RAREi
THE CANADIAN FORUM FOR
RARE DISEASE INNOVATORS

RAREi Submission

Response to PMPRB's Guidelines Scoping Paper

December 20, 2023

Thank you for the opportunity to contribute to the first phase of the Patented Medicine Prices Review Board's (PMPRB's) consultations on new price review guidelines for rights holders.

The Canadian Forum for Rare Disease Innovators (RAREi) is a network of 18 biopharmaceutical companies dedicated to improving the lives of patients with rare diseases by developing and commercializing treatments.

Since it was established in 2018, RAREi has actively engaged in all Health Canada and PMPRB consultation opportunities related to modernizing the *Patented Medicines Regulations* and the board's guidelines. It has consistently called for consideration of the particular challenges associated with developing and commercializing treatments for small populations and for care to be taken to ensure that Canadian medication review and approval process are not designed and operated in such a way as to disincentivize the creation and deployment of treatments for orphan conditions. All of RAREi's previous submissions are available on its website (www.rarei.ca).

Introductory remarks

As a starting point, RAREi wishes to acknowledge and congratulate the board for the constructive and step-wise approach that it is taking towards the creation of the new guidelines. This two-phase effort offers stakeholders the opportunity to help the board ground the guidelines in PMPRB's court-clarified mandate – how it can act as a monitor against excessive pharmaceutical pricing as a function of abuse of market exclusivity.

The second phase will delve more specifically into the details about how price reviews could be conducted, building on the feedback received during this first phase. This more collaborative approach to consultation on guidelines changes is more in line with the PMPRB's pre-2017 approach, which included working groups mandated to discuss and resolve specific issues, which generally led to pragmatic guidelines that worked reasonably well for stakeholders.

In this context, RAREi would like to offer some background on the rare disease treatment landscape and some of the unique challenges faced by rare disease patients. Canadians affected by often severe and debilitating rare disorders struggle to access needed treatments. This is in addition to the multiple other challenges they face, including the very long journey to reach a diagnosis, small patient populations, fewer health care resources available to treat the conditions and many unknowns about the disease. For many rare disease patients, there are no treatments available yet to treat their condition. That is why it is important to ensure that those that are developed can be made available to patients who need them as soon as possible.

In addition, it is challenging to operate a business focused on bring new orphan treatments to fruition because of the high degree of uncertainty tied to so many variables. There is huge variation in the prevalence and incident rates country to country, province to province and even region to region. For genetic conditions, differing mutations can affect the progression and severity of disease. How conditions are managed, who is eligible for treatment, and even by whom they are managed can also vary considerably.

In response to that reality, other developed nations – including in Europe, the United States, Japan and Australia – have implemented tailored review processes and incentives to encourage rare disease innovators to develop and commercialize orphan treatments. They do so because they realize that orphan medication development is an extremely risky and costly endeavour. Targeted incentives such as enhanced intellectual property, regulatory and reimbursement policies are needed to offset the business and clinical challenges that a small number of patients represents compared with medicines for common diseases.

Add to that the high upfront cost of doing business in Canada and the fact that Canada represents just 2% the global pharmaceutical market, and one can begin to see why it is vital that Canadian policymakers take care to implement regulatory, policy and funding initiatives that support and encourage innovation.

Considering just the fees charged for new product submissions to Health Canada and Canada's health technology assessment (HTA) agencies, the cost of bringing even one new medicine or a new indication into Canada can be in the millions of dollars. In addition, there are substantial additional outlays required to support those submissions that, taken together, cost more than in other comparable markets because of the need to comply with a broad range of unique regulatory, medical, reimbursement-related and commercial activities necessary to successfully deploy new medicines in this country. Moreover, Canada is often used as a benchmark for other markets – meaning that Canadian prices have a follow-on impact on higher population markets. According to a World Health Organization report, Canada is a reference country for Brazil, South Africa, Taiwan, Egypt, Saudi Arabia and the United Arab Emirates. Canadian prices are also indirectly referenced. For example, China references Taiwanese prices for some products and some Latin American countries reference Brazil. In addition, some European countries informally reference Canada if it is the first country of launch (or second after the US).[1] Corporate decisions about when (or even if) to bring medicines to Canada are necessarily sequenced to optimize market opportunities around the world.

