this issue, we strongly recommend the use of the highest therapeutic comparator price for any future application of therapeutic class tests, whether dTCC or iTCC.

12. **The PMPRB's excessive discretion on the timing and extent of reassessments introduces significant uncertainty and volatility:** The Guidelines not only lack guidance and clarity for manufacturers to set prices at launch but introduce significant uncertainty around pricing during the lifecycle of the medication by giving the PMPRB broad discretion on the timing and extent of reassessments. It is also unclear what happens if the pharmacoeconomic evaluations improve over time. Once a product is subject to lower prices as part of a PMPRB review, any upward adjustment to the price is no longer feasible.

13. **The decision to retain the median international price (MIP) to set the maximum list price (MLP) for new patented medicines will cause further product launch delays in Canada:** Due to reference-based pricing, medicine prices in Canada impact medicine prices in other countries, meaning that a low price in Canada could have follow-on effects in other markets. Given that companies need to be in compliance with the interim maximum list price (iMLP) at the point of launch, many will simply wait until their products have been launched in a number of more innovative countries before launching in Canada, both to retain value in other higher priced markets and to secure a better eventual list price in Canada. To illustrate our concerns, AstraZeneca's Roxadustat – a novel, first in class oral treatment for anemia – is currently under priority review by Health Canada. While AstraZeneca is responsible for the commercialization of Roxadustat in Canada, we do not possess marketing rights in ten of the eleven countries in the reference basket. As a result, we have no visibility into the launch sequencing or the prices that will be charged in each of the countries. Given that the MIP will be the sole factor in setting the iMLP and the MLP, we are faced with the difficult decision of whether to delay the launch in Canada until we have more clarity on the impact of the international prices. This will ultimately negatively impact Canadian patients, by depriving them of timely access to new and innovative medicines. Additionally, there are significant operational challenges associated with the new requirement of the compliance with the iMLP at launch as opposed to having one reporting period to come into compliance.

14. **A number of key operational questions remain that should have been the subject of this consultation, such as sources of international prices source and application of the Non-Excessive Average Price:** There are many questions that have not been clarified in the updated Guidelines, including international price sources, an explanation of the formula for calculating the pharmacoeconomic price (PEP), clarity on the use of the Non-Excessive Average Price (NEAP), and how reporting will change in the coming reporting periods. The NEAP in particular is problematic: it is based on confidential information and should not be

considered a ceiling for the list price. The PMPRB has given no guidance or clarity on how the NEAP would apply to grandfathered and "gap" products, or even which NEAP would apply (the 2019 NEAP or the 2020 NEAP). The promised Help Tool will be issued too late to support any business certainty in the coming months, and there is simply insufficient and inadequate consultation on these and other key operational issues.

Final thoughts

AstraZeneca is an innovative biopharmaceutical company with a long track record of pushing the boundaries of science to create life-changing medicines. We want to continue to be able to bring these cutting-edge therapeutics to Canadians who need them in a timely manner. However, the federal government's price controls, and the PMPRB's approach to operationalizing the Regulations, continue to perpetuate uncertainty, penalize innovation, and create barriers to commercializing medicines that will improve and save the lives of Canadian patients.

Given the ongoing COVID-19 situation and the recent Federal Court ruling invalidating provisions related to the disclosure of confidential rebates, the PMPRB should strongly consider taking a more measured and stepwise approach to implementing the new price controls. It should consider implementing one change at a time to better understand the impacts of each new intervention rather than moving forward with all changes at once. The current approach will make it impossible to assess the impacts of each new change. In this context, we strongly encourage the adoption of the new basket of countries change first.

In sum, we hope the Government of Canada, including the PMPRB, will revisit its current flawed approach to medicine price regulation and consider a more balanced pricing framework – one that supports an innovation-driven healthcare system and ensures that Canadians can continue to have access to the latest life-changing health innovations.