SERVIER CANADA

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BY EMAIL: PMPRB.Consultations.CEPMB@pmprb-cepmb.gc.ca
ATTENTION: New Draft Guidelines Consultation
Patented Medicine Prices Review Board
Box L40, 333 Laurier Avenue West
Suite 1400
Ottawa, Ontario
K1P 1C1

Please find herein Servier Canada Inc.'s (Servier) comments on the Patented Medicine Prices Review Board (PMPRB) Draft Guidelines (Guidelines) released on November 21, 2019, following the amendments of the Patented Medicines Regulations (Regulations) published on August 21, 2019.

Servier understands that the PMPRB intends to update its Guidelines within the framework of the amendments to the Patented Medicines Regulations, which are not yet in force. While Servier is committed to constructive engagement with the PMPRB on the draft Guidelines, Servier's response to this consultation is not intended and should not be interpreted as supporting the amendments to the Regulations. Servier continues to have grave concerns about the practicality and legality of the amended Regulations, which are the subject of ongoing legal challenge. Servier reserves the right to oppose any aspect of the Guidelines that exceeds the jurisdiction of the federal government under the relevant legislation.

Servier, as a member of both Innovative Medicines Canada (IMC) and BIOTECanada, is in agreement with, and fully supports, the comments submitted by these associations.

Servier is a research-based organization established in numerous countries around the world and focused on further improving health and bringing better care to patients. With more than 22,000 employees worldwide, Servier is managed by a Foundation and reinvests 25% of its global turn-over in Research & Development (R&D).

Servier has been present in Canada for more than 40 years. Servier's mission is to provide the Canadian medical community and its patients with innovative therapeutic solutions. Servier produces a number of innovative medicines used to treat diseases affecting the lives of many Canadians such as cancer, diabetes, heart disease, and high blood pressure.

Servier believes that all Canadians should have timely and optimal access to innovative medicines and is of the view that the Guidelines will have the unintended consequence of decreasing access to innovative medicines for Canadian patients and deterring companies from launching new drugs in Canada.

After careful analysis of the Guidelines, Servier would like to highlight the following main areas of concern:

➢ Predictability, Impact & Regulatory Approach

The mandate of the PMPRB, as established by the Patent Act (Act), is to ensure that prices charged by patentees for patented medicines sold in Canada are not excessive. The Guidelines, which are issued pursuant to subsection 96(4) of the Act, are intended to provide transparency and predictability to patentees in determining whether a patented medicine appears to be priced excessively in Canada.

The Guidelines, as currently proposed, do not foster a fair and predictable pricing and reimbursement environment. Instead, they create uncertainty, unpredictability and complexity in price setting for patented medicines from product launch to patent expiry. Their ultimate impact will be counterproductive as it will create further delays in patient access and potentially prevent new innovative medicines from launching in Canada, which defeats the government's stated policy objective of increasing accessibility to medicines for Canadians.

Here are some examples of elements proposed in the Guidelines that promote uncertainty, unpredictability and complexity with regard to setting allowable price ceilings for patented medicines in Canada:

I. Maximum List Price (MLP) for Non-Grandfathered Patented Medicines

a. Median International List Price (MIP)

During the introductory period, the proposed MLP ceiling of a new patented medicine is set at the median of the new basket of 11 comparator countries or lower based on additional tests. Following this period and until patent expiry, the MLP ceiling continues to be assessed against the MIP. This methodology significantly departs from the current practice whereby, once the introductory ceiling price is set, Canadian patented prices can increase in keeping with the Consumer Price Index (CPI) but never to the point of exceeding their highest international price within a basket of 7 comparator countries.

If PMPRB's mandate under the Act is to ensure non-excessiveness, why is the current methodology being changed from highest (a plausible measure of excessiveness) to median (a mid-point value)? If the median is used, this implies half of all countries in the basket will always have excessively-priced medicines. Yet no one truly believes that the new basket of 11 comparator countries is composed of countries which systematically tolerate excessively-priced medicines. Furthermore, a median price will be nearly impossible for patentees to predict from product launch to patent expiry especially when it involves 11 comparator countries who have their own distinct pricing regulations/policies. Price fluctuations in the MIP assessment throughout the product

lifecycle may delay or even reduce the likelihood of market entry of innovative medicines in Canada. Furthermore, investment in clinical trials will be negatively impacted given the pricing uncertainty caused by the proposed Guidelines thereby causing further delays or even a reduction in patient access to new innovative medicines ultimately resulting in a decrease in the standard of care for Canadians.

b. Median domestic Therapeutic Class Comparison (dTCC)

The proposed MLP ceiling also considers the median of the dTCC for non-grandfathered patented medicines. This methodology departs from current practice whereby the highest treatment cost for all comparators is used in various pricing tests, depending on the level of therapeutic improvement. The proposed dTCC uses the median treatment cost for all comparators no matter the level of innovation. Again, under a mandate of controlling excessiveness, why is the PMPRB using a median value to determine if the price of a patented medicine is excessive versus its comparators?