Much evidence exists that demonstrates that rare disease therapies are launched in Canada much later than in the United States and/or Europe and, in many cases, are not even available for patients in Canada. To put things in perspective, fewer than two-thirds of the rare disease treatments approved in Europe were submitted to Health Canada for regulatory approval, and among those approved by Health Canada, the rate of public reimbursement is low.[2] Meanwhile, only 54% of rare disease treatments approved by Health Canada are subsequently reimbursed by public drug plans in Canada.[3]

The reality is that no aspect of the current national medication review process, including pricing review, HTAs, product negotiations and funding frameworks, is organized to evaluate treatments designed for small populations appropriately. Moreover, the current processes are ill-prepared to respond effectively to the new innovative trial designs and adaptive studies that are common when researching new rare disease treatments.

For its part, the PMPRB has represented a unique challenge for rare disease innovators in that the effective price ceilings permitted have often represented major obstacles even before the changes to the regulations that prompted this consultation.

For example, the PMPRB has attempted in several cases in recent years to impose price ceilings that are the lowest among comparator countries. In the absence of any public consultations related to that approach, at least six voluntary compliance undertakings have been completed using the lowest price standard. Any further imposition of

[1] Dedet G. *Pharmaceuticals Pricing and Reimbursement Policies in Europe,* WHO TBS, October 2016.

[2] Ward et al, *An international comparative analysis of public reimbursement of orphan drugs in Canadian provinces compared to European countries*. Orphanet Journal of Rare Diseases, Issue 17, Article 113, March 4, 2022): https://doi.org/10.1186/s13023-022-02260-6.

[3] Rawson, Nigel, *Availability and Accessibility of Essential Drugs for Rare Disorders in Canada*. Canadian Health Policy, October 13 2021: https://doi.org/10.54194/HFEB4050 www.canadianhealthpolicy.com.

"lowest of" benchmarks will continue to send challenging signals to rare disease developers that deploying medicines in Canada may be subject to onerous and uncertain price controls. A price ceiling that is set at too low a level can, for obvious reasons, make the case for bringing a medicine to Canada untenable.

In addition, the draft guidelines proposed by the PMPRB in earlier attempts at rewriting the rules did not acknowledge or account for the additional challenges represented by rare diseases and would have significantly exacerbated the difficulties faced by rare disease patients, researchers, clinicians, developers and health systems. To state it plainly, the market uncertainty that has characterized the PMPRB's lengthy price review modernization journey has been damaging to Canada's attractiveness as a location for global investments in research and development.

From an administrative law and constitutional perspective, the PMPRB's scope has been clarified by the courts in recent decisions. In sum, guidelines that seek to control or regulate prices are not within the constitutional jurisdiction of the board, because the PMPRB's regulatory mandate is limited to monitoring, investigating and acting on cases of excessive prices that arise as a function of abuse of market exclusivity.

Given all of the above, RAREi recommends that the board take a pragmatic approach to price review and take pains to ensure that rights holders are provided with the certainty required to run a business effectively in Canada. The board also needs to stay clearly within its constitutional jurisdiction.

The following sections address each of the themes outlined in the PMPRB scoping paper.

Theme 1: Efficient Monitoring of Prices without Price Setting

Overall, RAREi is encouraging the board to adopt a more minimalist and balanced approach to price regulation that is more consistent with the PMPRB's recently clarified mandate – to ensure that patentees are not abusing their rights by pricing products excessively during a period of market exclusivity. The board's only job is to ensure that Canadian prices of patented medicines are not "excessive." In its July 2021 decision in the case of *Soliris*, the Federal Court of Appeal made it clear that, consistent with the board's limited mandate, it must be satisfied with monitoring pricing to prevent abusive behaviour by rights holders, which it defines as, "excessive pricing made possible by the abuse of the monopoly power given by a patent."[4]

It must be noted that since 1987, when the PMPRB was established, several effective price-lowering and value-enhancing initiatives have been established within the Canadian medication review and approval process that have helped ensure the public is benefiting from cost-effective treatments. The result has been the creation of a number of new entities within the Canadian health care system at the national, provincial and even private payer level which are focused on assessing and valuing innovation and ensuring that Canadian have access to innovation in a cost-effective manner.

Those mechanisms have contributed to more than two decades of moderate medication cost growth in Canada that has resulted in medications' contribution to overall health care costs to remain stable since at least the turn of the century. PMPRB's role in that context has been to provide an identifiable price ceiling, under which the rights holder is permitted sell at the ex-factory gate. In that context, it has served Canadians well as part of a suite of measures that offer protection against unsustainable medication cost growth.

[4] Alexion Pharmaceuticals Inc. v. Canada (Attorney General), 2021 FCA 157 (CanLII), [2022] 1 FCR 153: https://canlii.ca/t/jh8cg.

In this context, the PMPRB's role should be limited and grounded solely in its legislative and constitutional mandate – specifically – to prevent the *abuse* of market exclusivity, not the legitimate *use* of market exclusivity. Intellectual property is the most important driver of innovation, allowing developers to create and deploy new medicines that help save and improve lives. It is time limited, and during that period, RAREi believes that the PMPRB should confine its role to acting as a backstop to protect Canadians against excessive pricing of patented products while they remain on patent, not engaging in price controls or attempts to lower prices where there is no evidence of abuse.

A pragmatic approach to national price review is particularly important for rare disease innovators which, as indicated above, operate in a very challenging, highly competitive global market. The often very small patient populations to be served and the highly complex treatment areas in which we operate impose a wide range of challenges that undermine our ability to bring new medicines to Canada quickly, if at all. Predictability at every step, including the PMPRB review, would increase Canada's attractiveness for new medicines that many Canadians with rare diseases badly need.

RAREi recommends that the board consider obvious "excessiveness" as the only standard for opening an investigation. Given that the courts have made it clear that the PMPRB's mandate is limited to protecting against abuse of market exclusivity, the following recommendations should be considered:

- Any list price that is equivalent to or lower than what is being charged in other PMPRB11 countries should be deemed compliant at launch.
- Provided that list price increases are limited to the board's consumer price index (CPI)-adjustment factor, then it should be deemed to have remained compliant and therefore not subject to price review.
- In some cases, where there is clear unmet need or in therapeutic areas where there is a public policy rationale to support it, higher list prices than what are available in the PMPRB 11 could be warranted as a means of encouraging the commercialization of new rare disease medicines in Canada.

More precisely, the board should ask itself whether products that have been subject to successful national negotiations through the pan-Canadian Pharmaceutical Alliance (pCPA) on behalf of public payers or which are subject to national, hospital or blood product group and public purchasing processes should be subject a price review at all. Those pricing mechanisms have proven very successful in consistently securing high-value commercial arrangements on behalf of all Canadian jurisdictions, thereby limiting the necessity for PMPRB oversight.

In addition, RAREi's view is that therapeutic comparisons should only be used as a fall back in cases where no international prices are available within the PMPRB11. In those limited cases when therapeutic class comparisons are required, the chosen comparators must be selected very carefully and attention should be given to ensuring that the new treatments are not being equated with out-dated, unsuitable or irrelevant alternatives.

RAREi members have had negative experiences in the past when dealing with PMPRB staff where therapeutic comparators used to support price review investigations have included inappropriate or irrelevant comparators, such as unapproved products, without any link to clearly defined scientific evidence evaluation methods and which have been questioned by clinical experts.

In the event that a therapeutic class comparison is required, RAREi recommends that the comparator should be selected by independent, arms-length expert clinicians, In each case, an independent panel of clinicians who are familiar with the condition and have expertise in managing patients directly should be called upon to determine what the appropriate comparator ought to be. RAREi believes also that those expert opinions should be binding on PMPRB staff and the board.

To clarify, such comparisons should not include generics, biosimilars or non-prescription or non-approved treatments within the class. Comparing new innovative products to a class that includes such products undermines any incentives to research and launch new medicines in an existing class of products. The suggestion that price comparisons would be made within a therapeutic class without any recognition of the numerous evolutions in treatment that emerge all the time is non-sensical. That would mean that allowable prices would not distinguish between modern, cutting-edge treatments and older, often long-genericized medicines. By ignoring such improvements, and the clinical and quality-of-life improvements that arise from them, the board will undermine the innovation process and discourage medical progress.