The use of a median for the dTCC is inconsistent with an excessive price standard because this would force a new product to be priced lower than comparator products, even if the new product has a superior safety and/or efficacy profile relative to those comparators. Therefore, the highest treatment cost of the dTCC should remain the standard especially in light of the proposed removal of therapeutic improvement assessments in the Guidelines.

Also, the Guidelines indicate that the PMPRB may omit a medicine of the same therapeutic class if it believes it is unsuitable for comparison. No principled explanation is provided as to why a medicine will be considered "unsuitable", and instead, there is only an example of unsuitability provided. How are patentees expected to accurately evaluate the impact of the median dTCC on the MLP ceiling if at any time a comparator may be withdrawn from the dTCC evaluation by the PMPRB?

II. <u>Maximum Rebated Price (MRP) for Non-Grandfathered Patented Medicines</u>

a. Pharmacoeconomics

The proposed MRP ceiling for Category I drugs is calculated based on the cost-utility analyses prepared by a publicly funded Canadian organization, such as the Canadian Agency for Drugs and Technologies in Health (CADTH)-to be used as the typical source of pharmacoeconomic analysis, or the Institut national d'excellence en santé et services sociaux (INESSS)-to be used as a secondary consideration. It is important to note that these cost-utility analyses, which result in a statistical ratio, are based on estimates and assumptions, and involve a significant amount of subjectivity such that the analyses and resulting ratios may differ between CADTH and INESSS. Moreover, in order to estimate

the variability of this statistical ratio, a confidence interval encompassing the potential range of results is taken into consideration. These ratios are intended to inform payer reimbursement decisions and help with efficient allocation of healthcare resources. They are not intended to dictate a price. Nor are they used that way in practice. The PMPRB is not a payer and has no decision-making power with regard to drug reimbursement. Its mandate is to provide a consistent and predictable application of the Act through clear and objective measures. The use of cost-utility analyses to assess potential excessive pricing is inappropriate, which would explain why no other jurisdiction in the world uses this factor to establish price ceilings.

In an attempt to better understand the Pharmacoeconomic Price (PEP) formula as described in the Guidelines and its potential impact on future patented medicines, Servier reached out to the PMPRB in December 2019 to request further clarification and was told that additional information would only be provided at the end of the consultation period. How is this promoting transparency and predictability on PMPRB's part, and how are patentees supposed to truly understand the impact of this new factor on future business without open communication with the PMPRB during the consultation process?

Also, the PMPRB continues to proclaim that the MRP ceiling will remain confidential. How will this be possible when the MRP calculation methodology combined with publicly available data (e.g. CADTH review reports, IQVIA data, and price lists) could allow third party payers to reverse engineer or estimate net prices? Given the significant international sensitivity associated with this information, this potential breach in confidentiality would impact whether innovative patented medicines are launched in Canada or not and will create great uncertainty for future investments. It also places the PMPRB offside its own statutory duty to keep this information confidential, a duty which is clearly set out in sections 87 of the Act.

b. Market Size

Innovation should be recognized and incentivized, and not penalized as, will be the case with the implementation of the Guidelines given the de facto revenue control mechanism resulting from the application of the market size factor, which reduces the MRP ceiling as revenues grow. This revenue-based tiering approach has no relevance when establishing maximum price ceilings and is inconsistent with an excessive pricing review standard.

Therapeutic benefit should remain part of the allowable price ceiling assessment and should not be replaced by factors such as market size. The latter is relevant for payers when negotiating listings but is not relevant in assessing price excessiveness. The removal of therapeutic benefit from determining a price ceiling for an innovative patented medicine is inconsistent with the PMPRB's statutory mandate and should be reconsidered within the context of the Guidelines.

III. Relevant Indication

The Guidelines state that for patented medicines with more than one approved indication, the Relevant Indication for which the MLP and MRP (if applicable) ceilings will be assessed will be determined by the PMPRB. They further explain that the PMPRB will identify the indication that triggers the annual treatment cost criteria or the highest prevalence criteria depending on whether the medicine is classified as Category I or II and the extent to which the approved indication(s) triggers either criteria.

This methodology does not take into account the actual use and relevance of the medicine in clinical practice. Its purpose within the Guidelines is solely to ensure that the strictest pricing rules are attributed when establishing a price ceiling in Canada. This may discourage companies from seeking out additional indications for existing medicines, since adding a niche indication that has higher treatment cost could suddenly switch their drug from Category I to Category II, or otherwise impact pricing rules, even if that niche indication is of little practical importance compared to the main indication. This practice has no place in the price setting for innovative medicines that could significantly improve or save the lives of Canadian patients.

IV. Reassessment

The Guidelines also allow for the reassessment of prices for both grandfathered and non-grandfathered products at any time during their lifecycle. A reassessment may be conducted by the PMPRB in numerous circumstances such as the approval of a new indication, the increase in market size above a pre-determined threshold, the increase in total prevalence or the update of a cost-utility analysis.