Theme 2: Transition to PMPRB11 – New versus Existing Medicines

Regarding existing products – those that were marketed prior to July 1, 2022, RAREi recommends that the board apply the new basket of comparator countries prospectively only. In that context, all existing products that were priced at or below the previously accepted non-excessive average price on that date, and which did not increase beyond the board's existing CPI-adjustment factor in the meantime, should be deemed exempt from investigations.

Imposing new rules on existing medicines would lead to significant operational challenges and could result in supply disruptions. Therefore, the PMPRB should avoid investigations and excessive price determinations that would retroactively apply after final guidelines are published. Such an approach will reward patentees for longstanding compliance and avoid substantial disruption in the patented medicines marketplace in Canada.

Theme 3: Price Reviews during Product Life Cycle

In keeping with the minimalist approach to price review recommended by RAREi, the board should limit the review of products that are already in the market and subject to existing regulatory and competitive forces, as long as list prices do not increase beyond the board's existing CPI-adjustment factor allowances.

It must be stressed that ongoing uncertainty related to pricing can impose significant challenges on innovators. The uncertainty related to potential future list price reductions could have a similar impact as a system that initially imposes price ceilings that are too-low in the international context. Simply put, if innovative companies are unable to rest assured that an approved pricing level will remain compliant, it makes it all the more challenging to build the case for entry into the Canadian market.

Theme 4: Investigations and Referral to Hearing

As noted above, if the board pursues its mandate with a light touch that is concerned only with ensuring that rights holders are not abusing the market exclusivity rights accorded to them via patents and certificates of supplementary protection, then there should be only minimal cause to undertake an investigation. In such instances, dialogue and collaboration between the rights holder and board staff should be the preferred method for addressing any disputes regarding what would be a compliant list price.

With that in mind, RAREi proposes that the PMPRB should continue to rely on voluntary compliance undertakings to address any findings of excessiveness and only in the rare event of an inability to reach an agreement should any file be subject to a hearing.

Theme 5: Relation to pan-Canadian Health Partners, Insurers (Private and Public); and Alignment with Broader Government Initiatives

For RAREi, the PMPRB's current effort to define its new price review approach must be aligned and consistent with the broader policy platforms being pursued by the federal government and the national-level goal of encouraging a healthy, prosperous and globally competitive life sciences ecosystem in Canada.

Prior to this consultation, the board's approach to price review modernization has appeared to be at odds with other federal government policies that appear intended to improve access to medicines and grow the life sciences sector in this country. In fact, when announcing the most recent amendments to the *Patented Medicines Regulations* in April 2022, the government's press release stated, "the Government of Canada is committed to improving access to quality medicines for Canadians."[5]

Since the pandemic, the federal government has made it clear that it wants to nurture and support a vibrant and sustainable life sciences and biomanufacturing sector in Canada. It has signaled that intention in a variety of ways, including the establishment of a multi-year biomanufacturing and life sciences strategy, a genomics strategy, a pediatric medication development initiative, a variety of regulatory modernization initiatives related to health product review and approval and the national rare disease drug strategy.

All of these new strategies have been accompanied by multi-year funding commitments, demonstrating the government's commitment to their success.

Considering numerous clear statements of policy intent by the federal government, the PMPRB must take care to operate in a manner that contributes to helping it succeed in its stated policy goals. Its price review efforts must be organized in such a way that is consistent with those goals.

In addition to the Canadian government's desire to enhance innovation and support a prosperous life sciences sector, half the provincial governments across the country have active life sciences strategies and all jurisdictions are supporting economic development activities designed to encourage life sciences innovation.

Aligning with Canadian governments' common policy interest in supporting innovation and life sciences expansion and access to rare disease medicines – and what's happening internationally – means Canada needs to catch up. Reaching back into the old toolbox to determine how the PMPRB should operate into the future is not the best way to support that whole-of-government approach for rare diseases and life sciences.

Theme 6: Engaging with Patients, Health Practitioners, Pharmacy, and other Stakeholders

As a group representing rights holders, RAREi has little to add regarding theme six with the exception of a comment in response to the paper's content and questions related to "high-priced drugs for the treatment of rare diseases."