How can patentees make viable business decisions nationally and globally when the viability of their patented medicines can be negatively impacted by a reassessment at any time during their lifecycle and for multiple reasons, many of which are beyond the foreseeability or control of the patentee? Servier believes in investing in Research and Development in order to bring innovative medicines to all Canadians, but this approach will be challenged given the constant uncertainty created by continual reassessment.

➢ "Grandfathered" Products

By definition, grandfathered products should be exempt from new laws or regulations. Based on the Regulations and Guidelines, not only do "grandfathered" products face a new basket of comparator countries, they must also comply with a significant change in pricing methodology. Whereas in the current regime the price of an existing product can never exceed its highest international price comparator, the new regime does not allow for the price to exceed its median international price comparator. This change in methodology will drastically reduce the price of many "grandfathered"

products and create great uncertainty in forecasting their future pricing despite the fact that these products entered the Canadian market in good faith and in compliance with the rules and regulations in place at the time of their market entry and when the scope and impact of the new PMPRB regime could not have been reasonably foreseen.

It is inaccurate to state that existing patented medicines are being grandfathered under the new PMPRB regime. Changes of this magnitude are incongruent with the concept of grandfathering. Furthermore, existing medicines have already been subjected to assessment and negotiation by various Canadian agencies, and funding decisions based on value for money and affordability have already been made. Therefore, regulating existing medicines under the new PMPRB regime, at any level, is unfair to patients as well as to patentees who have already made significant investments based on business analyses done under an existing regulatory framework.

- **Rare Diseases**

The price setting methodology for rare diseases is significantly more restrictive than previously communicated by the PMPRB. The single QALY threshold for all patented medicines, regardless of the value they bring to patients, is inappropriate especially in the context of rare diseases, as evidenced by the fact that neither CADTH nor INESSS apply a single cost-effectiveness threshold across conditions.

By definition, not only are rare diseases comprised of small patient populations, but most are also severe, debilitating or life threatening. Generally, a new therapy not only addresses an unmet need but is also often the first therapy for the condition, with no alternative treatments for comparison or substitution. A "one-size-fits-all" assessment approach in establishing price ceilings undermines the value that innovative medicines bring to patients, especially those with rare diseases, which is why this approach should be reconsidered within the context of the Guidelines.

Servier's assessment of the new regime in the context of the potential launch of a rare disease drug indicated for the treatment of a rare and aggressive cancer did not allow for a reliable prediction of price ceiling at the time of introduction nor throughout the product lifecycle. Furthermore, the product in question would have been significantly impacted by the new economic factors, would have been classified a Category I drug and would have been under constant threat of reassessment until patent expiry. In these circumstances, the opportunity to recover the investment required to bring this product to the Canadian market to treat a rare disease was even more uncertain under the new regime than previously anticipated. Consequently, the business plan for launching this product in Canada was suspended.

In summary, when considering the enormous scope and potential implications of the proposed Guidelines as described above, it is crucial to take a measured approach in ensuring that all proposed changes are subject to extensive consultation in order to clearly identify and correct any unintended consequences. Additionally, numerous operational feasibility issues have yet to be addressed by the

PMPRB and an amended *Patentee's Guide to Reporting* has yet to be released which makes assessing all potential impact impossible. Patentees will need sufficient time to change their reporting and information systems to comply with new Guidelines.

The unprecedented complexity and uncertainty created by the proposed Guidelines combined with the significant increase in administrative burden for patentees does not make for a favorable commercial environment and increases the cost/risk of doing business in Canada. Recent exchanges with the PMPRB have demonstrated that even the PMPRB did not appreciate the extent of the complexity of the proposed changes. Servier believes that there is a simpler way to achieve the PMPRB's objectives via more predictable and less complex regulatory tools and would welcome the opportunity to work with the PMPRB, alongside other stakeholder, in order to develop them.

Servier is disappointed that Health Canada did not materially incorporate any of the stakeholder comments received with respect to the Regulations. Nevertheless, Servier is still hopeful that the comments provided to the PMPRB in this letter and by numerous stakeholders within this consultation period and via face-to-face meetings will be seriously considered and incorporated in the Final Guidelines. Canada's health care system is complex and implementing price ceilings as described in the Guidelines will reduce Canadians' access to new innovative medicines and impact highly skilled jobs and research partnerships.

Servier is committed to working with the government to help it achieve its goals of affordability and sustainability, but not to the detriment of patient access to innovative medicines. Providing access to innovative medicines allows Canadians to benefit from a world-class health care system, and Servier aims to provide the Canadian medical community and its patients with the best possible therapeutic solutions through the discovery and development of new innovative therapies.

As an important stakeholder in the healthcare system, we appreciate the opportunity to provide feedback on the Guidelines and we look forward to working collaboratively with the PMPRB and other stakeholders to address these serious concerns that ultimately affect all Canadians.

Yours sincerely,

Frédéric Fasano, PharmD, MBA
Chief Executive Officer
Servier Canada Inc.