RAREi has previously expressed concerns about PMPRB's characterization of rare disease medicines as "expensive drugs for rare diseases and/or as "high-cost" or "high-priced." These characterizations appeared to be directed at undermining stakeholder confidence in the value of such treatments. They do not offer any context regarding the potentially life changing or life extending value represented by many of these new treatments, the health care system savings they offer, the cost of rare disease treatments in comparison to other health care expenditures or the valid reasons why orphan treatments may be priced higher than medicines for more common conditions. RAREi believes that the very characterization of rare disease treatments as "high-priced" is pejorative and reflects a lack of

[5] Health Canada, *Statement from minister of health on the coming-into-force of the regulations amending the Patented Medicines Regulations*, April 14, 2022: https://www.canada.ca/en/health-canada/news/2022/04/statement-from-minister-of-health-on-the-coming-into-force-of-the-regulations-amending-the-patented-medicines-regulations.html.

appreciation for the important impact that such medicines have on patient lives. In general, RAREi request that the board and staff refrain from describing rare disease medicines as “high-cost” or “expensive.”

At the same time, RAREi is disappointed with what appears to be an attempt by the staff to influence the consultations by pointing out that a growing percentage of patented medicine sales are represented by treatments that cost more than $10,000 per patient per year. While true, the analysis does not offer the important contextual points that the proportion of national health care costs represented by medications has been falling in recent years and that the spending trends do not capture the substantial financial considerations provided to payers to offset the costs of the medicines they cover.

For perspective, a June 2022 review examining the magnitude of spending on patented medicines determined that between 1990 to 2020, such spending never exceeded 8.0% of national health expenditure. In addition, patented medicines’ share of national health care spending was virtually the same level in 2020 as it was in 2000 (6.4%) and they accounted for approximately the same percentage of gross domestic product (GDP) in 2020 (0.8%) as in 2003 (0.8%). That is true despite the growing influence of higher cost treatments over that same time period.

Conclusion and Recommendations

In light of the above, it is RAREi’s position that PMPRB should remain focused on its core mandate and operate as a passive oversight agency that guards against an abuse of market exclusivity, which is a high bar, especially in the context of so many other price-moderating and value-generating initiatives across Canadian public and private payers. Given that focused mandate, and the broader policy goal of promoting and encouraging innovation, RAREi takes the view that the board must undertake its oversight responsibility with care to avoid dissuading innovators from undertaking the research, development and commercialization of important treatments for Canadians and the world.

With that in mind, RAREi recommends that the new guidelines be developed in a manner that is consistent with the PMPRB’s limited legislative and regulatory mandate and with broader government objectives related to the life sciences sector and rare disease policies. Furthermore, guidelines should be designed to reduce uncertainty for rare disease developers.

In addition, it recommends that the PMPRB create a technical working group, comprised of medicine developers and other key stakeholders, to pressure test new guidelines, and undertake a case study approach to better understand how any draft price review processes would work in practice.

It must be stressed that this is an extremely exciting time for the rare disease community given the incredible scientific and technological advances underway. However, the benefits of many of these technologies will not reach Canadian patients in a timely manner if the PMPRB guidelines are not crafted carefully and in a way that would position Canada as an example to follow internationally in terms of providing timely access to rare diseases treatment and a place to pursue real innovation.

Thank you for your consideration. RAREi looks forward to working with the PMPRB, industry associations, patients, clinicians and other health system stakeholders to truly modernize the patented pharmaceutical price review process in Canada.

About RAREi

RAREi is a network of biopharmaceutical companies dedicated to improving the lives of patients with rare diseases by developing and commercializing treatments. This network includes the following members: Alexion Pharma Canada Corp, Amicus Therapeutics Canada Inc, argenyx Canada, Astellas Canada, Biogen Canada Inc, BioMarin Pharmaceutical (Canada) Inc, Boehringer Ingelheim Canada Ltd., GlaxoSmithKline Canada, Horizon Therapeutics Canada, Ipsen Biopharmaceuticals Canada Inc, Janssen Canada, Mitsubishi Tanabe Pharma Canada Inc, Recordati Rare Diseases Canada Inc, Sanofi Genzyme, Sobi Canada, Inc, Takeda Canada Inc., Ultragenyx Pharmaceutical Inc and Vertex Pharmaceuticals (Canada) Inc. For more information, please visit www.rarei.ca.